CARDIOLOGY

Abstracts

International Academy of Cardiology Annual Scientific Sessions 2015 20th World Congress on Heart Disease

Vancouver, B.C., Canada, July 25–27, 2015

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e-ISBN 978–3–318–05591–7

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Each abstract was graded by at least seven expert reviewers. Acceptance for presentation was based on the average score of all reviewers. A large number of excellent contributions were received and we thank both contributors and reviewers for their support, interest and effort.

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ABSTRACTS

NOVEL CELLULAR MECHANISMS OF ATHEROSCLEROSIS

001

VASCULAR RESIDENT STEM CELLS IN ARTERIOSCLEROSIS

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Resident stem/progenitor cells in the adventitia and intima of the vessel wall have been implicated in the pathogenesis of arteriosclerosis. Vascular lineage differentiation of stem cells can contribute to both tissue repair and exacerbation of vascular diseases leading to restenosis in response to angioplasty. The present presentation will focus on two aspects of progenitor cell plasticity in arteriosclerosis. Firstly, we provide evidence that macrophages can induce functional endothelial cell differentiation of the stem cells while simultaneously inhibiting their smooth muscle cell differentiation. Mechanistically, both effects were mediated by macrophage-derived TNF via TNF receptor 1 and canonical NF-kB activation. The lack of TNF in a knockout mouse model of vein graft resulted in significant reduction of endothelial repair that led to thrombus formation. Consistently, vessels from vein grafts carried out in knockout mice that received TNF+/+ bone marrow cells showed a rescue of vascularization and prevention of thrombosis. Furthermore, we found that treatment of the cells with sirolimus resulted in an induction of their migration and is mediated specifically by CXCR4 activation. Ex vivo experiments using a decellularised vessel in a bioreactor system confirmed the increment of vascular progenitor migration from the adventitial side into the intima where they form neointima-like lesions in response to sirolimus. These findings provide direct evidence of sirolimus-induced progenitor cell migration and differentiation into smooth muscle cells via CXCR4 and EGFR/ERK/beta-catenin signal pathways, implicating a novel mechanism of restenosis formation following sirolimus-eluting stent treatment. Finally, our group recently established a new method to directly reprogramme mature cells into endothelial lineage that was useful for promoting endothelial regeneration in vivo. Thus, vascular progenitor cells can differentiate into either endothelial cells to repair the vessel or smooth muscle cells to form neointimal lesions. A balance of stem/progenitor cell differentiation would be essential for vascular hemostasis.

002

EARLY DIAGNOSIS OF THE CARDIOVASCULAR SYSTEM - THE NANOMEDICAL EVALUATION OF ENDOTHELIAL DYSFUNCTION

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Background: Endothelial dysfunction can be directly related to the dysfunction of the cardiovascular system. The dysfunctional endothelium is characterized, among others, by the deficiency of bioavailable nitric oxide (NO) and excess production of cytotoxic superoxide (O2-) and peroxynitrite (ONOO-) – the main components of oxidative stress. The studies presented here focus on the early assessment of endothelial dysfunction and its risk associated with the development of cardiovascular diseases.
Methods & Results: We used a nanomedical approach (nanosensors with a diameter of 150-250 nm) to simultaneously measure the production of NO, O2-, and ONOO- in single HUVECs, of different ethnicities (Caucasian, African American, Native American) and different gene variants of endothelial nitric oxide synthase (eNOS). We introduced the parameter R, where R = [NO]/ [O2-] +[ONOO-], to measure the degree of endothelial dysfunction and the K as the rate of NO, ONOO- and O2- production in nmol/s. R varied from about 3.5±0.4 to 1.8±0.3, indicating a significant change in the function of eNOS variants. Dependent upon the eNOS gene variants and ethnicity, the rate K, of NO production also varied from 180±25 nmol/s to 60±15 nmol/s. In a set of separate experiments, [NO]/[O2-]+[ONOO-] balance/imbalance and the kinetics of NO, O2- and ONOO production were also elucidated in the presence of environmental factors like elevated glucose and/or elevated NaCl. Apparently, these environmental factors further increased endothelial dysfunction, unfavorably shifting the [NO]/[O2-] + [ONOO-] balance. This effect was additive to the effect of the gene variants.
Conclusion: The [NO]/ [O2-] +[ONOO-]ratio, as well as the rate of NO, ONOO- and O2- generation, accurately reflects the functional state of the endothelium. This model can be used to design a method for early diagnosis of cardiovascular diseases based on the analysis of a single endothelial cell.

003

NAVIGATING THE COMPLEXITIES OF APOPTOSIS AND AUTOPHAGY IN CARDIOVASCULAR DISEASE: CAN WE CHART A CLEAR COURSE?

K. Maiese
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The programmed cell death pathways of apoptosis and autophagy play a significant role in the reparative and regenerative processes of the cardiovascular system. Apoptosis can control tissue development and remodeling during the early stages of development. However, in mature cells the induction of apoptosis can result in cell death. In contrast, autophagy, a process that can promote cellular protection as well as cellular death involves the recycling of cytoplasmic components and discards defective organelles for tissue remodeling. Multiple pathways can ultimately influence apoptosis and autophagy in the cardiovascular system during injury, but a number of new therapeutic strategies are focusing upon the role of extracellular matrix associated proteins such as the CCN family of proteins. Of the CCN family members, Wnt1 inducible signaling pathway protein 1 (WISP1) is increasingly being recognized as an exciting target for tissue repair. WISP1 is intimately linked to pathways of regeneration that include phosphatidylinositol-3-kinase (PI 3-K), protein kinase B (Akt), and the mechanistic target of rapamycin (mTOR). Elucidating the potential of these novel reparative pathways and the ability to govern apoptosis and autophagy offers new hope for the treatment of acute and chronic disorders of the cardiovascular system.

004

THE SECRET SUPREMACY OF SMALL BLOOD VESSELS, AN ENDURING PUZZLE OF THE CARDIOVASCULAR SYSTEM: RESEARCH GAPS AND OPPORTUNITIES

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Small blood vessels are a critical component of the vascular system and essential for the maintenance and proper functioning of organs throughout the body. Their malfunction is a major contributor to local and systemic diseases. In spite of being part of the same system, small blood vessels have been studied traditionally within research and medical specialty silos aligning with specific organs and the diseases affecting them. The enduring challenge stems from the limited sharing and integration of the miscellaneous fundamental knowledge about diverse types of small blood vessel across body systems necessary to gain a cohesive understanding of how they individually and collectively function in health and disease. Emblematic for the "unity in diversity" of small vessels is the endothelium, the inner cell layer covering all blood vessels yet selectively mediating the local blood-tissue interactions. The endothelium can function as an only cellular layer of tiniest blood vessels that mediate most blood-tissue exchanges. Their complexity rests on anatomical and functional properties of specific endothelial cells, with extreme ability to respond to local environmental cues and functional demands. At the body level, endothelium functions as a complex mosaic layer, from creating completely tight barriers between blood and tissue to allowing translocation of entire cells. Even more puzzling are the mechanisms controlling local specificity of small blood vessel responses to systemic and long-range interactions, including mechanical, electro-chemical, and blood-borne signals. Lack of appreciation for small blood vessel complexity may be an important contributor to the bench-to the bedside gap in cardiovascular research. Advancement will require a systems approach for integrating information, from molecular to tissue to body level, informed by development of new sensitive biosensors and imaging. Understanding and harnessing the phenotypic and functional heterogeneity of small blood vessels may create new opportunities to specifically target tissues and organs for therapeutic interventions.

NOVEL CELLULAR MECHANISMS OF ATHEROSCLEROSIS

005

AGING, ESTROGEN, CELL SENESCENCE AND VASCULAR INFLAMMATION

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Aging is characterized by the development of systemic inflammatory changes, organ dysfunction and frailty. In females, loss of estrogen compounds these changes. Estrogen loss combined with aging leads to increased oxidative stress, increased inflammation, dysfunctional EPCs leading to impaired vascular repair, increased inflammation and increased monocyte adhesion. Cellular senescence was thought to be benign, but it is now evident that senescent cells are pro-inflammatory and may be associated with deleterious consequences in aging organisms that accumulate senescent cells. Senescent endothelial cells secrete more pro-inflammatory factors than non-senescent cells, and more disturbingly, may also incite pro-inflammatory secretion by healthy non-senescent cells along with other negative functional changes. We hypothesized that cell senescence, which increases with aging, is an important contributor to inflammation and vascular dysfunction seen with aging, and that prevention or reduction in cell senescence can mitigate the inflammatory changes associated with estrogen loss and aging. A corollary to this hypothesis was that 17beta-estradiol (E2) will mitigate aging changes. To investigate this issue, we co-cultured human microvascular smooth muscle cells (VSMC) with senescent (SEN) or early-passage (EP) human endothelial cells (EC), separated by a permeable membrane to allow both VSMC and EC to communicate with secreted factors. We found that the coculture of VSMC with EC synergistically elevated secreted pro-inflammatory factors, IL-6, IL-8, and MCP-1. While both SEN and EP cells promoted the cytokine and chemokine release, the amount released in SEN EC – VSMC coculture was about 1.5- to 2- fold greater than with EP EC – VSMC. In addition, when E2 was added to culture, the phospho-VASP/VASP ratio increased. These findings support the potential role of senescent EC in aggravating hypertension and the persistent inflammatory disorder that are common in older individuals, as well as the potential of E2 in aged individuals to improve vascular function.

NOVEL CELLULAR MECHANISMS OF ATHEROSCLEROSIS

006

CORONARY VASOMOTOR REGULATION BY CRP AND LOX-1 RECEPTORS

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Recent evidence suggests that C-reactive protein (CRP) is an independent cardiovascular risk marker and also a mediator of inflammation and atherogenesis. Studies in cultured endothelium implicate that lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) or Fc-gamma receptor II (CD32) contributes to the pro-atherogenic effects of CRP. However, it is unclear whether CRP exerts adverse action in the coronary microcirculation and the identity of the CRP receptors linking to vasomotor function remains unknown. To address these issues, porcine coronary arterioles (50-100 micrometer in diameter) were isolated for videomicroscopic analysis of vasomotor activity, dihydroethidium fluorescence detection of superoxide, immunohistochemical localization of receptors, immunoprecipitation of receptor/CRP interaction, and protein blot. Intraluminal treatment of pressurized arterioles with a pathophysiological level of CRP (7 μg/mL, 60 minutes) attenuated endothelium-dependent nitric oxide (NO)-mediated and prostacyclin (PGI2)-mediated dilations to serotonin and arachidonic acid, respectively. The adverse effect of CRP was prevented by superoxide scavenger Tempol and NADPH oxidase inhibitor apocynin. LOX-1 and CD32 were both detected in the endothelium of arterioles. Blockade of LOX-1 with either pharmacological antagonist κ-carrageenan or anti-LOX-1 antibody prevented the detrimental effect of CRP on vasodilator function, whereas anti-CD32 antibody treatment was ineffective. Denudation of endothelium and blockade of LOX-1 but not CD32 prevented CRP-induced elevation of superoxide in the vessel wall. CRP was co-immunoprecipitated with LOX-1 and CD32 from CRP-treated arterioles. Similarly, blockade of LOX-1 and CD32 both prevented CRP-induced arteriolar expression of plasminogen activator inhibitor-1 (PAI-1), a thrombogenic protein. We conclude that CRP elicits endothelium-dependent oxidative stress and compromises NO- and PGI2-mediated vasomotor function via LOX-1 activation. By contrast, both LOX-1 and CD32 mediate PAI-1 upregulation in arterioles by CRP. Thus, activation of LOX-1 and CD32 may contribute to vasomotor dysfunction and pro-atherogenic actions of CRP, respectively.

007

REGULATION OF EARLY GROWTH RESPONSE PROTEIN-1 IN VASCULAR SMOOTH MUSCLE CELLS

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Hyperactivation of proliferative and growth promoting pathways underlies the progression of vessel remodeling leading to vascular dysfunction. An upregulation of early growth response protein 1 (Egr-1), a zinc finger transcription factor has been observed in several models of vascular diseases. In an attempt to understand the mechanisms that contribute to the upregulation of Egr-1 in these models we have investigated the role of vasoactive peptides such as Endothelin-1 (ET-1), Angiotensin II (Ang II) and growth factors such as insulin- like growth factor -1 (IGF-1) on the expression of Egr-1 in vascular smooth muscle cells (VSMC) Here we show that ET-1, Ang II and IGF-1 potently enhanced both protein and mRNA expression of Egr-1 in these cells. Pharmacological blockade of ERK1/2, PI3K/PKB pathways by PD98059/Wortmannin/SC-66 respectively, significantly attenuated Egr-1 expression by these factors. DPI (Diphenyleneiodonium), an inhibitor of NAD(P)H oxidase, blocked the activation of ERK1/2 and PKB as well Egr-1 expression in response to these factors. In summary, these data demonstrate that ROS-dependent activation of ERK1/2 and PI3K/PKB, the key growth promoting pathways in VSMC, by vasoactive peptides and growth factors plays a critical role the upregulation of Egr-1 in vascular system. (Supported by CIHR).

008

CARDIOVASCULAR EFFECTS OF CARFILZOMIB, A NEW PROTEASOME INHIBITOR, ON CORONARY RESISTENCIES, VASCULAR TONE AND VASCULAR REACTIVITY

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Background: Carfilzomib (CFZ) is a new proteasome inhibitor used for the treatment of relapsed and/or refractory Multiple Myeloma. Cardiac failure events (7.2%) and myocardial ischemia have occurred following administration CFZ. Infusion reactions also include chest thightness and angina of unknown mechanism.
Aim of study: To test the effects of CFZ (10^{-9} to 10^{-7} mol/L) on the isolated rabbit heart and aorta.
Methods and Results: CFZ administered in the perfusate to the isolated heart did not substantially modify left ventricular pressure (LVP) and heart rate (HR), whereas coronary perfusion pressure (CPP) was only slightly increased at the highest concentration used (from 65.2 +/- 4.1 to 78.6 +/- 8.3 mm Hg; $p<0.05$). Conversely, administration of CFZ by pulse injection caused a significant increase in CPP at all concentrations used (all $p<0.05$) and a mild, though significant, rise in LVP and HR at the highest concentration. Carfilzomib administered directly into the organ bath significantly increased the basal tone of the isolated aortic strips (e.g. 0.58 +/- 0.04 at 10^{-7} mol/L) with plateau of contraction reached after 10 minutes (all $p<0.05$). Such spasmogenic effect was basically doubled following ablation of the endothelium. Pretreatment with CFZ for 60 minutes significantly amplified the vasospastic action exerted by 3 different agents, i.e. KCl, noradrenaline (NA) and angiotensin II (A), on aortic strips; and impaired vasodilation following administration of nitroglycerin (NTG) and nifedipine (NFP) on the plateau of contraction induced by KCl, NA and A (all $p<0.05$). Likewise, aortic strips pretreated with CFZ exhibited impaired relaxation, as compared to untreated strips, following administration of acetylcholine (Ach), an endothelium-dependent vasodilating agent, on the plateau of NA contraction ($p<0.05$).
Conclusions: CFZ increased CPP, resting vasoconstricting tone and the spasmogenic effect of different agents. Preincubation with CFZ decreased the anti-spasmogenic activity of NTG and NFP, as well as reduced by over 50% the vasodilating effect of Ach, suggesting that CFZ can impair vasodilation via an endothelium dependent mechanism. Further studies are warranted to establish its clinical safety in patients with known CAD and prior history of coronary spasm.

009

ASPIRIN-INSENSITIVE THROMBOXANE GENERATION AS A MARKER OF ENDOTHELIAL DYSFUNCTION

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Thromboxane A2 (TXA2) is a signal-dependent prostanoid generated from the metabolism of arachidonic acid by the cyclooxygenase (COX) and thromboxane synthase enzymes. In healthy adults, TXA2 is almost exclusively produced in platelets where it mediates platelet activation and vasoconstriction. Aspirin exerts its principle antiplatelet effect by suppressing TXA2 generation by irreversibly inhibiting platelet COX-1. Data from several clinical studies reveal that patients with cardiovascular disease and evidence of persistent TXA2 generation despite aspirin therapy are at increased risk of adverse cardiac events. In a study of patients undergoing cardiac surgery, we found that while aspirin was highly effective at suppressing platelet TXA2 generation, a substantial number continued to generate TXA2 from apparent non-platelet sources. This aspirin-insensitive TXA2 generation was found to be a novel risk factor for early graft thrombosis and strongly associated with increased oxidative stress. In vitro studies subsequently confirmed that endothelial cells are capable of generating TXA2 in response to a number of stimuli, including oxidative stress. Isoprostanes, generated by non-enzymatic metabolism of arachidonic acid under conditions of oxidative stress, appear able to act as mediators of endothelial TXA2 generation. Studies by several laboratories, including our own, suggest that TXA2 is capable of altering endothelial thromboresistance by modulating the expression of tissue factor and inflammatory adhesion molecules. This may provide an explanation for the increased risk of thrombotic events associated with aspirin-insensitive TXA2 generation observed in clinical studies. In contrast to platelet TXA2 generation, aspirin is ineffective at inhibiting TXA2 generation in endothelial cells given its short circulating half-life and the ability of nucleated cells to regenerate inhibited COX-1. Potential strategies to suppress endothelial TXA2 generation include TXA2 synthase inhibitors/receptor antagonists, antioxidants and/or polyunsaturated fatty acids.

010

REGULATION OF MYOCARDIN ACTIVITY IN VASCULAR SMOOTH MUSCLE

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Many vascular diseases result from dedifferentiation of vascular smooth muscle cells (SMCs). Myocardin (MYOCD) is a co-transcriptional activator of serum response factor (SRF) and stimulates the expression of SM genes and inhibits the cell cycle. In addition to its roles in the development, MYOCD is critically involved in the pathogenesis of proliferative vascular diseases. The expression and activity of MYOCD are tightly regulated in SMCs. MYOCD, when phosphorylated by GSK-3β, can be ubiquitinated by C-terminus of Hsc70-interacting protein (CHIP), a cytosolic E3 ligase, resulting in proteasomal degradation and reduction of MYOCD transcriptional activity. More recent studies from our laboratory have indicated that inhibition of MYOCD degradation blocks MYOCD activity and tumor necrosis factor-alpha phenotype-specifically regulates MYOCD activities in SMCs. In summary, the regulation of MYOCD activity may play a critical role in the pathogenesis of vascular disease.

011

ATHEROSCLEROSIS, CANCER AND WOUND HEALING; THE SYSTEMS BIOLOGY CONNECTION

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Serpins have critical regulatory roles in coagulation, inflammatory, and apoptosis, representing a large percentage of circulating proteins. Genetic serpin mutations cause severe disorders such as deficiency in alpha1 antitrypsin and neuroserpin or in sepsis with disseminated intravascular coagulation. Modified serpin activity is used in treating clinical disorders, i.e. heparin decreases clotting through activation of anti-thrombin (SERPINC1) and alpha anti-trypsin replacement (SERPINA1) is given to patients with genetic deficiency and emphysema. Prior studies report the use of serpin peptides for treatment in sepsis and HIV. Our research group is examining virus-derived serpins as potential therapeutics. Prior work demonstrated significant reductions in vascular disease with the Myxomaviral serpin, Serp-1, in models of arterial balloon angioplasty and aortic, renal and cardiac transplants. Serp-1 treatment also improved mortality in lethal Mouse gamma herpes virus (MHV68) infection where we detected marked reductions in pulmonary hemorrhage and congestion Serp-1 has also been tested in a phase 2A clinical trial after coronary stent implant for patients with unstable coronary syndromes (NSTEMI) with a demonstrated significant reduction in markers for myocardial damage. Another Myxomavirus derived serpin, Serp-2, that targets the infammasome and apoptotic pathways markedly reduced anti-inflammatory activity in animal models of vascular surgery, ischemia reperfusion injury and transplant, whereas CrmA from Cowpox was inactive. Related work using mammalian serpins such as neuroserpin (SERPINI1) also demonstrated anti-inflammatory activity and reduced tumor growth in animal models. In recent work we assessed the capacity of serpin reactive center loop (RCL) peptides to expand serpin functions and reduce inflammatory responses detecting reductions in plaque growth in an aortic transplant models and improved survival in lethal MHV68 infection model. In conclusion, viral serpins have evolved over many millions of years to form highly efficient regulators of central inflammatory pathways, identifying shared pathogenic pathways driving disease and new therapeutic horizons.

012

DETERMINANTS OF CARDIAC FUNCTION IN PATIENTS WITH DILATED CARDIOMYOPATHY

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Interstitial fibrosis is common in patients with advanced heart failure, including those with dilated cardiomyopathy (DCM). Echocardiography and right heart catheterization were utilized to assess left ventricular (LV) function and cardiac tissue was obtained to study myocardial structure and the gene and protein expression of several proteins that affect cellular function and fibrosis. LV systolic and diastolic function were significantly related to the mRNA and protein levels of SERCA 2a and PLB as well as mRNA levels of TTN N2B and N2BA. On the other hand, weak to no associations were present between myocardial function and interstitial fibrosis and its molecular determinants. LV systolic and diastolic functions in DCM are primarily associated with myocardial force generation/relaxation elements.

013

PREDICTING LONG-TERM RISK IN GENERALLY ASYMPTOMATIC PATIENTS: CARDIAC TESTING IN A MULTIMODALITY IMAGING WORLD

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Although coronary artery calcium score (CACS), exercise treadmill test (ETT), and stress myocardial perfusion tomography (SPECT) results predict patient outcome, there are no data comparing their relative value in risk stratification. We performed a prospective, observational study in 988 asymptomatic or low-risk symptomatic patients without prior coronary artery disease to define relative value of these tests in predicting long-term (median follow-up 6.9 years) cardiac events. Most patients (87%) were appropriate candidates for functional testing based on current guidelines. The cardiac event rate was 11.2% (1.6%/ year). Multivariate risk predictors in all patients and in the appropriate use cohort were abnormal SPECT (hazard ratio [HR]: 1.83 and 1.99), ETT ischemia (HR: 1.70 and 1.76), decreasing Duke treadmill score (HR: 1.07 for both), and CACS severity (HR: 1.29 for both), respectively. CACS improved risk prediction in all patients, in the appropriate use cohort and in those with low-risk ETT and SPECT results (all, $p<0.001$). Area under the receiver operating characteristic curve increased when CACS (from 0.63 to 0.70; $p=0.01$) but not ETT variables (from 0.63 to 0.65) were added to Framingham risk score (FRS). Net reclassification improvement significantly increased by adding CACS to FRS + functional variables ($p<0.0001$). Thus, CACS significantly improved long-term risk stratification beyond FRS, ETT, and SPECT results across all FRS groups, among those currently considered appropriate candidates for functional testing and in those with low-risk functional test results. Our findings support CACS as a first-line test over ETT or SPECT for assessing long-term risk in such patients.

014

CAC TESTING IN 2015: ROLE IN SHARED DECISION MAKING?

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In both the US and Europe, there have been significant declines in deaths due to cardiovascular disease (CVD) over the last two decades. The impressive reduction in mortality is reassuring evidence of the success of enhanced preventive efforts including lifestyle interventions and the appropriate use of preventive medications such as statins. The recent ACC/AHA guidelines on risk assessment and cholesterol treatment shifted the paradigm of statin eligibility in primary prevention from a combination of risk assessment and corresponding LDL cholesterol targets to a risk-based decision alone, shared between the provider and the patient. However with wide broadening of the scope of individuals meeting criteria for statin has brought new challenges. With current guidelines more than 12 million additional individuals in US and overall 1 billion individuals worldwide will be candidates for statins with the cost of generic statin to be around 1 trillion dollars in 2020. Moreover emerging evidence suggest that approximately half of those considered at high risk by current risk calculators are actually at lower risk of events resulting in appropriate use of statin. Coronary artery calcium (CAC) as a surrogate for coronary atherosclerotic burden has been consistently shown to identify those at higher risk and thus appropriate candidates for statin. Moreover absence of CAC (power of zero) have been noted in 30-50% of those considered at high risk by traditional strategies among whom statins can be safely avoided with a focus on lifestyle interventions. In 2015, CAC testing has the potential to appropriately identify candidates who will, and will not, benefit from lifelong statin therapy and facilitate shared decision making and resource allocation among the stakeholders.

015

CURRENT STATUS OF INTRAVASCULAR IMAGING

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Currently available intravascular imaging techniques that are used in clinical practice, have major limitations related to resolution and ease of imaging. There have been major innovations in the field of imaging to improve on these limitations and to incorporate novel imaging techniques that venture beyond the traditional delineation of anatomical intravascular structures. Intravascular Ultrasound (IVUS) imaging and Optical Coherence Tomography (OCT) are now widely used in clinical practice. However the frustrating impediment of lack of high grade resolution has been a major handicap for clinicians. Advances in ultrasound and tomographic physics have made possible major path breaking initiatives to improve axial, lateral and temporal resolutions. Ease of imaging has improved with technological advancement in catheter designs and in techniques that allow tomographic imaging without interrupting blood flow. Tissue imaging of subcellular components and chemicals can be combined with traditional imaging to obtain additional valuable information. Near infrared spectroscopy and time-resolved fluorescence spectroscopy are two novel imaging techniques that have potential to be incorporated into the traditional imaging techniques like IVUS, OCT, angioscopy, Computerized Tomographic angiography and Magnetic Resonance Imaging. Hybrid techniques involving two or more imaging methods will improve the applicability and utility of intravascular imaging in clinical practice.

016

SAFETY AND EFFICACY OF DUAL MOTION ROTATIONAL CORONARY ANGIOGRAPHY

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Background: Cardiac catheterization via standard angiography (SA) requires several angiograms while rotational coronary angiography (RA) employs the use of automated gantry acquisitions (LAO to RAO with a fixed cranial or caudal angulation) permitting complete visualization of the entire coronary tree via two injections of the left (LCA) (cranial and caudal) and one of the right coronary tree (RCA). XperSwing dual-axis rotational coronary angiography (DARCA) is a novel acquisition method wherein the gantry automatically rotates both LAO/RAO and cranial/caudal in one cine permitting complete visualization of a coronary tree with a single injection (Figure 1). We sought to compare DARCA to SA with respect to time, contrast and radiation dose.
Methods: 15 patients underwent SA and DARCA for both coronary trees. Contrast, dose-area product (DAP) and time (mean ±SD) were recorded for each and compared using a Student's t-test. For DARCA, blood pressure (BP), heart rate (HR), symptoms and ectopy were recorded for each prolonged coronary injection.
Results: DARCA significantly reduced the amount of contrast used (28.9±4.2 vs.55.3±12ml; p=0.0002), radiation dose (23.9±6.3 vs. 38.5±11.7 Gy/cm2: p=0.0003) and procedural time (158.5±40.2 vs. 221.9±61.5 seconds; p=0.0028) when compared to SA. There were no significant changes in BP, HR nor development of symptoms/ectopy during DARCA.
Conclusion: DARCA is a novel, safe and effective angiographic acquisition technique which significantly reduces contrast, radiation exposure and procedural time when compared to SA.

017

EMERGING NONINVASIVE TECHNIQUES FOR ASSESSMENT OF MYOCARDIAL STIFFNESS BY ECHOCARDIOGRAPHY

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Structural changes in the tissue brought by the disease (e.g., cancer, liver cirrhosis and fibrosis, myocardial infarction, heart failure, etc.) alter biomechanical properties of the tissue (elasticity and viscosity). Increasing evidence exists that measurement of tissue elasticity by ultrasound and magnetic resonance imaging can detect such alterations in liver, breast, thyroid, and prostate. The assessment of myocardial stiffness has been more challenging to achieve, and remains restricted to invasive techniques (pressure-volume measurements in the catheterization laboratory). Recent developments suggest that noninvasive estimation of myocardial elasticity by ultrasound and magnetic resonance imaging may be clinically possible in the near future. We recently introduced a new method that relies on analysis of intrinsic myocardial waves to estimate myocardial elasticity during diastole. This technique has been validated in animal studies, demonstrating that myocardial wave speed was highly correlated with the stress-strain derived elastic modulus measured by gold-standard invasive techniques. We have used this wave-based technique in >100 patients with various cardiac diseases. The results indicate that intrinsic myocardial wave speed is altered in left ventricular myocardium of patients with severe aortic stenosis, cardiac amyloidosis, heart failure with preserved ejection fraction, and hypertrophic cardiomyopathy compared to age-matched healthy subjects. Less severe changes were found in patients with degenerative severe mitral regurgitation. Preliminary results suggested that a higher wave speed was associated with reduced exercise capacity and peak myocardial oxygen consumption. Noteworthy, the wave speed measured by the intrinsic wave method was comparable to the shear wave speed produced by the ultrasound radiation force which is more challenging to apply effectively throughout the left ventricle at transthoracic imaging. In conclusion, measurement of myocardial stiffness has potential to become a new noninvasive imaging biomarker that may help with identification of structural changes in the myocardium caused by the disease.

018

COMPUTED TOMOGRAPHY CORONARY ANGIOGRAPHY: DIAGNOSTIC AND PROGNOSTIC VALUE

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Coronary multislice computed tomography (CT) is increasingly being used as a tool for non-invasive visualization of the coronary arteries (1). The technique provides information on atherosclerotic plaque burden and to some extent on plaque composition. The diagnostic value of coronary CT scan is high. In the last few year a flourish literature on the prognostic value of coronary CT has been published. Accuracy of coronary CT needs to be assessed in management outcome studies, in which diagnostic and therapeutic strategies would be decided based on CT alone, without reference to any coronary angiography results.

A main point is that plaque composition represents a long-term predictor of cardiac events. In a long-term follow-up study on the predictive value of coronary CT, Sozzi et al (1) demonstrated that non-calcified and mixed plaques carried a worse prognosis compared to calcified plaques. Referring to plaque vulnerability concept, Mann et al (2) studied 31 subjects who died suddenly of CAD. They found that lipid core size and minimal cup thickness, 2 major determinants of plaques vulnerability, were not related to absolute plaque size or degree of stenosis. Accordingly, atherosclerotic plaque growth and destabilization are highly variable. Many serial angiographic studies have demonstrated that most AMI occur due to the occlusion of coronary arteries that did not previously contain significant stenosis; furthermore the coronary artery with the most severe stenosis is usually not the “culprit” one. Thus, plaque progression and clinical outcome are not always closely related, and each is poorly predicted on clinical and angiographic grounds, as most plaques that underlie an AMI are <70% stenosed.

Previously, CT was associated with elevated radiation exposure. Radiation doses are rapidly decreasing with newer acquisition protocols, arriving to an exposure of 2 mSv per exam.

1. Sozzi FB, Civaia F et al. Long-term follow-up of patients with first-time chest pain having 64-slice computed tomography. AJC 2011;15:516-21.
2. Mann JM, Davies MJ. Vulnerable plaque. Relation of characteristics to degree of stenosis in human coronary arteries. Circulation 1996;94:928-931.

019

EXERCISE ECHOCARDIOGRAPHY: ADVANTAGES AND DISADVANTAGES

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The presentation will describe the advantages and disadvantages of exercise echocardiography (Ex Echo) for evaluation of coronary artery disease (CAD). Advantages and benefits of Ex Echo are the following:
1. Accuracy and availability;
2. Test is non-invasive (Ex Echo avoids the risks of invasive procedures) and inexpensive;
3. Ex Echo does not require the purchase, handling or disposal of radionuclides;
4. Ex Echo provides real-time global and regional information about the ventricles;
5. The resting echo also provides additional information about valvular disease, site and extent of MI, chamber dilatation, thrombi and aneurysm;
6. Ex Echo is convenient to clinical practice, it takes less time, can be scheduled immediately and can be scheduled any time during a day;
7. Stress echo requires minimal staff.
Disadvantages of stress echocardiography are the following:
A. Factors contributing to false positives: severe hypertension, cardiomyopathies (LV dysfunction of unknown etiology), idiopathic hypertrophic subaortic stenosis; left bundle branch block, arrhythmias, pacemaker; severe AI; insufficient level of exertion; reader is too sensitive to very mild hypokinesia and over-reading normally stiff segments.
B. Factors contributing to false negatives: single-vessel disease, normalization of wall motion abnormalities, extensive collaterals to occluded vessel, the influence of medications, resting wall motion abnormalities and technical problems.
Conclusion: In spite of some false-negative and false-positive tests accuracy of exercise echocardiography is high and it is an excellent tool for evaluation of CAD.

020

POINT OF CARE ULTRASOUND, THE NEW PHYSICAL EXAMINATION

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Background: Ultrasound technology has become a central part of modern day healthcare. Its use as a clinical tool will continue to expand as the technology becomes more portable.
Hypothesis: Point-of-care (POC) ultrasound will ultimately replace the prior medical paradigm of a physical examination centric approach to patient evaluation.
Limitations: 1. Cost of equipment 2. Access to devices 3. Reimbursement model for use of technology 4. Learning curve and scarcity of master clinician ultrasound educators 5. Legal barriers and potential regulatory barriers.
Methods for adoption: 1. Change reimbursement model to deliver population based care to include bundling of reimbursement 2. Engage new device delivery models that allow access to equipment with a lower cost of entry 3. Build in ultrasound curricula to all levels of medical and clinical training 4. Expand the Emergency Department model of standardized examinations (FAST scan) into focused systems based examinations for point-of-care hypothesis testing.
Possible initial strategies: 1. Start with specific actionable evidence based imaging (IVC, gall bladder, pleural effusions) 2. Enlist medical training programs to incorporate POC ultrasound into all facets of curricula 3. Expand users of POC ultrasound to health care extenders and ancillary health care professionals to acquire actionable imaging data for physicians remotely.

021

DO PELVIC VASCULAR BED CALCIFICATIONS CORRELATE TO CORONARY ARTERY CALCIFICATIONS IN MODERN AMERICAN POPULATION?

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Background: In recent years, computed tomographic (CT) assessment in ancient mummies revealed aortoiliac calcifications thought to represent atherosclerosis, challenging the assumption that atherosclerosis is a modern disease. In an effort to characterize the presence of atherosclerosis in the often incomplete anatomy of mummies, we sought to investigate the correlation of pelvic vascular calcifications to the presence of coronary calcifications. A study in modern Egyptians revealed that atherosclerotic calcifications seen in aortoiliac beds preceded the appearance of coronary calcifications by almost a decade. The goal of our study was to investigate a correlation between iliac and coronary artery calcifications in modern population.
Methods: We randomly selected 103 patients (64% male) who underwent screening body CT. Mean age was 57 +/- 11 years (range 31-84). Using these scans, coronary, right and left iliac artery calcifications were quantitatively assessed.
Results: Results revealed that coronary and iliac artery calcification scores correlated with age ($p< 0.0001$), but not BMI or BSA. The right iliac (54 of 103) and left iliac (51 of 103) artery calcifications correlated with each other ($r = 0.745$, $p<0.0001$). The total coronary calcification score correlated with both left ($r = 0.590$, $P < 0.0001$) and right ($r = 0.679$, $P < 0.0001$) iliac scores. Further analysis using the Fisher exact test revealed coronary calcification in 76.5% (39 of 51) of those with left iliac calcification, 79.6% (43 of 54) of those with right iliac calcification and 82.9% (34 of 41) of those with bilateral iliac calcification. In those without iliac calcifications, 30.8% (12 of 39) had coronary calcifications.
Conclusion: The presence of iliac calcifications is suggestive of coronary calcifications. However, the absence of iliac calcifications does not preclude coronary calcifications.

022

UPDATE ON THE TREATMENT OF THE CHRONIC TOTAL OCCLUSION

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A key goal in treating obstructive coronary disease is complete revascularization (CR). Multiple observational and registry studies have suggested the value of CR in maximizing survival, minimizing long-term adverse cardiac events, and improving the quality of life. The primary challenge to providing CR with percutaneous intervention (PCI) is treatment of the chronic total occlusion (CTO). Because of the technical challenges, the CTO is often ignored in PCI treatment citing the presence of collaterals filling the region and suggesting that the CTO is a rather "benign" lesion. The idea that collaterals adequately perfuse the myocardium in the CTO territory is a myth; that area is, in fact, a chronically ischemic zone and may account for the worsened outcome of CTO patients compared with matched non-CTO CAD patients. CTO PCI should align with guidelines and appropriate use criteria for management of the non-CTO lesion, governed by the same criteria, i.e. the extent of symptoms and ischemia and the adequacy of medical therapy. Available data have shown that revascularization with PCI of a CTO can improve symptoms, decrease the need for bypass surgery and improve ventricular function and may improve survival. Newer techniques have improved recanalization rates from the relatively poor 60-70% range as reported in large registries to the current 90% range in centers of excellence. These techniques include the antegrade dissection-re-entry technique with dedicated tools including the CrossBoss catheter, Sting-Ray balloon, and Sting-Ray re-entry wire and retrograde techniques, both intra-luminal and dissection re-entry. Currently no randomized trials have demonstrated that CTO PCI is more effective than medical therapy or bypass surgery in multivessel disease but such trials are ongoing and should provide increased clarity in decision-making.

023

A CONTEMPORARY PRACTICE PATTERN AND OUTCOME FOLLOWING TRANSRADIAL AND TRANSFEMORAL INTERVENTIONS IN RECENT ANTIPLATELET ERA: A PROPENSITY SCORE-MATCHED ANALYSIS

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Purpose: Radial artery is an access site for percutaneous coronary intervention. We compared clinical outcomes after transradial intervention (TRI) and transfemoral intervention (TFI) in contemporary antiplatelet era.

Methods: Among 6,973 patients enrolled in a nationwide, prospective, multicenter registry from February to September 2013, eligible 1,860 patients were divided into TRI (n=1,445, 77.7%) and TFI (n=415, 22.3%) groups based on the vascular access site. Bleeding and major adverse cardiac events (MACE; death, recurrent myocardial infarction, revascularization, or stent thrombosis) were compared. Propensity score (PS)-matched analysis was performed in 728 patients.

Results: TRI group had significantly lower bleeding rate than TFI group in the entire (1.5% vs. 4.8%, odds ratio [OR] 0.38, 95% confidence interval [CI] 0.19–0.78, p=0.008) and PS-matched (2.7% vs. 5.2%, OR 0.42, 95% CI 0.19–0.94, p=0.035) cohorts. In multivariate regression, TRI was associated with bleeding in the entire (odds ratio [OR] 0.381, 95% confidence interval [CI] 0.186–0.781, p=0.008) and PS-matched (OR 0.424, 95% CI 0.191–0.942, p=0.035) cohorts. Kaplan-Meier estimates showed that MACE-free survival was higher in TRI group than TFI group in the entire (93.3% vs. 87.5%, log rank p=0.026) and PS-matched (91.8% vs. 87.1%, log rank p=0.04) cohorts. In Cox proportional hazard analysis, TRI was an independent predictor of MACE in the entire (hazard ratio [HR] 0.65, 95% CI 0.45–0.93, p=0.02) and PS-matched (HR 0.61, 95% CI 0.39–0.96, p=0.034) cohorts.

Conclusions: This study showed that TRI was associated with a reduced bleeding rate and better clinical outcomes compared to TFI in contemporary real-world practice.

024

UTILITY OF FREQUENCY DOMAIN OPTICAL COHERENCE TOMOGRAPHIC EVALUATION OF ANGIOGRAPHICALLY OPTIMIZED STENTED LESIONS

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Purpose: Optical coherence tomography (OCT), given its high resolution, may be a useful clinical tool to optimize stent deployment. We evaluated the nature and frequency of post-stent deployment OCT findings prompting further intervention.
Methods and Results: We evaluated 100 patients (pts), 127 stents, and 127,894 stent struts with post-PCI OCT who had angiographically optimized coronary stent implantation: 44% with unstable angina/NSTEMI, pre-PCI diameter stenosis 81±16%, stent diameter 3.0±0.4 mm, length 24.7±10.3 mm. Post-PCI in-stent minimal lumen area was 6.6±2.4 mm2 and minimal lumen diameter 2.7±0.5 mm. OCT findings were classified as 'significant' if an OCT finding prompted further intervention. Specific findings on OCT are summarized in table below. OCT findings were considered significant in 50 pts (50%), requiring the following interventions: 78% further balloon dilatation, 14% another stent implantation 6% treatment with Gp IIb/IIIa inhibitors, and 2% aspiration thrombectomy.
Conclusions: Post-PCI OCT was helpful in improving stent deployment in half the studied cases. Inappropriate angiographic stent sizing was the most common reason for significant OCT findings prompting further treatment. This finding recommends pre-PCI OCT when feasible when feasible. Overall results suggest the value of OCT in optimizing stent deployment.

Table 1: Abnormalities Found on Post-PCI OCT

Abnormality	Percentage of Patients (%)
Any abnormality	73
Malapposition	44
Stent underexpansion	12
Plaque prolapse	9
Thrombus	6
Angiographically unrecognized lesion	5
Uncovered dissection flap	4
Other (lesion ulcer, calcification)	2

025

LONG TERM CLINICAL OUTCOMES FOLLOWING SIROLIMUS-ELUTING STENT IMPLANTATION IN DIABETIC VS. NON-DIABETIC PATIENTS

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3. Sahajanand Medical Technologies Pvt. Ltd., Surat, Gujarat, India

Objective: Objective of this registry was to compare the long term clinical outcomes of the Supralimus-Core sirolimus-eluting stent (SES) in complex, non-selected diabetic and non-diabetic patients.
Background: Drug-eluting stents (DES) reduce restenosis and target lesion revascularization (TLR) in both diabetic and non-diabetic patients. However, there are limited data on the long term safety and efficacy of DES in diabetic patients.
Methods: Between April-2008 and May-2014, 500 patients treated exclusively with biodegradable polymer-coated Supralimus-Core SES (Sahajanand Medical Technologies Pvt. Ltd., Surat, India) were consecutively enrolled in the non-randomized, observational, multicenter SCODA registry. Of these, 269 patients were diabetic, whereas 231 had non-diabetic. Primary endpoint was long-term combined major adverse cardiac events (MACE) including death, myocardial infarction (MI), TLR, target vessel revascularization (TVR)/ coronary artery bypass graft (CABG) and stent thrombosis. Clinical follow-up was obtained up to 6 years. Mean follow-up time was 4.0±1.8 years (range, 3 to 6 years) and was achieved in 64.6% (323/500) of patients.
Results: A total of 500 patients, with mean age of 55.1±10.4 years, were included in this registry. Diabetic patients had a higher prevalence of arterial hypertension (60.2% vs. 40.3%, p<0.001), hypercholesterolemia (72.1% vs. 41.1%, p<0.001) and unstable angina (41.6% vs. 29.4%, p=0.005) compare to non-diabetic patients. During 6 years follow-up, the cumulative incidence of MACE in patients with diabetes was comparable to that of non-diabetics [19 (7.1%) vs. 27 (11.7%), p=0.074]. The diabetic patients demonstrated a higher, but non-significant, incidence of TVR/CABG compared to non-diabetic patients [7 (2.6%) vs. 5 (2.2%), p=0.750]. The incidence of stent thrombosis was similar between diabetic and non-diabetic patients [1 (0.4%) vs. 0 (0), p=1.000)].
Conclusion: Despite complex lesion morphology, this multicenter registry demonstrates satisfactory and sustained six years clinical outcomes as evidenced by the low rates of MACE, for the Supralimus-Core SES, in diabetic and non-diabetic patients.

026

FERROMAGNETIC STENT-GRAFT FOR RAPID ENDOTHELIAL CELL-CAPTURE

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Objectives: Develop a stent-graft by combining electrospun polyurethane nano-fibers and a ferromagnetic stent to enhance endothelial cell-capture and retention.
Background: Stents-grafts are an important advancement in vascular interventions, but restenosis, thrombosis and distal embolism continue to be concerning issues. Stent-grafts were originally developed by sandwiching a polymer between stents. In this study, we have developed a stent-graft in which a ferromagnetic stent was encapsulated between 2 layers of polymer thereby becoming capable of capturing and retaining magnetically-labeled endothelial cells to promote healing.
Methods: An electrospinning system was developed for creating nano-fibers from medical-grade polyurethane (BioSpan®, DSM, Exton, PA). First, nano-fibers were electrospun on a 3mm diameter rotating mandrel to form a graft. Next, a previously developed ferromagnetic stent made from 2205 stainless-steel was placed on the graft and electrospinning was continued to form the outside layer. We manufactured 7 stent-grafts and inspected them microscopically for surface and construct integrity. Three of the stent-grafts were tested for crimping and expansion to verify mechanical competence. Finally, one stent-graft was tested *in-vitro* for endothelial cell-capture.
Results and conclusions: The stent-grafts developed in this study (Fig1a) were suitable for deployment using a standard trifold balloon (Fig1b,c). Microscopic evaluation showed that the electrospun fibers sandwiched the stent without any observed delamination between layers due to manufacturing and after deployment. Using fluorescence imaging, the magnetized stent-graft proved to attract and retain magnetically-labeled cells *in-vitro* (Fig1d, cells appear white). Thus, our proof of concept stent-graft showed promise for targeted cell seeding which can facilitate rapid healing.

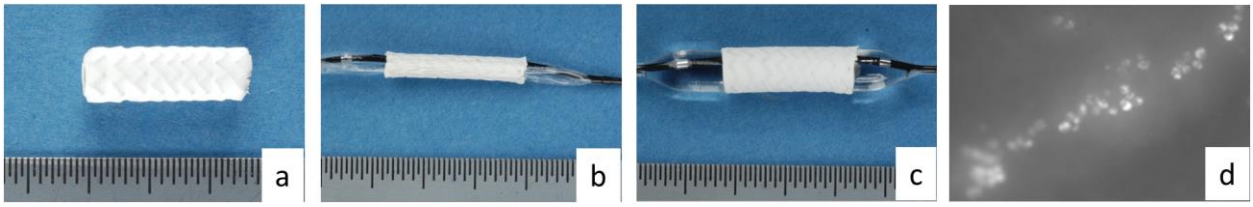

Figure1

027

RADIAL APPROACH TO CORONARY ARTERY BYPASS GRAFT ANGIOGRAPHY AND INTERVENTION REDUCES ACCESS SITE COMPLICATIONS

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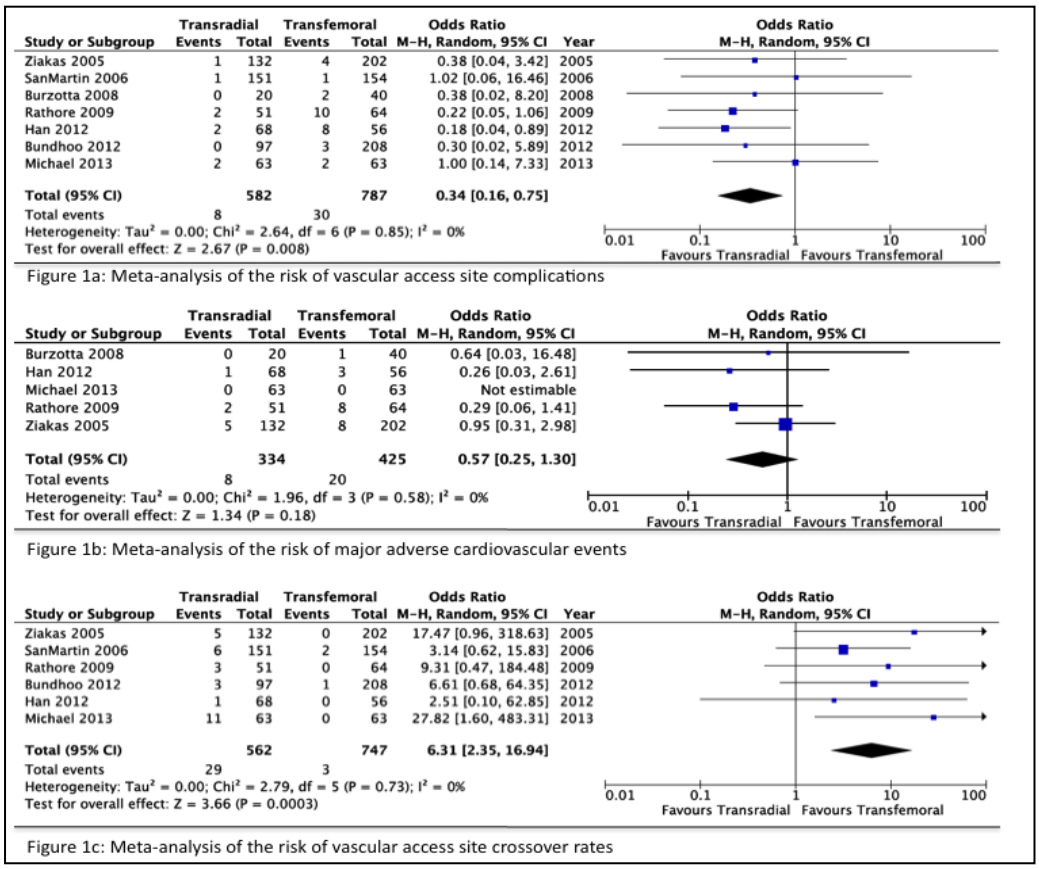
Background: Transradial (TR) approach to coronary artery angiography and intervention is gaining popularity with reduced morbidity and mortality compared to transfemoral (TF). Safety and effectiveness of TR approach in setting of bypass graft angiography and intervention is not well studied.
Methods: Systemic review of literature identified 1 randomized and 6 observational studies (n=1370) that addressed this issue. Meta-analysis compared characteristics and outcomes of each approach including vascular access site complications, major adverse cardiovascular events (MACE), access site crossover rates, fluoroscopy time, procedure time and contrast volume use.
Results: (figure). Baseline patient characteristics were similar in both groups. Compared to TF, TR had decreased vascular access site complications (1.4%-vs-3.8%; OR: 0.34, 95% CI 0.16-0.75; p=0.008) and a tendency towards lower MACE (2.39%-vs- 4.7%; OR 0.57, 95% CI 0.25-1.3; p=0.18). No difference was found in rates of major bleeding (0.17%-vs-0.57%; p=0.58) or in-hospital death (0.29%-vs-0.7%, p=0.54). Risk of vascular access site crossover was higher in TR (5.16%-vs-0.4%; p=0.0003). TR was associated with comparable fluoroscopy time, procedure time and contrast volume usage to TF (all p>0.05).
Conclusion: Transradial approach to bypass graft angiography and intervention reduces vascular access site complications and has comparable fluoroscopy time and contrast volume usage.



028

RELATIONSHIP OF INTRA-PROCEDURAL HEPARIN DOSE AND ACTIVATED CLOTTING TIME DURING PERCUTANEOUS CORONARY INTERVENTION

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Background: Heparin dosing is done at physician discretion during percutaneous coronary intervention (PCI).
Objectives: We aim to describe the effect of unfractionated heparin dosing on intra-procedural activated clotting times (ACT).
Methods: Retrospective analysis was performed of 70 patients who presented as ST elevation myocardial infarction (STEMI) and underwent PCI. Patients were given initial bolus of intravenous heparin on presentation. First ACT was recorded in the catheterization lab on arrival. Additional intra-procedural doses of heparin were at the discretion of the physician and second ACT level was recorded. The use of glycoprotein IIb/IIIa inhibitor was at the discretion of the physician. Nominal and continuous data were analyzed. Mean and standard deviations were calculated.
Results: Patient population was 74% male, 69% hypertensive, 26% diabetic and 56% smokers. Initial dose of approximately 50 IU/kg of unfractionated heparin (UFH) lead to first ACT time of 192 sec, 28 min after administration. Repeat dosing of 25 IU/kg lead to an ACT of 240 sec, approximately 25 min after administration.
Conclusion: Current guidelines emphasize weight based initial dosing of heparin for percutaneous coronary intervention. However, there is a lack of guidelines for subsequent heparin dosing. Heparin nomograms should be encouraged to help maintain appropriate therapeutic anticoagulation during PCI.

Table 1.

Parameter	**Value**
Mean age	59.5±11.9 yrs
Mean weight	86.6±18 kg
Average First heparin bolus/kg	49±10 IU/kg
Mean Time to First ACT check	28±2.5 min
Mean First ACT	192±26 sec
Percent of patients with First ACT less than 250 sec (N)	97% (68/70)
Average Second heparin bolus/kg	25 ±14 IU/kg
Mean time to Second ACT check	25.5±13.5 min
Mean Second ACT	240±57 sec
Percent of all patients with Second ACT less than 250 sec. (N)	61% (43/70)
Percent of patients on GPIIb/IIIa inhibitors (N)	53% (37/70)
Percent of patients on GPIIb/IIIa inhibitors with second ACT<250sec (N)	59% (22/37)
Percent of patients on UFH only during the PCI (N)	47% (33/70)
Percent of patients on UFH only during PCI and second ACT<250sec (N)	61% (20/33)

029

RIGHT ATRIAL MECHANICS PROVIDE USEFUL INSIGHTS IN IDIOPATHIC PULMONARY HYPERTENSION IN CHILDREN

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Background: Identification of impending right ventricular (RV) decompensation is inaccurate in children with idiopathic pulmonary hypertension (PH), since 6-minute walk distance and degree of tricuspid regurgitation (TR) do not deteriorate with increase in disease severity, as in adult PH. In absence of TR, current echo indices are poor predictors of disease severity. Right atrial (RA) mechanics may provide insight into state of RV compensation.
Methods: 16 patients (age 3-20 years) with severe PH but without significant TR and 12 matched controls were studied. RA longitudinal strain (RALS) & longitudinal displacement (LD) were calculated by speckle-tracking echocardiography. Area enclosed by RALS-LD loop measured atrial "work". RV area-change (RVAC) and tricuspid annular plane systolic excursion (TAPSE) served as indices of RV function. Mean pulmonary artery pressures (mPAP) were available within 6 months. RALS >40% was used to distinguish compensated from decompensated PH.
Results: mPAP & RALS showed significant correlation (r=0.71). RALS-LD loop area was preserved in compensated PH, but drastically reduced in decompensated PH (Figure 1). Defining RV decompensation as a state of low RALS allowed identification of a subgroup of PH patients with higher mPAP and lower TAPSE and RVAC.
Conclusions: RALS can identify both increasing mPAP and RV deterioration and may detect decompensation in pediatric PH.

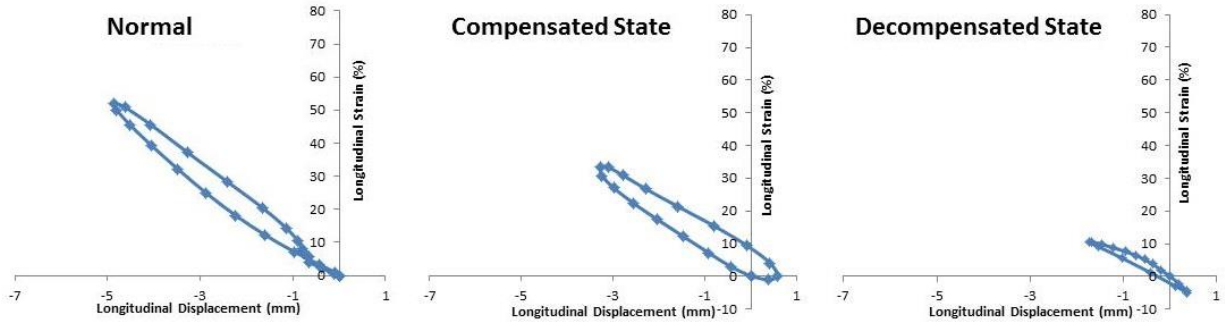

Figure 1

Table 1: Right Heart Data

	mPAP (mm Hg)	RALS (%)	Loop Area (u)	TAPSE (cm)	RVAC (%)
Normal		55.59 ± 6.99	46.03 ± 31.49	1.96 ± 0.33	51± 9
Compensated	51.38 ± 8.25	56.74 ± 14.33	39.69 ± 20.64	1.72± 0.49	42± 14 *
Decompensated	81.57 ± 18.28	26.10± 18.62 *¶	12.97 ± 31.83 *¶	1.53± 0.51 *	25 ± 12 *¶

(mean ± SD, * p<0.05 when compared with normal, ¶ p<0.05 decompensated versus compensated state. Newman-Keuls test

030

MORPHOLOGIC SEVERITY DOES NOT PREDICT MYOCARDIAL CONTRACTILE FUNCTION IN PEDIATRIC NONCOMPACTION CARDIOMYOPATHY

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Objectives: To evaluate in a pediatric population whether morphologic Noncompaction Cardiomyopathy (NCC) severity correlates with left ventricular contractile function.
Background: NCC is a likely under-diagnosed developmental disorder defined by morphologic criteria. It is associated with a high morbidity and mortality, mostly due to poor contractile function. Predictive markers have not yet been identified.
Patients and methods: 58 patients (age 6.2±6.7 years, 33% females) were diagnosed with NCC between 4/2006 through 4/2014 and qualified for retrospective analysis. 16 (29%) patients had associated congenital heart defects (CHD). NCC severity was graded by the number of cardiac segments affected as mild (<6), moderate (6-11), and severe (>11). Low left ventricular contractile function was defined echocardiographically by an ejection fraction (EF) <56%.
Results: NCC was mild, moderate, and severe in 27 (46%), 26 (45%), and 5 (9%) patients. EF was low in 19 (33%) patients. Patients with low EF were not different from patients with preserved EF in regard of age, weight, gender, associated CHD, or morphologic NCC severity. EF was low in 10 (37%) patients with mild NCC, 7 (27%) patients with moderate NCC, and 2 (40%) patients with severe NCC (p=0.37). Four patients (7%) required mechanical circulatory support or heart transplant; two patients (3%) died. Only one of these six patients (10%) was at high risk by morphologic severity criteria.
Conclusion: Morphologic NCC severity does not predict left ventricular contractile function in a pediatric population. Predictive functional markers for NCC are still urgently needed.

031

TRANSCATHETER CLOSURE OF PERIMEMBRANOUS VENTRICULAR SEPTAL DEFECT

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Background: Surgical closure is still considered as the most common treatment for significant perimembranous ventricular septal defects. Although perioperative mortality and morbidity rates became very low with advanced surgical techniques and improved postoperative management, this approach still carries the risks and complications of open heart surgery with cardio-pulmonary bypass. The transcatheter approach offers a valuable less invasive alternative with shorter hospital stay. Periprocedural complications include atrioventricular block - which reduced the popularity of the procedure, residual shunt, infective endocarditis and hemolysis. The NitOcclud Le coil initiates a revolutionary initiative that overcomes the atrioventricular conduction concern.
Objective: Assessing the efficacy, safety, short and long term results and complications of percutaneous closure of perimembranous ventricular septal defects using the Nitocclud Le VSD coil.
Methods: Twenty nine patients (17 F: 12 M; mean age 12 years, range 3-36 years) underwent transcatheter coil closure of perimembranous ventricular septal defects between May 2009 and November 2011. Success rate, adverse events, short and long term complication are reported. Multi variant analysis was performed to identify risk factors, positive and negative independent predictors.
Results: The success rate was 96.5% (28/29 procedures). Minor and transient short term complications were 31%, comprising coil related hemolysis, femoral artery thrombosis, catheter induced second degree atrioventricular and fascicular block. Two patients experienced major complications which required surgical intervention. One patient presented with late onset Kingiella Kingii endocarditis 6 months after the procedure and the second patient developed progressive tricuspid regurgitation. No long term atrioventricular block was observed by repeated ECG and ECG holter studies.
Conclusions: The transcatheter approach using the NitOcclud Le coil for the closure of perimembranous ventricular septal defect may be an effective and safe alternative to surgery.

032

PEDIATRIC POST-OPERATIVE ATRIO-VENTRICULAR BLOCK MEETS THE AFFORDABLE CARE ACT: A NEW STRATEGY FOR MANAGEMENT

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Introduction: Post-operative (post-op) complete atrio-ventricular heart block (CAVB) occurs after approximately 1-4% of pediatric cardiac operations. Current practice dictates implantation of permanent pacemaker (PPM) when post-op CAVB persists > 9 days. We propose that earlier PPM implantation may be the most cost-efficient methodology of caring for these patients since patient costs increase with extended length of stay (LOS).
Methods: Data on the probabilities of persistent post-op CAVB were extracted from published reports. This was utilized to create a decision-making model and a total cost analysis on post-op day 0-10 to determine the most cost-efficient day to implant a PPM. Cost variables included estimates of daily cardiac ICU care, cost of PPM implantation, LOS, cost related to possible superficial or deep infection based on published prevalence rates (2.3% and 4.9%, respectively) and need for explant due to deep infection or recovery of native conduction. The model assumes 5-day minimum LOS and 1 day increase in LOS with PPM implantation. Cost data were obtained from relevant billing codes and manufacturer list prices for PPM and leads. A secondary analysis evaluated probability of unnecessary PPMs implanted and excess costs.
Results: Post-op day (POD) 4 is the lowest total cost of PPM implantation for post-op CAVB, even when accounting for possible risk of either superficial or deep infection. A one-way sensitivity analysis accounting for variability of cardiac ICU care costs between centers ranging from $3,000-$9,000 per day consistently replicates POD 4 as the most cost-effective day for PPM implantation. Implant on POD 4 results in a 26% chance of unnecessary implantation.
Conclusions: The most cost-efficient day for PPM implantation for post-op CAVB is post-op day 4, which results in a minimum total cost savings of $17,422 per patient**.** Added costs due to risk of superficial or deep infection are marginal due to low prevalence of post-operative infection in this population.

033

HEART FAILURE CRT PACING IN CONGENITAL HEART: ACUTE VENTRICULAR PACED CONTRACTILITY (DP/DT) IS AN EFFECTIVE MARKER TO PREDICT CHRONIC EFFICACY

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Introduction: Patients (pts) with congenital heart disease (CHD) often develop heart failure (HF). Cardiac resynchronization pacing therapy (CRT) may improve HF. However, published pt selection criteria, including ejection fraction (EF) <35%, may not apply as EF is often inaccurate in many CHDs as well as pts with pacemakers (PM). This study evaluated acute ventricular (V) paced contractility (dP/dt) response pre-CRT implant to determine chronic CRT efficacy among CHD pts with HF.
Methods: Data from CHD pts being listed for heart transplant (HT) who underwent catheterization studies with temporary bi-V CRT-paced hemodynamics were reviewed. Positive CRT benefit was defined as >15% increase in dP/dt over baseline. Pts were given the option of CRT in addition to standard HF medical therapy and followed (2-144 months, mean 34) for outcome.
Results: EF could accurately be measured in only 20/32 pts (62%) measuring 16-62% (mean 35%). A positive CRT benefit was found in 22/32 pts (mean 22y age), 15/22 with preexisting PM (mean dP/dt increase from 551 to 823mmHg-sec, $p<0.006$). All 22 pts received CRT implant. During follow-up, all improved in NYHA class with improved HF symptoms and EF (36% vs 52%, $p < 0.01$) compared with pre-CRT values. Of these pts, 4 underwent HT (mean 56 mos later), 3 died (2 noncompliance (NC)) and 15 remain stable (NYHA class 1-3), off the HT list (repeat dP/dt mean 843mmHg-sec). Of the 10 pts with a negative CRT response (mean dP/dt 635 vs 662mmHg-sec, p=NS), 2 received HT (mean 12 mos later) and both died within 6y post HT, 2 died awaiting HT (NC), and 6 remain on the HT list (NYHA 2-4).
Conclusions: Pt response to CRT is often equivocal. Pre-selecting CHD pts by direct acute paced contractility (dP/dt) response assures greater CRT efficacy, can delay need for HT and improve pt well-being.

034

ABNORMAL FETAL Z-SCORES ARE A SENSITIVE PREDICTOR OF FETAL CONGENITAL HEART DISEASE

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Introduction: Current obstetric fetal cardiac screening recommendations fail to provide the proper tools necessary to accurately identify congenital heart disease (CHD). We sought to utilize 4 established normative fetal measurements to simplify screening for CHD. Hypothesis: Abnormal z-scores of 4 fetal cardiac measurements are a sensitive predictor of CHD.
Methods: We performed a retrospective review of fetal echocardiograms done on neonates with a post natal diagnosis of CHD from 2010 to 2013. Four anatomic measurements (aortic annulus, pulmonary valve annulus, right and left ventricular diameters) were performed according to ASE guidelines and compared to normative z-score reference ranges from published data. CHD lesions were categorized as right-sided lesions (tetralogy of Fallot, tricuspid and pulmonary valve abnormalities), left-sided lesions (hypoplastic left heart syndrome, aortic valve abnormalities, aortic coarctation and interrupted aortic arch), transposition of the great arteries (TGA), ventricular septal defects (VSD), and atrioventricular septal defects (AVSD).
Results: 120 patients with average gestational age of 28.2 weeks met criteria. At least 1 abnormal z-score was present in 93 of 120 patients. Overall sensitivity was 78 percent but varied by lesion subgroups. Sensitivity was lowest for VSD (53 percent), AVSD (62 percent) and simple TGA (33 percent) and highest for right sided lesions, left sided lesions and complex TGA. When VSD, AVSD and simple TGA were removed from the cohort, sensitivity improved to 90 percent.
Conclusion: Abnormal fetal z-scores are a sensitive predictor of CHD. Inclusion of z-scores of 4 fetal cardiac measurements in level 1 obstetric sonograms can identify patients needing referral for fetal echocardiography and improve detection rate of CHD. Additional focus on TGA and septal defects would further improve detections rates.

035

PRENATAL DIAGNOSIS AND OUTCOMES OF FETUSES WITH TRICUSPID ATRESIA IN A COUNTRY WITH LIMITED RESOURCES

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2. Mean Center of Family Medicine, Prishtina, Republic of Kosovo

Aim of this presentation was retrospective analysis of diagnosis, features and outcomes of fetuses with TrA diagnosed in our clinic.
Method and material: Between January 2001 and December 2012 were studied around 326 fetuses with congenital heart diseases; in 23 (7.0%) were found TrA. Age of gestation at time of diagnosis was 16 -38 weeks gestation. Retrospectively were analyzed characteristics and outcomes of 18 cases with known follow-up.
Results Characteristics: Three fetuses were twins, 2 fetuses were triple. Five fetuses (21.7%) had restrictive interatrial communication and balloon atrioseptostomy immediately were performed. Twelve of them had heart failure already at presentation, due to restrictive communication. All fetuses had nonrestrictive VSD, 5 of them had additional muscular restrictive VSD. Five fetuses (17.4%) had transposition of great arteries with nonrestrictive VSD, 8 fetuses (34.8%) had pulmonary stenosis, 2 (8.7%) had pulmonary atresia, 9 were (39.1%) with patent ductus, one with aortic coarctation, 6 had associated extracardiac anomalies.
Outcomes: Seven pregnancies (30.4%) were terminated, 6 with extracardiac anomalies. Out of 16 fetuses that continued pregnancies, 3 died in utero, 3 died shortly after birth and 3 died in second month of live waiting for surgery. The remaining 10 cases were operated with palliative procedures and latter underwent surgery (Glenn/Fontan procedure). Total intrauterine and postnatal mortality was 16/23 (69.6%).
Conclusion: Despite of improvement perinatal diagnosis management and outcomes of fetuses and children with TrA in Kosovo remain still poor. Negative prognostic factors were restrictive atrial communication, long term waiting for surgery, type and form of transport from Kosovo to destination center for surgery and still poor technical resources for follow up of this specific condition.

036

OUTCOME OF PEDIATRIC PATIENTS WHO UNDERWENT TETRALOGY OF FALLOT CORRECTION IN CORRELATION WITH THE SURGICAL TECHNIQUE USED IN RELIEVING THE RVOT OBSTRUCTION

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Background and Objectives: Before the advent of surgical intervention, about 50% of patients with Tetralogy of Fallot died in the first few years of life. In the advent of surgical repair, it has greatly improved the long-term survival of TOF patients. The objective of this study is to determine the outcome of pediatric patients who underwent tetralogy of fallot correction in relation to the surgical technique used in relieving right ventricular outflow tract obstruction (RVOT).
Methods: In this prospective study, 63 patients who underwent tetralogy of fallot correction were included. Postoperative complications of residual pulmonary stenosis, pulmonary regurgitation, and right ventricle systolic and diastolic dysfunction were determined and analyzed in correlation to the surgical technique used to relieve right ventricular outflow tract obstruction.
Results: Residual pulmonary stenosis was observed on all patients for both groups. RV systolic dysfunction was more common in transannular patching group at 56.5%, compared to pulmonary valve sparing group at 25%. RV diastolic dysfunction was present in 91.3% of transannular patching group and 85% in pulmonary valve sparing group. With regards to the distance travelled in 6 minute walk test, transannular patching group showed a mean of 297 + 71.3m while in pulmonary valve sparing group, it was 215.3 + 69.2m. 96.7% and 97.5% of transannular patching group and pulmonary valve sparing group respectively, were in functional class II.
Conclusion: Both RV systolic and diastolic dysfunction are present in the early postoperative period. Diastolic dysfunction was more common among patients who had transannular patching while systolic dysfunction was more common among patients who had pulmonary valve sparing. Pulmonary incompetence was more common among the transannular patching group. Most patients in both groups were in functional class II and had sub-optimal distance travelled in six minute walk test.

037

COMPARISON OF LONG-TERM CLINICAL OUTCOME OF ANGIOTENSIN-CONVERTING ENZYME INHIBITOR VERSUS ANGIOTENSIN II RECEPTOR BLOCKER IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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Angiotensin-converting enzyme inhibitor (ACEi) should be used as the first choice for post myocardial infarction (MI) and angiotensin II receptor blocker (ARB) should be considered in patients who are intolerant to ACEi. We consecutively enrolled acute myocardial infarction (AMI) patients who underwent percutaneous coronary intervention (PCI) from January 2004 to December 2009. Of 4,748 AMI patients, 2,332 and 1,245 patients were treated with ACEi and ARB at discharge, respectively. The primary endpoint was the incidence rates of all-cause death and landmark analysis for 1-year post-MI survivors and subgroup analyses were performed. Median follow-up duration was 43.8 months (interquartile range 29.8 to 60.5 months). In overall population, long-term survival was superior in ACEi group (201 death, 101.%) as compared with ARB group (150 death, 15.2%) ($p<0.01$). In multivariable Cox proportional hazards regression, adjusted HR is 1.37 (95% CI 1.10 to 1.70, $p<0.01$). Overall findings were consistent in propensity matched population. In landmark analysis at 1 year, the incidence rates of all-cause death within 1 year were similar in both groups (adjusted HR 0.90, 95% CI 0.60 to 1.35, $p=0.62$), whereas, survival after the first year was superior in ACEi group (adjusted HR 1.83, 95% CI 1.42 to 2.36, $p<0.01$). In subgroup analyses, there were significant interaction between preserved (HR 1.07, 95% CI 0.81 to 1.46, $p=0.69$) and decreased renal function (HR 1.78, 95% CI 1.22 to 2.60, $p<0.01$, p for interaction $p=0.04$) and between STEMI (HR 1.00, 95% CI 0.71 to 1.40) and NSTEMI (HR 1.78, 95% CI 1.26 to 2.50, $p<0.01$, p for interaction 0.019). Long-term survival of ACEi was significantly superior than ARB in patients with AMI treated with PCI. ACEi should be remained as the first-choice of treatment in AMI patients and ARB might be used as alternative with careful consideration of renal function or clinical diagnosis.

038

GLOBAL LONGITUDINAL STRAIN AND SEGMENTAL STRAIN PATTERN AS A PREDICTOR OF OUTCOME IN PATIENTS UNDERGOING AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA

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Introduction: 12-15% of patients diagnosed with multiple myeloma (MM), will develop clinical amyloidosis (AL) during the course of their disease. The majority of morbidity and mortality of clinical AL is related to cardiac involvement (CAL). Patients undergoing high-dose myeloablative chemotherapy are subject to a significant fluid and electrolyte shifts and severe systemic physiologic stressors. It is not known whether subclinical CAL will affect the outcomes of these patients. Echocardiography is the imaging modality of choice for the diagnosis of CAL using calculated global longitudinal strain (GLS) values and segmental longitudinal strain (SLS) patterns. We hypothesize that using this technique, we would be able to uncover patients with subclinical cardiac AL, and the values would be a potential predictor for outcomes.
Methods: 115 patients with MM undergoing pre-transplant echocardiography prior to autologous stem cell transplant (ASCT) were identified from June 2009 to June 2014. The GLS and SLS patterns were calculated using vendor independent software (EchoInsight®). These were compared to post-transplant outcomes (30 and 100-day readmission rates, mortality, new arrhythmia, heart failure, and ischemic events).
Results: Of the 115 patients identified, there were 12 deaths, 33 readmissions, 2 non-ST segment elevation myocardial infarctions, 11 new arrhythmias, and 10 heart failure episodes. Neither the GLS value nor SLS pattern provided a sufficiently strong signal for predication of these events in the patients studied.
Conclusion: In the 115 multiple myeloma patients studied at our institution, neither GLS nor SLS were able to predict transplant-related mortality or morbidity within the first 100-days. Our study was subject to the usual limitations of retrospective analyses, as well as the relatively low incidence of overall events, and the short follow-up. In order to overcome these limitations, and better risk-stratify patients, larger prospective studies using a combination of imaging and serum biomarkers is necessary.

039

LACK OF SOCIAL SUPPORT IS RELATED TO MORE DEPRESSIVE SYMPTOMS AND WORSE RENAL FUNCTION IN POST-ACS PATIENTS

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Background and objectives: Both depression and low social support (SS) have been associated with higher risk of cardiovascular (CV) disease development and mortality. We investigated potential mechanism though which these psychological factors affect CV prognosis in patients with acute coronary syndrome (ACS).

Method: Participants were 99 consecutive patients with ACS (mean age=61,SD=9;85% male).Anthropometric measures and fasting blood samples including levels of blood urea and creatinine were taken within 3 days after the CV event. Severity of the CV event was measured with peak levels of myoglobin and troponin, and the severity of the underlying coronary disease (UCD) with the number of obstructed arteries in the coronary angiography. Participants filled in a questionnaire including the Beck Depression Inventory and measures of perceived, actual, and tangible SS.

Results: Twenty-five percent of patients had mild to severe depression. Higher depression scores were not related to severity of the CV event or the UCD (ps≤.1) but were related to higher levels of urea(r=.397,p<.001) and creatinine(r=.396,p<.001). Similarly, higher perceived SS was not related to severity of the CV event or the UCD (ps>.1) but was related to lower levels of urea(r=−.212,p=.039) and creatinine(r=.−.267,p=.009). Multiple regression analyses controlling for standard risk factors showed that depression and social support had no independent effects on renal function. Rather, depression mediated the relationship between SS and renal function.

Conclusions: Although patients who perceived less SS in their lives did not present more severe CV event or UCV, they reported more depression symptoms shortly after the CV event and had worse renal function. A possible explanation could be an unhealthier lifestyle, worse hydration or less drug adherence.

These results suggest that SS has a protective effect on mental health in the face of a serious CV event and that impaired renal function can be an additional mechanism through which depression increases CVD recurrence and mortality in patients with ACS.

040

KNOWLEDGE OF CARDIOVASCULAR RISK FACTORS IN HIGH-RISK POPULATIONS: WHAT PHYSICIANS STAND TO LEARN

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Introduction: Asians in the US are heterogeneous but are grouped together when assessing risk of cardiovascular disease (CVD). South Asians (SAs) have higher CVD risk. Traditional risk factors for coronary artery disease (CAD) cannot fully account for increased CAD among SAs. Other factors, including lipoprotein (a) [Lp(a)], have been identified, and Lp(a) measurements are important for cardiovascular risk stratification of SAs. We determined physicians' understanding of CVD risk among SAs and the likelihood of physicians to pursue risk stratification testing.
Methods: We electronically surveyed 100 Internal Medicine and Cardiology physicians on CVD risk among SAs and on CVD testing.
Results: Among responders, 38% identified SAs as the ethnic group with the highest CAD risk, and 71% were "very likely" to order lipid testing in patients with a strong family history (FH) of CAD, but only 43% knew which type of advanced lipid testing to order. Physicians acknowledged FH was the strongest predictor of CAD in SAs (40%), followed by Lp(a) (28%) and elevated total cholesterol-to-HDL ratio (17%). Forty percent would not order genetic testing in patients with a strong FH of CAD; 88% did not know which genetic tests to order.
Conclusion: Despite strong data, most physicians are unaware of the high risk of CAD in SA and are unaware of how to pursue advanced lipid and genetic testing in high risk populations. In addition, physicians may be unaware of the risk stratification tools available and when to utilize these tests. Education and increased awareness regarding the increased risk of CVD in the SA population among physicians may decrease the high mortality and morbidity rates observed in this ethnic group.

LIPIDS, LIPOPROTEIN DISORDERS AND CAD

041

THE STATIN MYALGIA CLINICAL INDEX (SMCI): ENHANCEMENTS AFTER COGNITIVE INTERVIEWS WITH PHYSICIANS

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Background: Patients who experience muscle symptoms while taking statins often become non-adherent. However, attributing symptoms to statin use is clinically difficult. The new Statin Myalgia Clinical Index (SMCI), proposed by the National Lipid Association and included in a consensus statement of the European Atherosclerosis Society, evaluates the likelihood that statins caused a patient's muscle complaints rather than some other cause. We sought to revise the SMCI and prepare it for use in clinical practice.

Methods: The SMCI was revised based on structured qualitative interviews with three of the authors of the original publication and cognitive debriefing interviews with ten physicians (six cardiologists, two lipidologists, and two primary care physicians). To maximize the clarity of the SMCI, we applied rigorous methods recommended by the FDA and EMA for clinical outcome assessment development.

Results: Based on recommendations from the qualitative interviews, the revised SMCI includes new instructions and formatting to aid understanding, completion, and scoring. One instruction on distinguishing between two statin challenges was unclear to most clinicians; we significantly revised the layout and visual appearance of the SMCI in response. Where appropriate, clinicians' minor suggestions regarding language were implemented. Otherwise, clinicians generally found the SMCI items, response choices, scoring and interpretation clear and understandable.

Conclusions: The SMCI assesses the likelihood that muscle symptoms are due to statin use. In preparation for testing the SMCI in clinical practice, this study refined the SMCI based on cognitive interviews with clinicians. Tests of clinical application and inter-rater reliability are underway.

042

HYPERURICEMIA IS ASSOCIATED WITH WORSE LIPIDS PROFILE AND CARDIAC FUNCTION IN ELDERLY ATRIAL FIBRILLATION PATIENTS

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Objectives: To investigate factors associated with hyperuricemia in elderly patients with non-valvular atrial fibrillation (AF).
Background: AF and hyperuricemia are common diseases in elderly. Accumulated evidences indicate that hyperuricemia is a possible risk factor of cardiovascular diseases.
Methods: Consecutive elderly patients (over age 60) with non-valvular AF were retrospectively recruited in this study from the inpatient clinic between January 2012 and December 2013. We excluded subjects with cardiomyopathy, severe hepatic or renal dysfunction, thyroid dysfunction, chronic anemia, active inflammatory conditions, autoimmune diseases, and those who were taking uric acid-lowering drugs. The final study population included 611 patients (363 men and 248 women). Hyperuricemia was defined as serum uric acid (SUA) concentration > 7 mg/dL.
Results: The prevalence of hyperuricemia was 22.7% in the non-valvular AF population, 69.1% and 30.9% in men and women, respectively. Body mass index was significantly higher in hyperuricemia group than SUA normal group ($p < 0.001$). Consistently with elevated SUA, higher levels of serum creatinine, blood urea nitrogen and lower estimated glomerular filtration rate were found in hyperuricemia group (all p values < 0.001). Patients with hyperuricemia also had higher level of triglyceride and lower level of HDL than those in the SUA normal group ($p < 0.001$), indicating a worse lipids profile in hyperuricemia group. Besides, levels of B-type natriuretic peptide, left atrial diameter, LV mass index and percentage of NYHA class III/IV were significantly higher in hyperuricemia group than SUA normal group, indicating worse cardiac function (all p values <0.01). Treatment with diuretics and angiotensin-converting enzyme inhibitors were more prevalent in hyperuricemia group ($p < 0.001$).
Conclusions: Among elderly non-valvular AF population, elevated SUA was combined with poorer renal function. Worse lipids profile and cardiac function existed in patients with hyperuricemia.

043

LEFT ATRIAL ENLARGEMENT AS A MARKER OF SEVERITY OF DIASTOLIC DYSFUNCTION AND CORRELATION WITH DEMOGRAPHICS

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Objective: To determine the prevalence of left atrial (LA) enlargement and its relation to left ventricular (LV) diastolic dysfunction.
Methods: We retrospectively reviewed 2,265 medical records of patients receiving Echocardiograms at a University hospital between 2008 year and 2012 year. The patients were divided into four groups according to level of diastolic dysfunction. LV diastolic function was evaluated by measuring the peak velocity of early (E) and late (A) diastolic transmitral blood flow, peak early diastolic mitral annular velocity (E') by Tissue Doppler echocardiography, and pulmonary venous sampling.
Results: In this study, correlations between LA index and echocardiographic features of left ventricular (LV) diastolic function. Bivariate analyses showed higher mean LA index values in patients with Pseudonormal and Restrictive DD compared with controls and in patients with impaired relaxation (22.7, std. dev.9.4, 22.6, std.dev. 9.9, 29.5 std. dev 13.8, and 33.0, std.dev. 11.3, $p<0.0001$).In the logistic regression model with LA index, BMI and Age as predictor variables for the outcome of DDX severity, both LA index and Age were statistically significantly associated with DDX severity (LA index: OR=1.022, 95% CI=1.010-1.034, p=0.0004; Age: OR=1.051, 95% CI=1.041-1.060, $p<0.0001$). In the model with LA volume, BMI and Age, both LA volume and Age were statistically significantly associated with DDX severity (LA vol: OR=1.010, 95% CI=1.004-1.017, p=0.0009; Age: OR=1.051, 95% CI=1.042-1.060, $p<0.0001$).
Conclusions: LA Index and LA volume were higher in patients with Pseudonormal and Restrictive Diastolic Dysfunction than in control. Age was an independent predictor for DD. BMI was an independent predictor for DD.

044

LEFT ATRIAL ENLARGEMENT IN PATIENTS WITH ATRIAL FIBRILLATION AND STROKE AND DIASTOLIC DYSFUNCTION

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Background: Whether LA enlargement is a predictor for atrial fibrillation and stroke in patients with DD is unknown.
Objective: We conducted an analysis to investigate the association.
Methods: We retrospectively analyzed echocardiograms of 1568 patients performed at University hospital. 154 with atrial fibrillation, & 157 with stroke. For this analysis, there were 717 patients with complete data.
Results: In the logistic regression analysis we found that LA Index/LA volume was a predictor marker for development of Atrial fibrillation in patients adjusting for DD (LA volume: OR=1.021, 95% CI=1.010-1.032, p=0.0002). The model with LA index yielded similar results (OR=1.044, 95% CI=1.020-1.068, p=0.0002). Furthermore, we examined the outcome of stroke with the predictor variables AF, DD, and LA volume. Neither LA volume (p=0.3397) nor LA index (p=0.3390) were associated with Stroke in patients in models adjusting for DD and Atrial fibrillation (p=0.4834). DD was the only covariate found to be significantly associated with stroke (OR=1.911, 95%CI=1.031-3.539, p=0.0395).
Conclusion: Increased LA volume and LA index are both significant predictors of AF in patients adjusting for DD. No association between either LA volume or LA index was found with stroke as the outcome.

045

PROGNOSTIC VALUE OF RIGHT ATRIAL FUNCTION AND DIMENSION IN PATIENTS WITH PULMONARY HYPERTENSION

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Introduction: Clinical assessment is essential when evaluating patients with suspected pulmonar hypertension (PH), however, echocardiography is a key screening tool in the diagnostic algorithm. Right ventricular dysfunction has been associated with adverse outcomes but few studies have focused on the structure and function of the right atrium (RA).Objectives: To determine the prognostic value of RA dimensional and functional parameters in patients with PH.
Methods: Prospective study of patients with PH undergoing clinical and echocardiographic evaluation, focusing on RA dimensions and deformation analysis. Association with the composite endpoint death or hospitalization for cardiac causes was tested using the Kaplan-Meier analysis and Cox multivariate regression analysis. The prognostic accuracy was evaluated by the area under the receiver operator curve.
Results: Seventy-seven patients (75% female; 55 ± 16 years; 68% with group 1 PH) were included. At baseline atrial dimensions were: diastolic area - 24.4±13.1 cm2; systolic area - 19.3±11.1 cm2; longitudinal diameter 4C view - 56.9±12.9 mm. During a median follow-up of 25 months, 9 patients died and 29 were hospitalized for cardiac causes. The composite endpoint occurred in 39% (N = 30) and the risk increased with the RA size and reduction of atrial systolic deformation. The risk of events increased 6% per cm2 of increased area (HR: 1.06; 95% CI 1.03-1.10; p=0.001). Longitudinal systolic strain of all septal segments and lateroapical segment were strong prognostic predictors. The risk of events increased 7% for each 1% of deformation reduction (HR: 1.07; 95% CI 1,02-1.13; P=0.003). Midseptal segment longitudinal systolic strain was the strongest prognostic predictor by multivariate Cox regression analysis (including all RA echocardiographic parameters) (HR: 1.10; 95% CI 1.02 to 1 18; P = 0.012).
Conclusions: RA function and dimension showed prognostic value in PH and should be considered in the echocardiographic assessment of these patients.

PULMONARY CIRCULATION ASPECTS, PULMONARY HYPERTENSION

046

DETERMINANTS OF SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Background: Patients with obstructive sleep apnea (OSA) have increased cardiovascular risk. In these patients, intermittent hypoxia increases sympathetic activity, systemic inflammation and oxidative stress which may all contribute to accelerated atherosclerosis. Our aim was to investigate relationships between carotid intima-media thickness (IMT) and OSA severity, markers of oxidative stress and systemic inflammation.
Methods: 84 subjects [mean age (mean±SD) 47.1±9.7 years, body mass index (BMI) 30.1±4.1 kg/m2] underwent overnight polysomnography (Alice 4, Respironics, Murrysville, USA). Subjects were divided into three groups: no OSA [apnea-hypopnea index (AHI) 3.2±1.1 events/hour]; mild-moderate OSA (AHI 15.8±6.7 events/hour), and severe OSA (AHI 48.3±16.0 events/hour). Carotid intima-media thickness (IMT) was assessed by B-mode ultrasound (Philips HD11 XE), arterial pulse wave velocity (PWV) was measured using the automatic Complior device.
Results: Both IMT and PWV increased from subjects with no OSA to patients with mild-moderate, and to those with severe OSA (0.54±0.10 vs 0.59±0.07 vs 0.62±0.11 mm, p=0.037; 8.9±1.0 vs 10.3±1.3 vs 9.8±1.6 m/s, p=0.026, respectively). In addition, circulating oxidized LDL (oxLDL) and lipopolysacharid levels increased with OSA severity (p=0.007, p=0.046, respectively). In multivariate models, age (p<0.001), oxygen desaturation index (p=0.031) and oxLDL (p=0.005, r2=0.329) predicted IMT independently of gender and BMI.
Conclusions: In patients with OSA, older age, nocturnal intermittent hypoxia reflecting OSA severity and oxLDL were independent correlates of ultrasonographic carotid atherosclerosis.
Support: APVV-0134-11, Ministry of Education, Slovakia

047

ROLE OF THE ELECTROCARDIOGRAPHY FOR EARLY RISK STRATIFICATION IN ACUTE PULMONARY EMBOLISM

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Objective: We investigated 12-lead electrocardiographic (ECG) patterns in acute pulmonary embolism (PE) to evaluate the role of the ECG score in risk stratification of patients with acute PE.
Background: Date on the usefulness of combination of different ECG abnormalities in risk stratification of patients with acute PE are limited.
Methods: Our study enrolled one hundred thirty four(134) consecutive patients admitted in Emergency Hospital "Pirogov" with the diagnosis of acute PE(confirmed by spiral computed tomography scan) from June 2007 to December 2014.We analyzed ECG patterns and calculated the ECG score in all patients. The ECGs were recorded at standard gain (10mV/mm) and speed (25mm/s).We evaluated right ventricular systolic pressure (RVSP) (n=76) and right ventricular(RV) hypokinesia (n=87) using echocardiography for risk stratification of acute PE patients. Subjects with undeterminet onset of PE or without available ECGs were excluded from the present study. Given the fact, that echocardiography may be of poor quality in overweight and mechanically ventilated patients, or in those with chronic pulmonary disease, these groups of patients were also excluded from the study.
Results: Among several ECG findings sinus tachycardia (90%), right axis deviation (76%), inverted T waves in leads V1-V4 (65%) and right bundle branch block (40%) were observed most frequently. The mean ECG score and RVSP were 7.38 ±6.32 and 53 ±20 mmHg respectively. The ECG score correlated with RVSP(r=0.266, p=0.015).The patients were divided into two groups: high ECG score group (n=98) with ECG score>12, and low ECG score group (n=36) with score<12, based on the ECG score with the maximum area under the curve. RV hypokinesia was observed more frequently in the high ECG score group, than in the low ECG score group (p=0.006). Multyvariate analysis revealed that a high ECG score was an independent predictor of high RVSP and hypokinesia.
Conclusions: ECG may be a useful, simple, non-costly tool for initial risk stratification of patients with acute PE in the Emergency Departments and for guiding further diagnostic work-up decisions. Using the ECG for management warrants prospective evaluation.

048

PULMONARY HYPERTENSION IN A PATIENT WITH CONGENITAL HEART DEFECTS AND HETEROTAXY SYNDROME

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Background: Heterotaxy syndrome is a rare clinical entity characterized by presence of abnormal position of the viscera, congenital heart defects and splenic malformations. There have been very few reported cases of heterotaxy syndrome that manifest with pulmonary hypertension in adulthood.
Case: 26 year old male with history of heterotaxy syndrome diagnosed as a fetus with multiple cardiovascular surgeries presented to the hospital with shortness of breath. Anatomical abnormalities related to heterotaxy syndrome in our patient included double outlet right ventricle with complete AV septal defect (Rastelli type A), asplenia, pulmonary atresia, interrupted inferior vena cava with azygous continuation to the right superior vena cava and total anomalous pulmonary venous return to the innominate vein. Echocardiogram was done during the hospital course that revealed elevated pulmonary artery pressure. The pulmonary pressures obtained through right heart catheterization six months prior were normal. To confirm the diagnosis of pulmonary hypertension, right heart catheterization was repeated which revealed elevated pulmonary artery pressure at 71/38 mm Hg with mean of 51 mm Hg and elevated pulmonary vascular resistance (PVR) of 4.9 Wood Units. Pulmonary capillary wedge pressure was within normal range. Vasoreactivity test was negative. Patient was started on bosentan for management of pulmonary hypertension.
Conclusion: There has been one previously reported case of pulmonary hypertension in an adult with heterotaxy syndrome in a structurally and functionally normal heart. To the best of our knowledge, pulmonary hypertension has not been previously described as the prominent clinical feature of patients with heterotaxy syndrome with congenital heart disease. Development of pulmonary hypertension may be secondary to congenital heart defects resulting in left-right blood shunting, vascular malformations leading to portopulmonary shunts or non-cardiac malformations such as asplenia.

049

MASSIVE PULMONARY EMBOLI FOLLOWING DISCONTINUATION OF RIVAROXABAN

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Introduction: The use of novel oral anticoagulants (NOACs) for stroke and systemic embolism prevention in non-valvular atrial fibrillation and as treatment of pulmonary and systemic venous thromboembolism (VTE) has become increasingly common. To date, data regarding patient outcomes following discontinuation has not been well studied. We present a patient who developed massive bilateral pulmonary emboli (PE) following discontinuation of rivaroxaban.
Case Study: A 69 year old male initially presented to our facility with a right thalamic intracranial hemorrhage. The patient was chronically on rivaroxaban for paroxysmal atrial fibrillation, which was discontinued on admission. Two days later he developed shortness of breath. A Computed tomography angiogram revealed multiple bilateral PE. Ultrasound of the lower extremities did not reveal deep vein thrombosis (DVT). An inferior vena cava filter was placed. The patient was discharged to inpatient rehab. On hospital day 32, the patient developed acute respiratory failure. Echocardiography revealed a severely dilated right ventricle. The patient went for emergent pulmonary embolectomy at which time massive bilateral thrombosis was noted. Ultrasound of the lower extremities revealed bilateral acute and subacute DVT.
Discussion: Our patient presented with massive bilateral PE after discontinuation of rivaroxaban following an acute intracranial bleed. To our knowledge, this is the first case of post marketing massive pulmonary emboli following discontinuation of rivaroxaban. Workup revealed no other obvious cause for hypercoagulable state . This case brings to light the potential complications with discontinuation of NOAC therapy. Whether or not NOACs promote a hypercoagulable state remains unclear and deserves further investigation.

050

NOVEL ECG PREDICTORS FOR PULMONARY EMBOLISM

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Background: Acute pulmonary embolism (PE) is a common and highly morbid disease with a mortality rate approaching 30 percent if left untreated. Presenting symptoms can mimic acute coronary syndrome. Though CT angiography (CTA) is gold standard for diagnosis, it carries risk for contrast induced adverse effects and radiation exposure. Electrocardiogram (ECG) is an inexpensive tool that can aid in diagnosis of PE, and help expedite therapy. However, current data is based mostly on small retrospective studies.
Methods: We identified 300 patients diagnosed with acute PE by CTA, and retrospectively gathered data including patient characteristics, type of PE, its hemodynamic significance and associated ECG findings in hopes of discerning which of the previously associated ECG changes had an acceptable diagnostic sensitivity for acute PE.
Results: We found that ECG changes, including classic ones like sinus tachycardia (25%; CI 19.5 to 30.3) and S1Q3T3 (11%; CI 7.1 to 15.0), had very limited sensitivity in our patient sample. The most common ECG changes in our cohort included 1. T wave inversion in leads III and a VF (43%; CI 36.6 to 49.1), 2. T wave inversion in any 2 contiguous leads (53%; CI 46.8 to 59.3), 3. Atrial arrhythmias of any type (39%; CI 33.0 to 45.3), and 4. Slurred S waves in leads V1 and/ or V4 (38%, CI 32.2 to 44.5). Significantly, the associations became stronger as the size of the PE increased. Furthermore, saddle PE was significantly associated with a tall R wave >1.5mm in lead aVR (40%; CI 0.05 to 0.75).
Conclusion: By using the largest cohort of patients ever examined for ECG changes in acute PE, we showed that classic markers have limited utility in PE diagnosis. We propose novel ECG markers that have stronger predictive value for PE, and, when present, can also be suggestive of PE size.

CARDIOVASCULAR ASPECTS IN RENAL DISEASE

051

ASSOCIATION OF CORONARY ARTERY CALCIFICATION AND ARTERIAL MICRO-CALCIFICATION OF THE VASCULAR ACCESS IN INCIDENT HEMODIALYSIS PATIENTS

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Background: We have reported that arterial micro-calcification (AMC) of vascular access has a negative impact on access patency and cardiovascular mortality in hemodialysis (HD) patients. Reasons behind increased cardiovascular mortality in AMC are not fully understood, but it is believed that aortic stiffness is a major contributing factor. Whereas, coronary artery calcification (CAC) is quite common in HD patients and it is known as predictor of future cardiovascular events and all-cause mortality in HD patients. The aim of this study was to explore the relationship between AMC and CAC in HD patients.
Methods: 95 HD patients who received vascular access operation were included in this study. The AMC was diagnosed by pathologic examination of arterial specimen by von Kossa stain, which was acquired during the operation. All patients underwent a multi-detector computed tomography (MDCT) imaging procedure and coronary artery calcium score (CACS) was calculated. Patients were classified into two groups, according to the CACS, as high (>100), in 56 patients, and low (<100), in 39 patients. We compared AMC and several parameters between the patients with high and low CACS groups.
Results: Mean age was 65.4 +/- 12.7 years and the male gender was 63.2% (n=60). The incidence of AMC was 55.8% (n=53). The mean CACS was 456.7 +/- 697.2 and distributed from zero to 3880. Patients with high CACS group were older (69.6 +/- 9.5 vs. 59.4 +/- 14.1, p=0.007), and showed a significantly higher prevalence of diabetes mellitus (75.0% vs. 53.8%, p=0.027). High CACS group showed high incidence of AMC compared to low CACS group (71.4% vs. 33.3%, p<0.001). By binary logistic regression, AMC was independently associated with high CACS (OR: 4.228, 95% confidence interval [CI]: 1.513-11.817, p = 0.006).
Conclusion: The present study suggests that AMC is closely associated with CAC in incident HD patients.

052

INCREASE OF SEMAPHORIN 3C EXPRESSION IN POLYCYSTIC KIDNEY ACCOMPANIED BY ENDOTHELIAL-TO-MESENCHYMAL TRANSITION

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EndMT is a phenomenon that an endothelial cell loses its characteristic and acquires mesenchymal cell specific feature. It is known to be crucial for heart development. However, as it was found that EndMT was involved in the cardiac fibrosis, pathological effect of EndMT has not been identified in other organs. Polycystic kidney disease (PKD) is a genetic disease and accompanied by EndMT. However, regulatory mechanism between EndMT and PKD progression is not clear. In this study, we focused on Semaphorin 3C to elucidate mechanism of PKD development derived by EndMT. Specific markers for EndMT were quantified in various PKD mouse models. Also, expression of Semaphorin 3C level was validated in PKD mouse models and PKD patient. To confirm the effect of Semaphorin 3C on EndMT and polycystic kidney, specific disease markers were evaluated in Semaphorin 3C KD or OE cells. As a result, markers for EndMT were significantly changed in experimental mouse compared to control. Also, it was found that Semaphorin 3C expression was correlated to EndMT and PKD progression. In conclusion, we suggest that EndMT is the one of contributors to PKD progression, which is associated with dysregulated expression of Semaphorin 3C.

CARDIOVASCULAR QUALITY IMPROVEMENT AND OUTCOME

053

OBSERVATION UNIT CARE: A COMPARISON OF SPECIALIZED CARDIAC VERSES GENERALIZED OU DESIGN

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Given the escalating costs of medical care in the United States hospitals have faced significant pressure to reduce costs, particularly from unnecessary admissions and readmission of patients. One approach suggested to improve quality of care and reduce cost burden has been the Observation Unit (OU). The impact of OU care on specific patient groups, however, is a field not well studied. Our study aims to compare the resource utilization of a specialized Cardiac Care OU with a general medical OU. We reviewed charts for 83 patients in the CCOU and 295 GMOU at our tertiary care academic center (55% female, average age 56). Data was retrospectively collected on floor time, time of discharge, consults ordered, imaging studies, EKGs, and labs ordered. Mean total floor time was found to differ between the two groups, with CCOU averaging 34 hours and GMOU averaging 41 hours (p=.019). No difference was found in the discharge delay, or the time from discharge order to patient discharge (2.5hrs vs 2.7hrs for GMOU OU, p=.56). CCOU patients received more EKGs than GMOU patients (1.8 vs 1, p<.001). However, there was no difference in total resource utilization (labs, imaging studies, or consults ordered) between the two groups (8 vs 8.3, 1.5 vs 1.4, .6 vs .5, p>.05). Interestingly, 23% of CCOU patients and 28% of GMOU patients had no procedures, labs, or imaging studies conducted during the 12 hour overnight period prior to discharge. This could suggest that patients are unnecessarily waiting for a discharge order while medically ready for discharge. Additionally, shorter mean total floor time with equal resource utilization suggests that the specialized CCOU was more efficient at providing the same quantitative level of care. Further research into the impacts of specialized OU care is warranted to improve patient outcomes.

CARDIOVASCULAR QUALITY IMPROVEMENT AND OUTCOME

054

NEGLECTED GUIDELINES OF STAPHYLOCOCCUS AUREUS BACTEREMIA

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Introduction: Staphylococcus aureus is a leading cause of both community-acquired and healthcare-acquired bacteremia resulting in mortality. There are increasing concerns in health care community regarding the physician's compliance with recommended guidelines. Literature has suggested that with bundle management, there has been documented improved morbidity and mortality. Our study reveals increased mortality in patients diagnosed with staphylococcus aureus bacteremia and infective endocarditis.
Hypothesis: Staphylococcus aureus bacteremia predisposes patients to endocarditis, not following recommended guidelines predisposes to mortality and complications.
Methods: Retrospective chart review of hospital patients admitted from January 2011 to December 31 2012. Covariables which predisposed to infection were documented: age, sex, history of bacteremia or endocarditis, IV drug abuse, line infections, and an immunocompromised state. Our analysis consisted of 200 patients with primary outcome of endocarditis and secondary outcomes of use of repeat blood cultures, transthoracic echocardiograms, transesophageal echocardiograms, and infectious disease consults.
Results: 152/200 (76%) patients had repeat blood cultures, 122/200 (61%) patients received transthoracic echocardiograms, 48/200 (24%) patients received transesophageal echocardiograms, and 153/200 (76.5%) patients had infectious disease consults. Out of the 200 patients with MRSA bacteremia, 20/200 (10%) were diagnosed with endocarditis, 5/20 patients with endocarditis died revealing a 25% mortality rate. Overall, 24% of patients did not receive repeat blood cultures, 24% patients did not receive infectious disease consults, and 33% patients did not receive imaging (TTE/TEE). The national mortality of endocarditis is 18%, our hospital system revealed 25% mortality.
Conclusion: According to the IDSA guidelines of staphylococcus aureus bacteremia, transthoracic echocardiography is a class I A recommendation in all suspected cases of infective endocarditis. We recommend imaging in all suspected cases of infective endocarditis, involving infectious disease specialists, and repeating blood cultures to document clearance of infection. We hope that applying these guidelines, there is an opportunity to decrease mortality.

055

DIAGNOSTIC YIELD AND INFLUENCE ON MANAGEMENT OF ECHOCARDIOGRAPHY PERFORMED FOR EVALUATION OF SYNCOPE

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We investigated the utility of an echocardiogram performed on arrival in patients presenting to the ED with syncope and whether results would affect subsequent acute in hospital clinical management. Our study included 200 consecutive patients with transthoracic echocardiogram performed for evaluation of syncope. The study cohort consisted of 50% females, 38% current smokers, 60% with history of hypertension, 32% with CAD and 8% with prior MI, 6% with chest pain on admission, 22% with diabetes, 8% with history of heart failure, and 9% with prior CVA. All echocardiograms were performed at a single academic medical center for the primary indication of syncope. Echocardiographic findings changed the diagnosis and affected the management in 10.6% of cases. Discharge following the echocardiogram was twice as likely if the echocardiogram was unrevealing (35% vs. 16%, p=0.095). Bradycardia, complete heart block, or atrial fibrillation was noted in 36% of cases. Subsequent arrhythmias during hospital stay led to diagnosis change in 16 patients and of these, the echocardiogram was unrevealing in 75% of cases. Echocardiographic findings associated with change in management included cardiomyopathy (n=8), pulmonary hypertension (n=8), inter-atrial shunting (n=4), and RV dysfunction (n=4). Change in management was more likely in males (16% vs. 4% in females, p=0.008) and in patients with chest pain (16% vs 5%, p=0.06). The change was less likely in patients with history of CAD (5% vs. 13%, p=0.112) or CVA (0% vs. 11%, p=0.149). Thus, echocardiographic yield in the evaluation of syncope is modest and is significantly influenced by associated co-morbidities, arguing against protocol-driven routine use of echocardiography in all syncope patients. More studies of this important subject are warranted to better understand the role of echocardiography in the evaluation of syncope.

056

THE ECHOCARDIOGRAPHY APPROPRIATENESS USE CRITERIA PARADOX: MORE STUDIES FOR APPROPRIATE REASONS?

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Background: The use of inpatient echocardiography has increased dramatically in recent years. The impact of this increase in volume on the adherence to the echocardiography appropriate use criteria has not been well studied.
Material and Methods: Our pilot study involved a review of 529 medical charts and consecutive inpatient transthoracic echocardiograms performed at a single medium-sized academic medical center for the indications of coronary artery disease (CAD), congestive heart failure (CHF), and infective endocarditis (IE) to determine appropriateness based on 2011 appropriate use criteria (AUC).
Results: We have observed a significant rise in utilization of echocardiography for these indications. For congestive heart failure alone, there was an increase of 142% in February 2014 and 495% in July 2014 compared to the same months in 2010. Of 529 echocardiograms, 126 (23.8%) were for CHF, 23 (4.3%) for IE, 26 (4.9%) for CAD. A sample of 80 consecutive echocardiograms was reviewed and scored for appropriateness: 23 (29%) CHF, 28 (35%) CAD, and 10 (13%) IE. Nineteen (24%) cases were not scored due to limited information in the EMR. Overall, 58 (95%) cases were deemed appropriate.
Conclusions: Despite the dramatic increase in the utilization of echocardiography in recent years, for CHF, CAD, and IE, the vast majority of studies met appropriateness use criteria. Wider dissemination of AUC criteria may actually lead to a large number of appropriately ordered tests. Additional studies of this important subject are required.

CARDIOVASCULAR QUALITY IMPROVEMENT AND OUTCOME

057

HEART FAILURE SUPPORTIVE CARE CLINIC: DOES IT IMPROVE QUALITY OF LIFE?

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Objectives: To evaluate the Heart Failure Supportive Care (HeF) Clinic at St. Paul's Hospital in Vancouver, BC. The goal of the clinic, which opened in January 2011, is to assess and treat patients with advanced heart failure (HF) who have severe symptoms despite maximal medical therapy. We hypothesized that early referral to the HeF Clinic would improve quality of live (QOL) and decrease hospital admissions for decompensated HF.

Background: Heart disease is one of the leading causes of death in Canada and is associated with high morbidity and mortality, a negative impact on QOL, and high health care costs. However, too few patients with advanced HF are offered appropriate palliative care and few resources are directed to the palliative needs of those patients.

Methods: We conducted an observational descriptive study to validate the suggested clinical benefit of the HeF Clinic. Data was collected from the clinical reports of the clinic's patients. Outcome measures included Edmonton Symptom Assessment System (ESAS) scores and number of hospital admissions for HF.

Results and Conclusions: Approximately 75% of patients were NYHA Class III or IV. Patients' QOL as measured by ESAS was improved or stabilized in most patients (67% of patients had improved ESAS scores and another 11% had stable scores). Furthermore, of the 28 most recent patients, only 7 were admitted to hospital for decompensated HF. Most patients with HF can be effectively managed by their family physician, however, patients with severe symptoms and multiple co-morbidities may benefit from early referral to this clinic.

COMPUTERS IN CARDIOLOGY

058

NOVEL SIMULATION-BASED TRAINING IN CARDIOLOGY: TRAINEE FEEDBACK AND EVALUATION OF A PILOT STUDY

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Background: Simulation is used to enhance safety in non-medical and medical professions. Our unit has previously validated carotid simulation training. This paper presents initial trainee feedback for a novel course for cardiology.
Methods: Participants 33 cardiology trainees were recruited, from ST3 to advanced training levels.
Training Facility & Simulator Device: 7 pilot cases utilized the Imperial Distributed Simulation Concept. 26 sessions used the ORCamp suite (ORZone), comprising an integrated VR simulator (Mentice VIST®-C), simulated patient (trained actor) and multidisciplinary team.
Testing Format: Scenarios were allocated from a portfolio of 16 cases, commencing with case history, leading on to decision-making (e.g. type of procedure, tool selection), proceeding on to simulated complications/crises.
Evaluation Techniques: Participants rated the realism of the simulator and evaluated the training experience, including potential for implementation.
Statistical Analysis: Quantitative data was analysed using the Statistical Package for the Social Sciences (SPSS), Version 22.0.
Results: Demographics Twelve ST3's, eight ST4'a, six ST5's, five ST6, two interventional fellows.
Evaluation & Feedback
1. Realism of Simulator
Participants agreed that the simulated model is realistic (mean = 4.68, std. dev = 0.476 and useful for training interventionalists (mean = 4.76, std. dev = 0.523).
2. Evaluation of the Training Environment & Experience
Participants rated the experience positively in terms of replicating the workplace and pathway, for team training and as a format to assess workplace performance.
3. Potential for Training Implementation
Simulation was deemed most useful for crisis training and transfer to clinical practice.
Conclusion: Simulation training can be a helpful learning tool for cardiology trainees, successfully replicating serious and life-threatening scenarios encountered in the catheterization laboratory. This has the potential of improving patient safety by providing trainees with the necessary skills to manage such cases prior to hands-on experience with real patients.

059

IPHONE ACQUIRED HEART RHYTHM: IS IT RELIABLE FOR CLINICAL DIAGNOSIS?

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The purpose of this study was to validate the reliable use of an iPhone acquired heart rhythm for clinical diagnosis of cardiac arrhythmias to help make early diagnosis of cardiovascular diseases. Each patient underwent a conventional 12-lead ECG, and, within minutes, underwent a lead 1 ECG rhythm recording using the iPhone based AliveCor application; ECG interpreted by two cardiologists.

Out of 105 patients studied, 92 had normal sinus rhythm, 9 had atrial fibrillation, 2 had junctional rhythm, and 2 had paced rhythm by a 12 lead electrocardiograph. An 83.8 percent correlation, 14.3 percent indeterminate, and 1.9 percent different diagnosis rate from the AliveCor heart monitor compared to the 12-lead ECG was obtained. Out of 92 normal sinus rhythm cases, 88 percent correlation, 11 percent indeterminate, and 1 percent different diagnosis rate was obtained. Out of 9 atrial fibrillation cases, 67 percent correlation, 22 percent indeterminate, and 11 percent different diagnosis rate was attained.

The 16.2 percent of all cases that had either an indeterminate or inaccurate diagnosis from the AliveCor Heart Monitor indicate substantial technical errors, most commonly caused by the presence of baseline artifacts produced by a combination of movement, muscle tremor, and poor contact surface. My findings suggest the use of alcohol swabs and electrode gel on patient hands and AliveCor sensors limit baseline artifact.

After statistical analysis, values above a 95% confidence level for the Chi-squared method with the statistically significant p-value of less than 0.001, estimates of population prevalence, sensitivity, specificity, predictive values, and likelihood ratios, the study suggested the 83.8 percent correlation supports the hypothesis that an iPhone acquired heart rhythm can be used reliably for clinical diagnosis of cardiac arrhythmias. My findings suggest the AliveCor application can be used to recognize previously undiagnosed atrial fibrillation, allowing early initiation of anticoagulants to prevent stroke.

060

CLINICAL PERFORMANCE OF THE HEARTBUDS, AN ELECTRONIC SMARTPHONE LISTENING DEVICE, COMPARED TO FDA CLASS I AND CLASS II STETHOSCOPES

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Background: Auscultation with stethoscopes is essential to the physical exam. However, the stethoscope has not appreciably changed since Leared and Cammann developed the first binaural stethoscopes in the mid 1800s. Because of technological advances, it is possible to use smartphone technology to auscultate patients, and the HeartBuds, a listening device that integrates with an iPhone app to achieve this purpose. The purpose of this study was to compare HeartBuds' acoustic superiority over the FDA approved class I blue disposable stethoscopes, which are commonly used in practice to reduce hospital infection rates, and demonstrate equivalence to the gold standard FDA class I analog stethoscope, the Littmann Cardiology III, and the FDA class II digital stethoscope, the Littmann Electronic 3200.
Methods: 50 patients were auscultated with the above-mentioned stethoscopes. Two examiners independently used these stethoscopes and rated their acoustic quality in addition to filling out surveys documenting body sounds heard.
Results: The disposable stethoscope was significantly worse at identifying cardiac murmurs ($p<0.002$), and performed poorly when auscultating for carotid bruits ($p<0.058$). The HeartBuds was equivalent to its more commonly used counterparts, the Littmann Cardiology III and the Littmann Electronic 3200. Examiners also found it to be of comparable acoustic quality to these models.
Conclusion: HeartBuds is a smartphone compatible listening device that was superior in examining cardiovascular sounds to approved FDA Class I disposable stethoscopes, and equivalent to FDA approved class I and class II Littmann stethoscopes. Considering HeartBuds equivalence to more expensive stethoscopes while costing much less, the HeartBuds can potentially reduce infection rates without sacrificing quality. This can be achieved all while reducing healthcare costs, which begs the question whether healthcare providers should rethink using the device they have grown used to hanging around their necks.

061

VIEWING HEART FAILURE AS INTERSTITIAL CANCER: DIAGNOSTIC AND THERAPEUTIC AVENUES

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In contrast to public perception, the morbidity and mortality as well as the resultant health care costs associated with chronic heart failure (HF) are increasing and arguably reaching epidemic proportions, but improvements in diagnostic and therapeutic strategies for this disease have not been forthcoming. The factors that contribute to this relative paucity of new clinical tools for HF are multifactorial but likely include the need to recognize and differentiate HF phenotypes and to move beyond conventional thought regarding biological pathways, which regulate myocardial growth and function. To that end, there are many lessons that can be learned from research in the cancer field that are potentially translatable to the HF process. For example, the most numerous cell type in the heart is the fibroblast, and with HF, this cell type undergoes a differentiation process not dissimilar to that of cancer metastasis. Specifically, HF myocardial fibroblasts express transcriptional and protein markers similar to those observed in a process of mesenchymal-epithelial transformation described in cancer. Moreover, this laboratory and others have identified proteolytic enzymes which degrade the tissue space - the extracellular matrix (ECM) emerges in both patients and animal models of HF. The aims of this presentation will be 3-fold. First, examine and identify the phenotype classifications of clinical HF and relate these phenotypes to abnormalities in ECM and fibroblast growth and function. Second, present basic and translational studies regarding fibroblast transformation in HF and pathways that may form therapeutic targets, which may actually parallel chemotherapeutic strategies. Third, present new studies regarding novel molecular imaging approaches and therapeutics for HF.
The conclusion to be drawn is that new findings in cancer research can be translated to target the transdifferentiated fibroblast in HF as a form of interstitial cancer.

062

BENDAVIA (MTP-131), A MITOCHONDRIA TARGETING PEPTIDE, NORMALIZES DYSREGULATION OF MITOCHONDRIA FISSION AND FUSION PROTEINS IN MYOCARDIUM OF DOGS WITH CHRONIC HEART FAILURE

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Introduction: Studies of mitochondria (MITO) ultrastructure in heart failure (HF) reveal considerable structural abnormalities along with marked hyperplasia and reduced organelle size. MITO are highly dynamic organelles whose morphology, distribution and activity is regulated by fission and fusion proteins that are also dysregulated in HF. We previously showed that chronic therapy with Bendavia (BEN, MTP-131), a novel mitochondria-targeting peptide, improves LV function in dogs with HF and normalizes MITO respiration and rate of ATP synthesis.
Objective: In this study, we tested the hypothesis that chronic therapy with BEN in dogs with HF can reverse the dysregulation of MITO fission proteins (Fission-1, Fis1 and Dynamin-Related Protein-1, Drp1) and fusion proteins (Mitofusin-2, Mfn2 and Dominant Optic Atrophy-1, OPA1) in LV myocardium.
Methods: 14 HF dogs were randomized to 3 months therapy with subcutaneous injections of BEN (0.5 mg/kg once daily, HF+BEN, n=7) or saline (HF-Control, n=7). LV tissue was obtained from all dogs at end of therapy and from 6 normal (NL) dogs for comparison. Protein level of Fis1 and Drp1 and of Mfn2 and OPA1 was measured with specific antibodies using Western blotting. In addition Porin, a MITO protein that is unaltered in HF, was also measured as internal control and all bands were quantified in densitometric units (du).
Results: Porin level was unchanged among the 3 study groups. Compared to NL, levels of Mfn2 and OPA1 were significantly reduced, and levels of Fis1 and Drp1 were significantly increased in HF-Controls. BEN restored protein levels of OPA1, Mfn2, Fis1, and Drp1 to near normal.
Conclusions: Long-term therapy with BEN reversed the dysregulation of MITO fission and fusion proteins in LV myocardium of dogs with HF. These findings support the observations of improved MITO respiration and rate of ATP synthesis and the improved LV function seen in dogs with HF after chronic treatment with BEN.

063

GENE-TARGETING OF NATRIURETIC PEPTIDE RECEPTOR-A ENHANCES THE EXPRESSION OF RAAS COMPONENTS LEADING TO INFLAMMATORY HYPERTENSIVE HEART DISEASE

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Atrial natriuretic peptide (ANP) was discovered over 30 years ago in the atrium of heart and has been extensively investigated with regard to physiology, pathophysiology, and cardiovascular disease therapeutics. ANP and brain natriuretic peptide (BNP) bind to guanylyl cyclase-A/natriuretic peptide receptor-A (GC-A/NPRA), which produces the intracellular second messenger cGMP and exhibit diuretic, natriuretic, and vasorelaxant effects with novel properties, including antihypertrophic, antifibrotic, antiproliferative, and antiinflammatory actions with a pivotal role in cardiovascular remodeling. GC-A/NPRA signaling antagonizes the cellular and physiological effects mediated by the renin-angiotensin-aldosterone system (RAAS). Genetic disruption of Npr1 (coding for GC-A/NPRA) increases 35-40 mmHg higher systolic blood pressure and a 63% greater heart weight/body weight (HW/BW) ratio leading to congestive heart failure in null mutant (Npr1-/-) mice compared with wild-type (WT; Npr1+/+) mice. The expression levels of angiotensin-converting enzyme (ACE) and angiotensin II type 1a receptor (AT1a) mRNA were increased by 4- to -5fold in Npr1-/- mice hearts compared with the WT mice hearts. The cardiac angiotensin II and aldosterone levels were also significantly increased in Npr1-/- mice than WT controls. Concomitantly, the expression of interleukin-2 (Il-2), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), and transforming growth factor-β1 (TGF-β1) were also increased by 4- to 5-fold, in null mutant mice hearts as compared with WT mice. The expression of nuclear factor-kappa B (NF-kB) and its binding activity in the nuclear extracts of Npr1-/- mice hearts was increased by 3- to 4-fold compared with WT mice. Treatment with captopril or hydralazine equally reduced the blood pressure, but only captopril significantly decreased the HW/BW ratio and proinflammatory cytokine gene expression in Npr1-/- mice hearts. The results suggest that the disruption of ANP/NPRA/cGMP signaling leads to augmented expression and activation of RAAS-mediated signaling pathways that enhance the expression of proinflammatory cytokines and promote cardiac hypertrophy, dysfunction, and heart failure.

064

ALTERED NUCLEAR AND CYTOSKELETAL MECHANICS IN CARDIAC MYOCYTES WITH D192G NUCLEAR LAMIN MUTATION

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Atomic force microscopy whole-cell loading/unloading curves were used to study the mechanical behavior of cardiomyocytes carrying the LMNA D192G mutation which is known to cause a severe form of dilated cardiomyopathy. Here, combining atomic force microscopy (AFM) with molecular and cellular biology methodologies, we studied both nuclear and whole-cell biomechanical behavior in Neonatal rat ventricular myocytes (NRVMs) expressing the LMNA D192G mutation and compared this with both control cells and those expressing wild-type LMNA. LMNA protein expression was confirmed up to day 6. Live-cell AFM force-deformation curves from days 1 through 6 showed that LMNA D192G nuclei displayed increased stiffness compared to controls with a peak at 72 hours ($p < 0.05$), with a 3 time increase in nuclear Young modulus. Furthermore, mutant NRVMs showed an unexpected reduction in the adhesion area between AFM probe and cell membrane compared to control and wild-type. Finally, D192G NRVMs displayed altered cytoskeletal deformation measured as force decays with time (relaxation force test) compared to wild-type and control NRVMs, suggesting loss of cytoskeleton elasticity. The altered mechanical behavior of LMNA D192G NRVMs was rescued by wild-type LMNA expression in mutant cells. Our results suggest that the LMNA D192G mutation has a profound effect on the whole-cell biomechanics in cardiomyocytes, extending beyond the increased nuclear stiffness, indicating cytoskeletal structural modifications and reduced cell membrane adhesion, changes that can be rescued by wild-type LMNA. These findings extend our understanding of the pathophysiology of this, and perhaps other, gene-specific causes of cardiomyopathy and provide a cell-based assay for their analysis and potential novel therapies.

065

MOLECULAR REGULATION OF DOXORUBICIN INDUCED HEART FAILURE

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Doxorubicin is known for its cardiotoxic effects and inducing cardiac failure, however, the underlying mechanisms remain cryptic. Earlier we established the inducible - death protein, Bcl-2-like Nineteen- Kilodalton- Interacting - Protein 3 (Bnip3) to be crucial for disrupting mitochondrial function and inducing cell death of cardiac myocytes. Whether Bnip3 underlies cardiotoxic effects of doxorubicin toxicity is unknown. Herein we demonstrate a novel signaling pathway that functionally links activation and preferential mitochondrial targeting of Bnip3 to the cardiotoxic properties of doxorubicin. Perturbations to mitochondria including increased calcium loading, ROS, loss of mitochondrial membrane potential and mPTP opening were observed in cardiac myocytes treated with doxorubicin. In mitochondria, Bnip3 forms strong association with Cytochrome c oxidase subunit1 (COX1) of respiratory chain and displaces uncoupling protein 3 (UCP3) resulting in increased ROS production, decline in maximal and reserved respiration capacity and cell viability. Impaired mitochondrial function was accompanied by an accumulated increase in autophagosomes and necrosis demonstrated by increase release of LDH, cTnT and loss of nuclear High Mobility Group Protein 1 (HMGB-1) immunoreactivity. Interestingly, pharmacological or genetic inhibition of autophagy with 3-methyl adenine (3-MA), or Atg7 knock-down suppressed necrotic cell death induced by doxorubicin. Loss of function of Bnip3 restored UCP3-COX complexes, mitochondrial respiratory integrity and abrogated necrotic cell death induced by doxorubicin. Mice germ-line deficient for Bnip3 were resistant to doxorubicin cardiotoxicity displaying normal mitochondrial morphology, cardiac function and survival rates comparable to vehicle treated mice. The findings of the present study demonstrate that doxorubicin provokes maladaptive autophagy and necrotic cell death of ventricular myocytes that is mutually dependent and obligatorily linked to Bnip3.

066

CALCIUM SIGNAL, TRANSCRIPTION AND DCM

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Cytosolic calcium levels critically determine and contraction/relaxation cycle of cardiomyocytes. The calcium signals also regulate cardiac cell growth through gene/protein expression. The calcium signal is translated through calcium binding proteins and phosphorylation mechanisms at the level of the contractile machinery and the cardiac genome. In particular a family of protein kinases (PKs) activated by calcium and calmodulin (CaM) has been shown to translate the calcium signal to promote cardiac growth and modulate contractile state. Data on the distinct members of the calmodulin activated protein kinases and how there activity impacts cardiac dysfunction, ventricle dilation and growth will be discussed with a view to design novel therapy.

067

THE ROLE OF MICRORNAS IN PERIPARTUM CARDIOMYOPATHY

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Peripartum cardiomyopathy (PPCM) causes considerable morbidity and mortality in young women during their reproductive years. The presentation is usually in the month preceding delivery up to 5 weeks post-partum. This overview will address some of the new developments in the field of molecular medicine using micro RNAs for diagnosis and also as therapeutic targets. In normal pregnancy reactive oxygen species increases ROS production reverting to normal levels in the post-partum period .However the total anti-oxidant capacity also increases during pregnancy and continues to be elevated post-partum. Studies on mice with Stat3 deletion have revealed the link between oxidative stress and prolactin. The increase in reactive oxygen species (ROS) in this murine model was associated with cleavage of the hormone prolactin (PRL) by ROS-activated Cathepsin D. These mice showed increased expression/activity of cathepsin D associated with the generation of a cleaved antiangiogenic and proapoptotic 16 kDa form of prolactin. Bromocriptine prevented PPCM in the STAT3 deleted mice. The 16 kDa form of prolactin impaired the cardiac capillary network and function in the myocardium resulting in the cardiac phenotype of PPCM. The micro RNA mir146-a has been implicated in the regulation of the prolactin signaling pathway. The 16K prolactin fragment exerts negative effects in endothelial cells by up regulating miR-146a. Additionally mir-146a levels were increased in patients with PPCM which resolved after treatment with bromocriptine possibly defining the role of prolactin in the pathophysiology of PPCM.

068

ARRHYTHMIAS IN ADULT CONGENITAL HEART DISEASE

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There are now more adults living with congenital heart disease (CHD) than children with CHD, due to the remarkable improvements in medical, interventional, and surgical care of these complex patients. However, despite increased survival and longevity, the long-term hemodynamic abnormalities and suture lines leave these patients with substantial electrophysiological sequelae. The vulnerability to sinus and atrioventricular nodal dysfunction increases risk of eventual need for permanent pacing, while atrial and ventricular tachyarrhythmias may develop due to the underlying anatomic substrates, which may lead to the need for catheter ablation procedures and/or implantable cardioverter defibrillators. Systemic ventricular dysfunction may also be treated with cardiac resynchronization pacing. These electrophysiologic interventions may require special circumstances and unique treatments due to variations in venous and cardiac anatomy. For example, transvenous access may not be feasible for adults with CHD who have interrupted vena cava, single-ventricle Fontan physiology, or other congenital anomalies or surgically-acquired obstructions. Unique routes of implantation may be necessary for placement of pacemakers, defibrillators, and resynchronization leads. Epicardial access may also be challenging, due to prior cardiac surgeries, adhesions, and congenital anomalies. Therefore, novel approaches and hybrid procedures may be indicated for electrophysiological interventions in adults with congenital heart disease. These procedures should be performed at regional expert centers of adult CHD care, by electrophysiologists experienced in congenital heart disease. Knowledge of the detailed anatomy and surgical procedures is necessary to fully understand the nuances of performing these procedures, and pre-intervention imaging is helpful to delineate the electrophysiologic procedural plan. Despite the additional complexities, with proper planning and collaboration, an experienced adult CHD team can provide excellent electrophysiological outcomes.

069

THE 2014 AF GUIDELINES: WHAT'S NEW?

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The 2014 AHA/ACC/HRS Guidelines for the management of patients with atrial fibrillation (AF) are derived from published clinical trials, basic science, and comprehensive review articles. They supersede the ACC/AHA/ESC 2006 Guidelines and two subsequent focused updates from 2011. Key new recommendations impacting patient care are: 1) usage (Class I) of the CHA2DS2-VASc score to assess risk of stroke in patients with nonvalvular AF; 2) usage (Class I) of oral anticoagulation (warfarin, dabigatran, rivaoxaban, or apixaban) for patients with nonvalvular AF with a history of stroke, transient ischemic attack, or a CHA2DS2-VASc score of 2 or greater; 3) omission (Class IIa) of antithrombotic therapy for patients with nonvalvular AF and a CHA2DS2-VASc score of 0; 4) for patients with nonvalvular AF and a CHA2DS2-VASc score of 1, choice (Class IIb) of no antithrombotic therapy, oral anticoagulation, or aspirin; 5) avoidance (Class III harm) of dabigatran, rivaroxaban, or apixaban for patients with AF and a mechanical or bioprosthetic heart valve; 6) avoidance of flecainide, propafenone, dofetilide, and sotalol in patients with severe left ventricular hypertrophy and AF; 7) prescription (Class I) of oral anticoagulation for patients with hypertrophic cardiomyopathy and AF irrespective of CHA2DS2-VASc score; 8) catheter ablation is useful (Class I) for patients with symptomatic, paroxysmal, AF who have not responded to or tolerated antiarrhythmic medications; and 9) catheter ablation is reasonable (Class II) in selected patients with symptomatic, paroxysmal, AF prior to a trial of medical therapy, provided it can be performed at an experienced center.

070

GLOBAL ATRIAL FIBRILLATION BURDEN: PREVENTION RATHER THAN TREATMENT MUST BE THE GOAL!

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The estimated number of individuals with AF globally in 2010 was 33.5 million (20.9 million men] and 12.6 million women. Burden associated with AF, measured as disability-adjusted life-years, increased by 18.8 in men and 18.9% in women from 1990 to 2010. In 1990, the estimated age-adjusted prevalence rates of AF (per 100 000 population) were 569.5 in men and 359.9 in women. Mortality associated with AF was higher in women and increased by 2-fold and 1.9-fold in men and women, respectively, from 1990 to 2010. There was evidence of significant regional heterogeneity in AF estimations. The incidence of atrial fibrillation is twice as high in developed countries compared to the developing countries. The increase of AF incidence was 70% in the developed countries compared to only 11 % in the developing countries.
There are several risk factor for atrial fibrillation which could be influenced: obesity, diabetes, hypertension, inflammation, and sleep apnea. Weight reduction and cardiometabolic risk factor management can reduce the burden of atrial fibrillation. In addition the recurrence rate could be reduced with an intensive cardiometabolic risk factor management either after pharmacological treatment or after catheter ablation of AF
C*onclusion:* These findings provide evidence of progressive increases in overall burden, incidence, prevalence, and AF-associated mortality between 1990 and 2010, with significant public health implications. Cardiometabolic risk factor management can further reduce the burden of atrial fibrillation in addition to conventional treatment options.

071

HYBRID ATRIAL FIBRILLATION FOR ADVANCED ATRIAL FIBRILLATION

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Atrial fibrillation (AF) is the most common sustained arrhythmia and is associated with a nearly five-fold increased risk for stroke as well as over two-fold increased risk of death. For symptomatic drug-refractory AF, percutaneous ablation has been used with good success in paroxysmal AF. For patients with persistent AF, the results of catheter ablation are not very good. Surgical AF using minimal-invasive approaches may be offered to this cohort. We analyzed our data in thoracoscopically-performed ablation of AF on the beating heart, and found this to be technical feasible, achieving high success rates with low procedure-related morbidity in early follow-up.
The next frontier in treatment of atrial fibrillation is hybrid atrial fibrillation. This is the most aggressive and arguably the most effective approach in advanced AF. The patient undergoes initially a thoracoscopic Maze with complex left atrial lesion set. At three months, an EP evaluation of the left atrial lesions are performed, and additional lesion performed as needed. Furthermore, the right-sided isthmus lesion is performed. The results of the hybrid approach are discussed along with on-going DEEP trial investigating global outcome with hybrid Maze.

072

LEFT VENTRICULAR REVERSE REMODELING WITH BIVENTRICULAR VERSUS RIGHT VENTRICULAR PACING IN PATIENTS WITH ATRIOVENTRICULAR BLOCK AND LEFT HEART FAILURE IN THE BLOCK HF TRIAL

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Background: In patients with heart failure (HF), biventricular pacing (BIV) attenuates adverse left ventricular (LV) remodeling in addition to improving survival and relieving symptoms. However, little is known about the effects of BIV pacing in HF patients with atrioventricular (AV) block.
Methods: The BLOCK HF trial randomized patients with AV block, NYHA class I-III heart failure, and LV ejection fraction (EF) less than or equal to 50% to BIV or right ventricular (RV) pacing. Doppler echocardiograms (DE) were obtained at randomization (30-60 days post-implant) and at 6, 12, 18, and 24 months. Data analysis comparing changes in 10 pre-specified echo parameters over time was conducted using a Bayesian adaptive design and all objectives were evaluated with intention-to-treat analyses. *Results*: There were 624 subjects among the 691 randomized subjects who had paired DE data for one or more analyses. LV volumes, EF, diastolic function and intra-ventricular mechanical delay (IVMD) were estimated at all time points. BIV pacing resulted in LV reverse remodeling, with significant reduction in LV end systolic and end diastolic volume indices and in IVMD and improvement in EF. By contrast, none of these parameters changed with RV pacing, indicating that no reverse remodeling occurred post-randomization.
Conclusions: Patients with AV block, depressed LV function, and HF symptoms benefit from BIV pacing with regard to cardiac structure and function. This DE analysis has important clinical implications in supporting the use of BIV pacing rather than RV pacing for patients with HF and AV block.

073

SYNCOPE VS PSEUDOSYNCOPE: DIFFERENTIATION, DIAGNOSIS AND TREATMENT

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Background: Syncope is common in the pediatric population. Pseudosyncope (PS) can be difficult to distinguish from classical syncopal episodes. Head-up tilt table (HUTT) has been employed as a diagnostic test for PS in adults; however, its use in the pediatric population is currently not described. The purpose is to describe the diagnostic utility of HUTT to elicit the diagnosis of PS in the pediatric population.
Design/Methods: A retrospective chart review from 11/12 to 10/14 of all patients less than 23 yrs of age referred for HUTT, consisting of a 30-minute, 80-degree HUTT with continuous monitoring of ECG and pulse ox. Blood pressure and heart rate were obtained supine, at 80-degree tilt, and every minute. Symptoms were recorded with vital signs taken concurrently.
Results: 51 patients were referred for HUTT [median age 16 yrs (5-23); 13 (25%) male]. The majority (27, 53%) had a negative HUTT , 24 had a positive HUTT, (vasovagal 13, postural orthostatic tachycardia syndrome 4, and idiopathic 3 . The remaining 4 (17%) were diagnosed with PS [median age 16 yrs (15-17); 1male]. Pretest probability for PS was high 1) failed appropriate management, 2) atypical episodes, 3) occurrence during exercise, or 4) prolonged duration. Due to high suspicion, prior to HUTT the likelihood of episode was discussed with patient. Episodes of PS occurred: 2 had PS within 2 minutes and 2 had episodes > 15 minutes into HUTT. PS was verified by normal vital signs and disruptive maneuvers: verbal response to questions, hand clap, sternal rub.
Conclusions: PS should be considered in patients that have failed appropriate management or who exhibit atypical episodes of syncope. PS can be identified with a HUTT if specific prompting of patients is utilized. Disruptive maneuvers, hand clap, sternal rub, etc., are excellent adjuncts to confirm diagnosis.

074

SUCCESS OF ATRIAL FIBRILLATION ABLATION IN VARIOUS SUBSETS

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Atrial fibrillation is an increasingly common clinical problem as the age of the population in North America has significantly increased. Medical therapy in terms of stroke prevention is improving. However, rhythm restoration is undergoing significant research and evolution. Medications to restore sinus rhythm have been minimally effective and therefore, invasive strategies such as percutaneous ablation have become increasingly common. Percutaneous ablation is seems to be more effective in certain sub groups such as shorter duration of disease, no structural heart disease and no significant valvular heart disease. Identifying success of the ablation in various sub groups is critical for good clinical outcome.

075

ZHANG'S PHENOMENON (HIS ELECTROGRAM ALTERNANS) AND A NEW MODEL OF ATRIOVENTRICULAR NODE DUAL PATHWAY CONDUCTION

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Zhang's phenomenon (originally His electrogram alternans), a new index of dual pathway atrioventricular (AV) node conduction, indicates that there are dual inputs rather than a final common pathway from the AV node into the His bundle. Our recent data revealed that during fast pathway (FP) conduction, the electrical excitation in the AV node propagates in a superior to inferior direction across the AV conduction axis. In contrast, this superior-inferior activation fails within the superior nodal domain during slow pathway (SP) conduction. This then permits electrical excitation to proceed longitudinally along the AV conduction axis through the inferior nodal domain. This transverse versus longitudinal electrical propagation in the AV node produces superior-fast and inferior-slow dual inputs into the His bundle during dual pathway conduction (the electrophysiological basis of Zhang's phenomenon). We believe that the peculiar anatomical location and fiber orientation of the AV node are mainly responsible for the unique electrical conduction pattern. The AV node is open only superiorly and posteriorly to atrial excitation. Fibers inside the AV node are largely aligned longitudinally along the AV conduction axis. Electrical propagation across fiber orientation (in a superior to inferior direction) is possible during FP conduction. However, this cross-fiber activation results in a longer effective refractory period and, thus, this activation will fail at short prematurities (i.e., SP conduction). Longitudinal activation along the fiber orientation results in a short effective refractory period. The failing of superior-inferior activation permits excitation to proceed along fiber orientation in the inferior nodal domain during SP conduction (i.e., at short prematurities). In summary, the transverse versus longitudinal electrical propagation within the AV node, the resulting functional dissociation in the distal node, and the superior-fast and inferior-slow dual inputs into the His bundle form the main features of the new model of dual pathway AV conduction.

076

LONG TERM OUTCOMES OF SURGICAL AF ABLATION: ASSESSMENT OF EFFICACY USING IMPLANTABLE CARDIAC MONITORS

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Background: Pulmonary Vein Isolation (PVI) is an effective treatment in recurrent atrial fibrillation (AF). However, no consensus exists on the definition of PVI success. Existing data are limited to intermittent holter or event recordings with reliance on patient symptoms.
Objective: We sought to determine the outcomes of surgical PVI and post ablation AF surveillance with implantable cardiac monitors (ICM) (Reveal XT, Medtronic Inc.). *Methods*: We designed a prospective study using ICM with an inherent algorithm for automatic recognition and detection of AF post PVI and followed patients to assess the natural course of AF recurrence. AF recurrence was defined as weekly AF burden > 5% as recorded by the ICM within a 3 month rolling window. Consecutive 65 patients underwent limited thoracotomy, video assisted epicardial PVI, were implanted with cardiac monitors and were followed. Data was downloaded weekly using CareLink® system. All transmitted events were analyzed for arrhythmias.
Results: 65 patients were followed after PVI for a mean of 27 ± 2 months. AF recurrence was highest in first 3 months (68%) and substantially decreased over 12 months (22%) post PVI. However, late AF recurrence was common. Overall freedom from AF recurrence at follow-up completion (27 months) was 48%.
Conclusions: Our study is unique in using ICM after ablation to obtain an objective measurement of success. Late recurrence of AF is common but not associated with symptoms in a significant percentage of patients. ICM should be considered standard for future studies aimed at defining success of AF ablation procedures.

ASSESSMENT AND MANAGEMENT OF CARDIOVASCULAR RISK / MODIFICATION OF LIPOPROTEINS

077

LIFE-EXPECTANCY DIFFERENCES BETWEEN OLYMPIC HIGH JUMPERS AND DISCUS THROWERS

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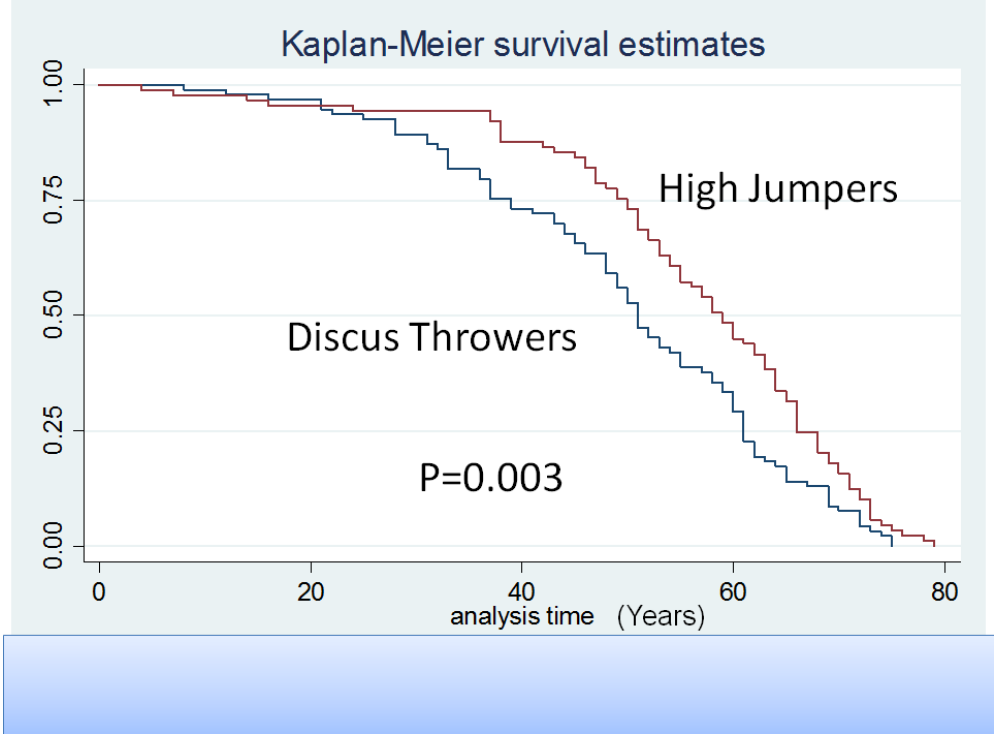
Background: Several studies have demonstrated that body habitus is associated with survival. We sought to determine if survival differed between elite ectomorph (high jump) and mesomorph (discus) athletes.
Methods: For each Olympics between 1924 and 1948 we identified the top (up to 20) Olympic male and female finishers in the high jump (HJ) and the discus. We determined date of death using internet searches and calculated age-specific expected survival using published US life tables. We adjusted life-expectancy for country of origin based on Global Burden of Disease data.
Results: We identified a death date for 182 of 224 (81%) Olympic athletes (61 male HJ, 59 male discus, and 32 female HJ, 30 female discus). Discus throwers were older during the Olympics by a mean of 2.8 ± 0.6 years, p<0.0001), heavier by 33 ± 4 lbs, p<0.0001, and taller by 0.9 ± 0.4 inches, p=0.04. Survival was higher for HJ (**Figure**). Observed-expected survival was 8.9±14.8 years for HJ and 5.0±13.5 years for discus athletes (p=0.06). In multivariate analysis, mortality was lower for HJ compared to discus throwers (HR 0.64, 95% CI 0.46-0.88, p=0.006) after adjustment for age, year of Olympics, and gender. However, after additional adjustment for weight, the effect of HJ was no longer significant (HR 0.89, 95% CI 0.56-1.40, p=0.61).
Conclusion: We found that elite high jumpers live longer than elite discus throwers, and this is explained in large part by body habitus (weight).



078

CHOLESTEROL GOALS & TARGETS: SHOULD WE IMPROVE-IT?

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Appropriate intensity statins are recommended by the ACC/ AHA Blood Cholesterol Guidelines as first line lipid therapy for both high risk secondary prevention patients with established atherosclerotic cardiovascular disease (ASCVD) and post-acute coronary syndrome (ACS). The IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) is the first randomized prospective clinical outcomes trial to demonstrate that stain therapy plus a non-statin agent (ezetimibe) reduced ASCVD events (6.4% relative risk reduction of the primary composite endpoint). It is likely this study will impact future guideline recommendations. Despite established benefits of statin therapy for secondary prevention there appears to be substantial underutilization of well-validate guideline-directed therapies, and a significant lack of medication adherence. Strategies to assess gaps in care delivery, improve awareness of guideline-driven recommendations, and patient adherence to therapies may be more important ways to IMPROVE-IT.

079

THE EFFECTS OF PLANT-BASED, MEDITERRANEAN, PALEOLITHIC, AND DASH DIETS ON CARDIOVASCULAR DISEASE RISK

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Background: Cardiovascular disease (CVD) is the leading cause of death in the United States for middle-aged men and women despite the fact that prevention and control of CVD is achievable by modifying risk factors through lifestyle changes and diet therapy. We examined the impact of four diet programs (plant-based (Vegan), Mediterranean, Paleolithic (Paleo) and DASH diets) on the CV risk factor profile of adults in the Hampton Roads area of Virginia.
Methods: Nondiabetic adults (ages 35-85) with one or more risk factors for CVD were invited to participate in 1 of the 4 diet arms. Participants underwent a comprehensive nutrition education program prior to 60-day diet intervention in which they kept daily food logs and met weekly with a multi-disciplinary study team. An initial health screen was performed to assess weight, blood pressure (BP), fasting glucose (FPG), A1C, lipids and lipoprotein particles, and repeated after 60 days on the diet and at 6-months follow-up.
Results: 279 subjects completed the 60-day dietary intervention (58 Vegan, 80 Mediterranean, 76 Paleo, 65 DASH), and 199 returned for 6-month follow-up. Most subjects were female, Caucasian, mean age 56, mean BMI 33 kg/m2. At baseline, mean FPG, TG and HDL-C were within the normal range, whereas LDL-P and BP were elevated. After 60 days on the respective diets, subjects lost an average of 9 lbs (4.7% body weight, total 2,576 lbs), which was associated with improvements in BP across all groups. Subjects on the Vegan and Paleo diets lost the most weight (6.5%) and showed the greatest improvement in lipid risk factors (11-14% decrease in LDL-P; 10-20% decrease in VLDL and TG).
Conclusion: All four diets promoted weight loss and improved BP but had variable effects on lipid risk factors. Effects were greatest and sustained in those subjects that attended regular diet support group meetings.

ASSESSMENT AND MANAGEMENT OF CARDIOVASCULAR RISK / MODIFICATION OF LIPOPROTEINS

080

QUANTIFYING THE ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND CARDIOVASCULAR DISEASE: A META-ANALYSIS

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Background and objective: The relationships between physical activity (PA) and cardiovascular disease (CVD) have predominantly been estimated using categorical measures of PA. In this systematic review and meta-analysis we derive a single continuous physical activity metric to directly compare the association between activity and CVD, both before and after adjustment for a measure of body weight.

Data sources: A systematic review was conducted through searching electronic databases such as MEDLINE and EMBASE for studies published between 1981 and 2014.

Study eligibility criteria and participants: Prospective cohort studies were included that measured PA levels where at least two of the following domains were measured: leisure, active travel and occupational activity. The relative risk needed to have been reported in healthy individuals and been adjusted for a measure of body weight. The PA exposure in each study was converted to MET hours per day. Various transformations were explored to parametrically describe the dose-response relationships, as well as a non-parametric categorical approach.

Results: A total of thirty-six studies were included in the analysis. An increase from inactive to achievement of recommended PA levels 150 minutes of moderate-intensity aerobic activity reduced the risk of CVD mortality by 23% and CVD incidence by 17% (RR 0.77 (0.71-0.84) and (RR 0.83 (0.77-0.89) respectively, after adjustment for body weight. Overall, there were a total of 3,439,874 participants, with 179,393 events occurring during an average follow up period of 12.3 years.

Conclusions: and implications: A single continuous metric for PA levels allowed us to directly compare the effect of physical activity on CVD incidence and mortality including myocardial infarct (MI), coronary heart disease (CHD) and heart failure. Effect sizes suggested that the greatest gain in health is associated with moving from inactive to small amounts of physical activity.

ASSESSMENT AND MANAGEMENT OF CARDIOVASCULAR RISK / MODIFICATION OF LIPOPROTEINS

081

ASPIRIN FOR PRIMARY PREVENTION OF CARDIOVASCULAR AND ALL-CAUSE MORTALITY: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Objectives: To assess the safety and impact of aspirin on cardiovascular outcomes in primary prevention.
Background: The use of aspirin in primary prevention without established coronary heart disease is still controversial. We performed a meta-analysis of randomized controlled trials (RCTs) comparing Aspirin to placebo for the primary prevention of cardiovascular events and mortality.
Methods: We searched PubMed, Medline, Embase and Cochrane for RCTs that compared Aspirin versus placebo in patients without established coronary artery disease. Trials that included patients with or without cardiac risk factors who were randomized to either Aspirin or placebo and that reported at least one of the studied outcomes were included. Study quality was assessed using the Jadad score. Heterogeneity of the studies was analyzed by Cochran's Q statistics. Mantel Haenszel relative risk and mean difference were calculated using the random effect model.
Results: Ten RCTs met our inclusion criteria and included 113900 patients with hypertension, dyslipidemia, tobacco smoking, or diabetes mellitus. The use of Aspirin was associated with lower non-fatal myocardial infarctions (MI) when compared to placebo (RR 0.79; 95% CI 0.64 –0.97; P=0.03). No significant difference in the incidence of fatal MI (RR 0.99; 95% CI 0.75 –1.29; P=0.92) or cardiovascular mortality (RR 0.95; 95% CI 0.83 –1.08; P=0.42) was observed between the two groups. There was an increase in the overall bleeding with the use of aspirin compared to placebo. (RR 1.33; 95% CI 1.16 –1.53; P<0.001). Lower all-cause mortality was noted in the Aspirin group compared to placebo (RR 0.94; 95% CI 0.89 –1.00; P=0.04).
Conclusions: Our findings suggest that the use of Aspirin in primary prevention is associated with a reduction in non-fatal MI and all-cause mortality at the cost of increased risk of bleeding. The use of aspirin should be made on a case-by-case basis.

082

RISK OF MYOCARDIAL INFARCTION AND STROKE IN WOMEN WITH FAMILY STRESS IN GENERAL POPULATION 25-64 YEARS IN RUSSIA: WHO EPIDEMIOLOGICAL PROGRAM MONICA-PSYCHOSOCIAL

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Objective: To explore the influence of family stress on relative risk of myocardial infarction (MI) and stroke in female population aged of 25-64 years in Russia over 16 years of follow-up.
Methods: Under the third screening of the WHO "MONICA-psychosocial" (MOPSY) program random representative sample of women aged 25-64 years (n=870) were surveyed in Novosibirsk. Questionnaire MOPSY was used for assessment of family stress. From 1995 to 2010 women were followed for the incidence of stroke and MI with using "Myocardial Infarction Registry" data. Cox regression model was used for relative risk assessment (HR) of MI, stroke.
Results: The prevalence of high family stress level in women aged 25-64 years was 20.9%. HR of MI over 16 years of follow-up in women with family stress was 5.59-fold higher (95.0%CI:1.99-15.70, p=0.001) compared to those without stress. HR of stroke in women with family stress was 3.53-fold higher (95.0%CI:1.82-6.84, p<0.001). There were tendencies of increasing MI and stroke rates in married women experienced stress in family compared to divorced and widowed with the same stress level. As the tendency a stroke more likely developed in women with high and elementary school education having family stress. With regard to occupational class the tendency of higher stroke rates was found for "physical workers" with family stress compared to those without it (÷2=3.69 df=1 p=0.055) and MI rates were tend to be higher in "managers" and "engineers" experienced stress in family.
Conclusions: The prevalence of high stress in family in female population aged 25-64 years is more than 20% in Russia. Women with high family stress had significantly higher relative risk of MI and stroke over 16-th years of follow-up. Rates of MI and stroke development were more likely in married women with low educational level and high family stress in professional class "managers" and "physical laborers".

083

DECREASED SERUM VASPIN LEVELS ARE ASSOCIATED WITH CORONARY ARTERY DISEASE: A META-ANALYSIS

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Background: Vaspin is a serine protease inhibitor and a newly identified adipokine linked with obesity and insulin sensitivity. Vaspin is shown to exert anti-inflammatory and anti-apoptotic effects on endothelial cells and vascular smooth muscle cells via inhibition of NADPH oxidase mediated production of reactive oxygen species. The association between serum vaspin and coronary artery disease (CAD) is obscure.
Objective: The aim of the present study is to conduct a meta-analysis to evaluate the relationship between serum vaspin levels and CAD.
Methods: We searched MEDLINE, CINHAL and COCHRANE databases for studies reporting serum vaspin levels in the CAD and non CAD study population. We included case controls, cohort and cross-sectional studies. We calculated the weighted standardized mean difference (SMD) in serum vaspin levels between the CAD and control groups.
Results: Our search strategy yielded 36 articles and we included 5 studies enrolling 2236 participants. The median age of the CAD group was 64.5 yrs. (IQR 64-66) compared to 62yrs (IQR 61-63) in the control group. The median body mass index in the CAD group was 25 kg/m2 (IQR 24 – 27) compared to 25 kg/m2 (IQR 24 - 29) in the control group. The unweighted median serum vaspin levels in the CAD group were 0.69 ng/ml (IQR 0.47 - 0.71) compared to 1.6 ng/ml (IQR 1.6 – 1.9) in the control group. The SMD of serum vaspin level was -0.829 (95% CI -1.013,-0.645) $p<0.001$ comparing those in the CAD group and control group.
Conclusion: Serum vaspin levels are significantly and negatively associated with CAD. Current findings warrant the need to further investigate the role of vaspin in the development of CAD and its potential to predict incident CAD events.

084

GEOGRAPHIC VARIATION OF CARDIOVASCULAR DISEASE MORTALITY IN ASIAN AMERICAN SUBGROUPS

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Background: Geographic variation in Black/white disparities in cardiovascular disease (CVD) morality in the U.S. has been documented. However, it remains unknown whether similar geographic variation in CVD mortality may exist among Asian American subgroups. *Objective:* This study examines geographic differences in CVD mortality rates among Asian American subgroups living in the U.S.
Methods: Age-adjusted CVD mortality rates per 100,000 population and standardized mortality ratios (SMRs) were calculated for the six largest Asian-American subgroups (Asian Indian, Chinese, Filipino, Japanese, Korean, and Vietnamese) compared to non-Hispanic whites (NHWs), using U.S. death records from 2003-2011 and interpolated counts from 2000 and 2010 U.S. Census data (n=104,223 CVD deaths). States with 100 or more deaths for the specific Asian American subgroup were included in the analysis.
Results: Among the Asian subgroups, Filipino males in Hawaii (270.5 per 100,000, 95% CI: 259.8-281.7) and females in Oklahoma (232.3 per 100,000, 95% CI: 152.9-345.6) had the highest age-adjusted CVD mortality rates. When compared to NHWs, all Asian subgroups had lower CVD mortality rates in the majority of states. However, higher CVD mortality rates relative to NHWs were consistently observed across Asian subgroups in Arizona and Nevada. This difference was largest for Asian Indian males (SMR: 3.2) and females (SMR: 3.7) in Arizona compared to their NHW counterparts from the same state.
Conclusions: Geographic and racial/ethnic disparities for CVD mortality were present among certain Asian American subgroups, particularly Filipinos and Asian Indians concentrated in the Southwest states. Tailored prevention and intervention efforts should be provided to the populations and geographic areas with higher CVD burden.

085

MAJOR CAUSES OF DEATH FOR EAST ASIAN SUBGROUPS IN THE UNITED STATES COMPARED TO COUNTRIES OF ORIGIN (2003-2011)

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Background: As populations migrate, evidence shows that disease risks can become more pronounced or attenuated depending on context and self-selection into migration. While Asian Americans are typically considered the "healthy minority", very little is known about their mortality burden relative to Asian countries of origin and by nativity.
Objective: This study reports the major causes of death among East Asian subgroups in comparison to respective countries of origin (with Hong Kong as a proxy for high-income Chinese in Asia).
Methods: We examined U.S. mortality records for Chinese, Japanese, and Korean decedents from 2003-2011 and ranked the major causes of death. Age-adjusted mortality rates were calculated by age groups and standardized to WHO 2000 standard population. Proportionate mortality (PM) was calculated for each cause of death by Asian subgroup and nativity status (foreign-born vs. U.S. born). Data for countries of origin come from the WHO Mortality Database.
Findings: Cancer was the leading cause of death for all groups except for Japanese men in the U.S. Consistent with later epidemiologic transition in Asia and the "healthy migrant effect", all-cause mortality rates were higher in countries of origin than in the U.S (40% and 70% higher in Hong Kong, 5% and 38% in Japan, and 58% and 113% in Republic of Korea for women and men, respectively). Cause-specific mortality rates were also higher in countries of origin; however, Asian subgroups in the U.S. experienced greater PM due to the leading causes of death, especially heart disease, reflecting in part fewer competing risks. PM of heart disease increased with proportion born in the U.S.
Conclusion: Our findings highlight differences in mortality between East Asian American subgroups and countries of origin. More research would help to understand how childhood exposures, socioeconomic status, self-selected migration, and acculturation interact to explain these differences.

086

TREATMENT OF OBSTRUCTIVE THROMBOSED PROSTHETIC HEART VALVE

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A systematic review of the literature from 1996 -2012 revealed 9 studies with 48 patients with tricuspid OT PHV in whom thrombolytic therapy was successful in 88%. For left sided OT PHV, 17 studies comprising 756 patients had received thrombolytic therapy (TT) and in 13 studies comprising 662 patients had received surgical therapy (ST). Females were present 59% (TT) and 66% (ST). All but 3 patients had a mechanical valve. In 10 ST comprising 518 patients, thrombus was present in 41%, pannus in 38%, thrombus + pannus in 21%. Anticoagulants were described as inadequate in 39%. Mitral valve was involved in 68% (TT), 73% (ST); remainder had aortic valve; NYHA Class III/IV 65% (TT) 81% (ST); remainder were in NYHA Class I/II. Recurrence rate was 13% (TT) 6% (ST); CVA/Emboli 14% (TT) 6% (ST). In TT, complete success was 70%. 30 day mortality was 8%. In (TT) failure rate was 30% with mortality up to 28%. In TT Failure group, 15 patients died while waiting for surgery. In ST, complete success occurred in 100% with 30 day mortality of 15%. Suggested therapeutic strategies: Tricuspid OT PHV Thrombolytic TT is first choice. Left sided OT PHV: TT first choice in NYHA FCI/II, those with very severe co-morbid conditions, ST not a viable option or patient refuses surgery. Left sided OT PHV: ST is first choice if prosthesis replacement is necessary or appropriate, coronary flow is compromised TT is contraindicated, pannus is a significant contributor, TT fails.

087

LEFT ATRIAL APPENDAGE – A NOVEL TECHNIQUE FOR EXCLUSION

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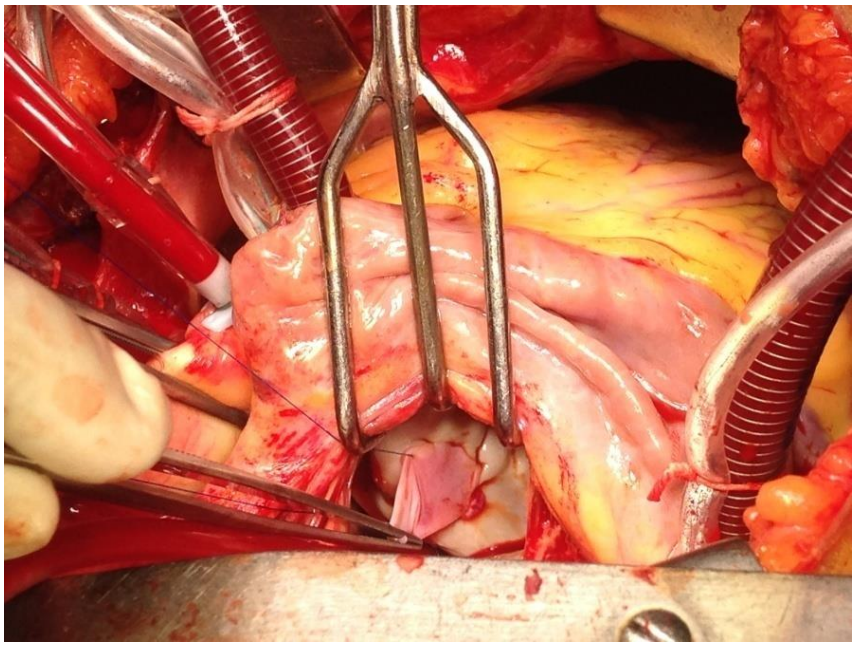
Objective: Left atrial appendage (LAA) is a frequent site of clot formation in patients with mitral valve disease, especially in those with atrial fibrillation. Ligation of LAA is commonly performed during mitral valve surgery. A number of surgical techniques are available for LAA exclusion, but a failure rate is nearly 60 %. We present here a novel technique to exclude the LAA during mitral valve surgery. Completeness of LAA ligation was 100 % with this technique which was confirmed by transesophageal echocardiography (TEE) in the follow up.
Methods: We used this technique in 24 patients with rheumatic mitral valve disease with atrial fibrillation / LAA thrombus who underwent mitral valve replacement over a period of approximately six months. We used fresh autologous pericardium of appropriate size to close LAA orifice using 4-0 polypropylene sutures in a continuous manner (Figure 1). In the follow up after 3 months TEE was done in all patients. A history of thromboembolic phenomenon after surgery was also recorded,
Results: None of the patient presented with any thromboembolic phenomenon in the follow up. Transesophageal echocardiography after 3 months showed no residual connection between the LA and LAA. LA clot was present in none of the patients and complete LAA obliteration was observed in all the patients.
Conclusions: Using an autologous pericardial patch to exclude the LAA, appears feasible with a low risk of distortion, injury, thrombus migration and incomplete exclusion.



088

WHICH STEM CELL TYPE IS MORE EFFICIENT AS AN ADJUNCTIVE TO SURGICAL TREATMENT OF SEVERE ISCHEMIC HEART FAILURE; EXPANDED MESENCHYMAL OR RECYCLING STEM CELLS?

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Objective: Bone marrow mesenchymal stem cells (MSCs) are used for the treatment of cardiac disorders. Recycling stem cells (RSC) are a marrow stromal cells with rapid self-renewal capacity and multipotential differentiation. In a prospective randomized controlled study, we compared 36-month follow-up results of intramyocardial injection of MSC and RSC on cardiac function in patients with severe ischemic heart failure undergoing CABG.
Methods: 27 patients with severe ischemic cardiomyopathy were randomly allocated into three groups; in control group, patients underwent CABG alone whereas in MSC and RSC groups, stem cells were injected in the border zone of the infarcted myocardium, respectively.
Results: There were no morbidities or mortalities in any of the groups in the study period. In dobutamine stress echocardiography, the LVEF in MSC group improved significantly (+6.1%) compared to control (-0.95%) and RS (+1.43%) groups ($p<0.05$). The wall motion score index of LAD territories improved in MSC group only, although the differences among the groups were not statistically significant (-0.18 in control group, -0.27 in MSC group, 0.00 in RS group; $p>0.05$).
Conclusions: Despite potential abilities of recycling stem cells in proliferation and differentiation, it seems that intramyocardial injection of MSCs is more efficient than RSC on improvement of cardiac function as an adjunctive treatment in patients undergoing CABG.

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EXAMINING THE COMPLEMENTARY EFFECTIVENESS OF THE ADDITION OF WARFARIN TO ASPIRIN ON PREVENTION OF SAPHENOUS VEIN GRAFT THROMBOSIS

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Objective: To determine if the addition of warfarin to aspirin prevents SVG thrombosis within 1 year of surgery.
Background: Coronary artery bypass grafting (CABG) is known to improve patient survival and alleviate symptoms of angina. Saphenous vein graft (SVG) thrombosis, a major cause of morbidity and mortality is seen in 15-45% of implanted grafts within the first year.
Methods: A retrospective analysis of patients who underwent CABG and repeat coronary angiography within one year of surgery at Carilion Roanoke Memorial Hospital between 2005 and 2012. Subjects were stratified into two groups, aspirin or aspirin+warfarin, based on the medications administered at the time of discharge. Surgical and cardiac catheterization reports were reviewed. Sample size at 95 % confidence interval was calculated for the aspirin group to be 50 patients which was then used for the comparison for the rate graft thrombosis.
Results: 3390 patients in the aspirin group and 385 patients in the aspirin+warfarin group were identified. Symptom driven repeat coronary angiography was performed in 10.7% (364) of patients treated with aspirin only while 3.6% (14 p=0.0001) of patients in the aspirin+warfarin group underwent the same procedure. In the aspirin group (N:50) there were 99 SVG implants and of those 55 thrombosed (56%). In the aspirin+warfarin (N:15) group there were 50 SVG's implanted and of those 9 thrombosed (44 % p=0.02). *Conclusion*: The addition of warfarin to aspirin therapy decreases the incidence of Saphenous thrombosis and symptom driven repeat coronary angiography within 1 year.

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RISK FACTORS FOR AAA IN SUBJECTS LESS THAN 65 YEARS OF AGE

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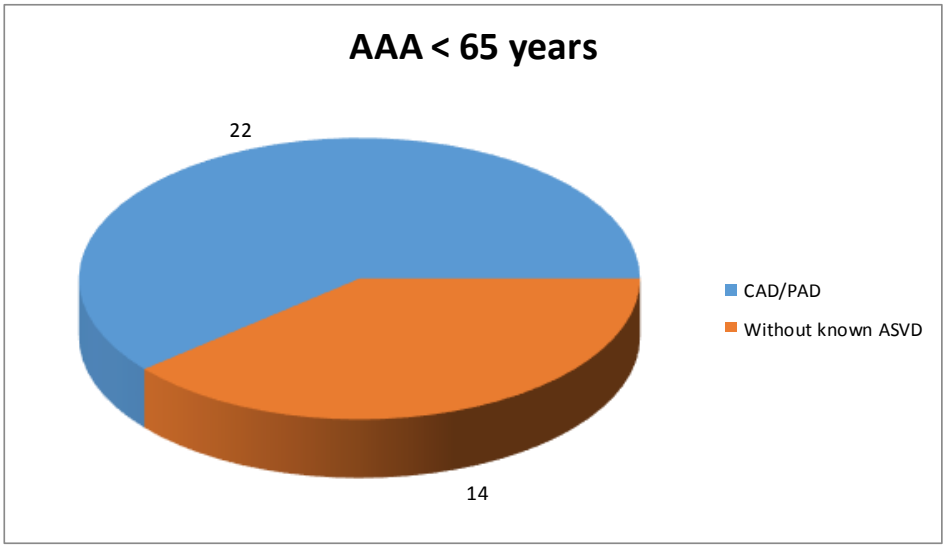
Background: The estimated prevalence of abdominal aortic aneurysm (AAA) is 4 to 9 percent, which increases with age. Rupture is a potentially catastrophic complication of undiagnosed AAA. Current United States preventive services task force guideline recommends screening of men who are ages 65 to 75 and who have ever smoked.
Methods: Data was reviewed on subjects (n=99) who underwent AAA repair at Salem VAMC from 1998 - 2012. Out of 99- patients with AAA, 36 (36%) were diagnosed with AAA prior to the age of 65-years and 29 out of 36 (80%) required surgery prior to the age of 65. Demographics/ risk factors of this subgroup were reviewed. Male gender, tobacco abuse (past or active), Hypertension were almost universal. 13 out of 36 (36 %) patients were known to have history of CAD, MI, PCI/CABG. 12 out of 36 (33 %) patients were noted to have peripheral artery disease (PAD). 22 out of 36 (61%) subjects had either CAD/PAD or revascularization (PCI/CABG).MACE (TIA/CVA, MI, and Death) was noted at day 7 and day 30, only one patient had an event who developed an MI the day of surgery and died subsequently on day 17 after surgery.
Conclusions:
*A significant number of subjects (36%) were diagnosed with AAA before 65 years of age and required surgery.
*61% of patients from this younger cohort had evidence of atherosclerotic vascular disease noted elsewhere (CAD, PAD).
*Clinicians should have a high index of suspicion and consider ultrasound screening for AAA in similar high risk subjects even if they *do not* meet current USPTF guidelines.



091

IMPELLA 2.5: TIME FOR A MORATORIUM?

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Background: Cardiogenic shock (CS) in a patient with acute myocardial infarction (AMI) portends a poor prognosis with mortality rate of 51-76% despite the use of Intra-aortic balloon pump or Impella 2.5 for hemodynamic support. In the current study, we describe our real world experience with Impella 2.5 at Kettering Medical Center (KMC) a large community teaching hospital.
Methods: 25 consecutive patients who received Impella 2.5 devices at KMC from May 2011 to January 2014 was reviewed. The primary end-point was 30-day mortality.
Results: The average age was 70.5 + 12.19 years. Baseline data showed they were all Caucasians, mostly males (78%) with co-morbidities of: prior AMI (43%), hypertension (80%), diabetes (78%), chronic kidney disease (33%), and prior stroke (21%). The mean systolic blood pressure before and after Impella 2.5 placement was 89.64 mmHg + 27.3 and 105.54 mmHg + 16.59 respectively. The overall mortality was 71% with all deaths occurring within five days of Impella 2.5 placement (mean of 2.5 days + 1.64). Multivariate analysis using logistic regression model did not show any significant difference in mortality based on factors specified for the secondary endpoints.
Conclusions: The real world 30-day mortality rate in patients with CS in the setting of AMI remains high despite use of Impella 2.5. This taken together with previously published data calls into question the utility of Impella 2.5 devices in the setting of CS. If circulatory support is needed Impella 5.0 or Ventricular assist device should be considered before the Impella 2.5 device.

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EXAMINING THE EFFECTIVENESS OF DUAL ANTIPLATELET THERAPY WITH ASPIRIN AND CLOPIDOGREL IN PREVENTING SAPHENOUS VEIN GRAFT THROMBOSIS GIVEN ITS PROVEN BENEFIT WITH CORONARY THROMBOSIS

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Objective: To determine if the addition of clopidogrel to aspirin prevents SVG thrombosis within 1 year of surgery.
Background: Coronary artery bypass grafting (CABG) is known to improve patient survival and alleviate symptoms of angina. Saphenous vein graft (SVG) thrombosis, a major cause of morbidity and mortality is seen in 15-45% of implanted grafts within the first year.
Methods: A retrospective analysis of patients who underwent CABG and repeat coronary angiography within one year of surgery at Carilion Roanoke Memorial Hospital between 2005 and 2012. Subjects were stratified into two groups, aspirin or aspirin+clopidogrel, based on the antiplatelet agent(s) administered at the time of discharge. Surgical and cardiac catheterization reports were reviewed. Sample size at 95 % confidence interval was calculated for the aspirin group to be 50 patients which was then used for the comparison for the rate graft thrombosis.
Results: 3390 patients in the aspirin group and 605 patients in the aspirin+clopidogrel group were identified. Symptom driven repeat coronary angiography was performed in 10.7% (364) of patients treated with aspirin only while 4.5% (27 p=0.0001) of patients in the aspirin+clopidogrel group underwent the same procedure. In the aspirin group (N:50) there were 99 SVG implants and of those 55 thrombosed (56%). In the aspirin+clopidogrel (N:27) group there were 50 SVG's implanted and of those 22 thrombosed (44 % p=0.18).
Conclusion: The addition of clopidogrel to aspirin therapy in patients undergoing CABG using a SVG decreases the incidence of early thrombosis and symptom driven repeat coronary angiography within 1 year of implant.

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INFLAMMATION IN HEART DISEASES

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The main objective of this study was to determine whether or not inflammation plays a role in heart diseases. We will demonstrate presence of inflammation in pre-diabetic (PD) cardiomyopathy and diabetic infarcted heart. We will define the role of monocytes and their differentiation into pro-inflammatory M1 and anti-inflammatory M2 macrophages. In PD cardiomyopathy model our data suggest that there was a significantly increased infiltrated monocytes and associated pro-inflammatory cytokines that induces adverse cardiac remodeling, and heart dysfunction in the PD group. Following BMP-7 treatment in PD cardiomyopathy group we observed increase in M2 macrophage polarization that are associated with an increase in anti-inflammatory cytokines. Enhanced anti-inflammatory cytokines reduced adverse cardiac remodeling, and improved cardiac function in the PD+BMP-7 group. In conclusion, our data suggest, that diabetic cardiomyopathy is associated with increased monocyte infiltration, released of pro-inflammatory cytokines, which contributes to adverse cardiac remodeling, and cardiac dysfunction.

CELLULAR AND MOLECULAR MECHANISMS OF CARDIOPROTECTION, CARDIAC REGENERATION AND REMODELING

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C-REACTIVE PROTEIN MODULATION OF INFLAMMATION IN ACUTE CORONARY ARTERY DISEASE

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C-reactive protein (CRP) is an acute-phase reactant and an active regulator of innate immunity. Clinical studies have shown that elevated baseline serum CRP levels confer, albeit to varying degrees, additional prognostic value for future coronary artery disease (CAD) and death and may be useful for risk-guided therapy. CRP has been implicated in multiple aspects of atherogenesis and acute CAD; however, whether CRP plays a direct causal role in these events remains controversial. Studies in rodents yielded conflicting results on atherosclerosis development. CRP has at least two conformationally distinct forms, native pentameric (p) CRP and monomeric (m)CRP. Loss of pentameric symmetry in pCRP, yielding mCRP, is associated with expression of distinct bioactivities. Using CRP isomer-selective antibodies, we detected mCRP, but not native CRP in human coronary artery atherosclerotic lesions with more pronounced mCRP staining in advanced fibro-fatty plaques than fatty streak lesions. The mCRP staining frequently co-localized with neutrophils and macrophages in advanced lesions. In vitro, mCRP is considerably more potent activator of human coronary artery endothelial cells and monocytes than pCRP, whereas mCRP and pCRP exert opposing actions on neutrophil trafficking and apoptosis through distinct Fc-gamma receptors and lipid rafts. Unlike pCRP, mCRP is susceptible for proteolysis, resulting in peptide 201-206 that exhibits potent anti-inflammatory and anti-platelet activities. These findings may explain how sequential conformational changes in CRP's structure could lead to expression of distinct biological activities that may modulate inflammation underlying plaque destabilization and acute CAD.

(Grant support: CIHR).

CELLULAR AND MOLECULAR MECHANISMS OF CARDIOPROTECTION, CARDIAC REGENERATION AND REMODELING

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CARDIOPROTECTIVE EFFECTS OF THERAPEUTIC T3 TREATMENT IN MYOCARDIAL INFARCTION AND ISCHEMIA REPERFUSION

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Background: Myocardial Infarction (MI) leads to cardiac tissue hypothyroidism, a condition that by itself can lead to heart failure (HF). Potential improvements in LV remodeling and function with a therapeutic T3 dose after MI and ischemia/reperfusion (IR) are not clear.
Objectives: We hypothesize that a safe, low-dose T3 treatment/monitoring regimen will lead to significant cardioprotection in rats following MI and 60 minute IR.
Methods: MI was produced in adult rats by LAD ligation. T3 (4-5 μg/kg/day) in drinking water was started after MI and continued for 2 months (Mo). Vehicle (V) was used in MI controls (n=16-20/group). The same 2 month treatment protocol was used for rats with IR.
Results: Infarct size was similar in MI and MI+T3 groups. D3 mRNA expression increased in MI+V (2.7-fold) and was reversed in MI+T3 (0.49-fold). MI+T3 improved ejection fraction by 51% at 1 Mo and by 47% at 2 Mo post-MI as assessed by magnetic resonance imaging (MRI). Mean MRI wall thickness was increased at both latter time-points. Histologically, non-infarct area and wall thickness increased significantly (30% and 18% respectively). Non-infarct length was also increased. Remarkably, following MI, the incidence of atrial tachyarrhythmias that persisted following discontinuation of experimental atrial tachypacing was significantly diminished by 63% with T3. T3 did not affect heart rate. The T3 dose led to feedback inhibition of Thyroid-Stimulating Hormone (TSH) but no significant change in serum T3. T3 treatment for 2 months after IR also led to an increase in viable myocardium and improvement in LF function.
Conclusion: Results demonstrate a safe and effective post-MI and IR T3 treatment strategy that dramatically improves LV function, atrial arrhythmogenesis, non-infarct tissue remodeling, and myocyte survival with no adverse effects. This study describes an effective, translatable, treatment/monitoring protocol for T3 treatment of MI and IR.

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REGULATION OF INTESTINAL GENES BY AN ORAL PEPTIDE REDUCES SYSTEMIC INFLAMMATION AND ATHEROGENESIS

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A high fat, high cholesterol diet (Western diet, WD) increases the levels of the potent growth promoter unsaturated lysophosphatidic acid (LPA) in small intestine and plasma of LDLR-/- mice. Supplementing mouse chow with unsaturated LPA produced dyslipidemia and inflammation. WD increased the expression of the genes Acadl, Acot1 and Angptl4 while reducing that of Reg3g. The transgenic plant reversed the changes in gene expression. We now report that supplementing chow with unsaturated LPA resulted in aortic atherosclerosis, which was ameliorated by adding a transgenic 6F plant powder. Supplementing chow with lysophosphatidylcholine (LysoPC) 18:1 resulted in dyslipidemia similar to that seen on adding LPA 18:1 to chow. A specific inhibitor of autotaxin (PF8380) significantly ameliorated the dyslipidemia induced by LysoPC 18:1. Supplementing chow with LysoPC 18:1 markedly increased the levels of unsaturated LPA in small intestine, plasma and liver. This increase was ameliorated by PF8380 indicating an autotaxin-dependent conversion of LysoPC 18:1 to LPA 18:1. Adding LysoPC 18:0 to chow increased levels of LPA 18:0 in small intestine, plasma and liver. This was not altered by PF8380 indicating that conversion of LysoPC 18:0 to LPA 18:0 was not autotaxin-dependent. We therefore conclude that a) autotaxin mediates the conversion of unsaturated LysoPC to LPA, and b) intestinally-derived unsaturated LPA can cause atherosclerosis in LDLR-/- mice.

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ALTERATIONS OF MACROPHAGE GSH/GSSG STATUS REGULATE CD36 EXPRESSION AND FOAM CELL FORMATION: IMPLICATION OF GSH-ANTIOXIDANT SYSTEM IN ATHEROSCLEROSIS

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The glutathione (GSH)-dependent antioxidant system has demonstrated to inhibit atherosclerosis. Macrophage CD36 uptakes oxidized low-density lipoprotein (oxLDL) thereby facilitating foam cell formation and development of atherosclerosis. It remains unknown if GSH can influence macrophage CD36 expression and foam cell formations. Herein, we report that treatment of macrophages with L-buthionine-S,R-sulfoximine (BSO) decreased the cellular GSH production and ratio of GSH to glutathione disulfide (GSH/GSSG) while increasing production of reactive oxygen species. Associated with decreased GSH levels, macrophage CD36 expression was increased which resulted in foam cell formation. In contrast, N-acetyl cysteine and antioxidant enzymes (catalase and superoxide dismutase) blocked BSO-induced CD36 expression and foam cell formation. In vivo, administration of mice with BSO increased CD36 expression in peritoneal macrophages and kidneys. BSO had no effect on CD36 mRNA expression and promoter activity but still activated CD36 protein expression in macrophages lacking PPARgamma expression suggesting it induced CD36 expression at the translational level. Indeed, we determined that BSO enhanced CD36 translational efficiency. Taken together, our study demonstrates that cellular GSH levels and GSH/GSSG status can regulate macrophage CD36 expression and foam cell formation, and further supports the important role of the GSH-antioxidant system in anti-atherosclerosis by providing molecular and cellular evidence.

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RELAXIN, A POTENTIAL THERAPY FOR ATRIAL FIBRILLATION

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Relaxin, a hormone of reproduction and has been identified as an insulin-like peptide with pleiotropic actions throughout the body including important cardiovascular actions. We recently demonstrated that Relaxin suppresses atrial fibrillation (AF) in spontaneously hypertensive rat (SHR) hearts by remodeling the extracellular matrix, modulating cardiac ion channels and reducing cell hypertrophy. Here, we test the potential therapeutic effects of Relaxin in a geriatric model of AF based on old rats (F-344, 24-months). Rats were implanted with osmotic mini-pumps (Alzet) to deliver Relaxin for 2-weeks (0.4 mg/kg/day) or to deliver the vehicle as controls. Heart rate, blood pressure and serum relaxin were measured at the onset and at the end of the 2-weeks treatment. Hearts were perfused in a Langendorff apparatus to optically map action potentials and Ca2+ transients, conduction velocity (CV), restitution kinetics, programmed stimulation (10-S1-S1 impulses at 300 ms CL, decreasing S1-S2 intervals) was applied to assess AF susceptibility, then atrial tissues were prepared for analysis by immuno-cytochemistry and RT-PCR. In control hearts, sustained AF was readily elicited (n=7/8) whereas AF was suppressed in relaxin treated rats (n=0/8). Relaxin increased CV by ~2-fold, reversed fibrosis and cellular hypertrophy. Consistent with these cardiac effects, collagen (I&III) deposition was reduced as well as transcripts of fibrosis (TGF-beta, collagen I and III, metalloproteinase 1 and 9) and upregulated voltage-gated Na+ channels Nav1.5 protein by 1.8 fold compared to untreated old-rats. In whole cell voltage-clamp experiments, atrial myocytes incubated with 100 nM relaxin for 24-48 hours had a 2-fold increase in current density compared to myocytes incubated with vehicle. These results may explain the clinical trial results of greater survival (37%) of patients with acute heart failure whom received relaxin (2-days,i.v.) and suggest that Relaxin may be a transformative therapy for AF.

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IMPACT OF PERCUTANEOUS INTERVENTION OF CORONARY CHRONIC TOTAL OCCLUSION ON LEFT VENTRICULAR EJECTION FRACTION

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Background: Percutaneous coronary intervention (PCI) of coronary artery chronic total occlusion (CTO) has been gaining popularity with reported high success rates in these anatomically complex and challenging lesions. However, changes in left ventricular ejection fraction (LVEF) associated with successful PCI have not been well studied.
Methods: We performed a systemic review of the literature and identified 14 prospective and 2 retrospective studies that specifically addressed this issue. Meta-analysis was performed to compare the changes in left ventricular EF associated with successful versus unsuccessful PCI.
Results: A total of 615 patients were included in this meta-analysis from 16 studies. Mean age of study patients was 60.5 years and 81% were men. Median duration of follow up was 6 months (range 1 to 36). LVEF was measured by invasive angiography (3 studies), cardiac magnetic resonance imaging (7 studies) and two-dimensional echocardiography (6 studies). Mean improvement in ejection fraction was 4.09% (95% confidence interval 2.91 to 5.28; p<0.00001) in those with successful PCI of CTO lesions [Figure]. An improvement in systolic wall thickening in CTO territory was also observed in 3 studies (p<0.001).
Conclusion: Successful PCI of coronary artery CTO improves LVEF and systolic wall thickening in selected patients.

Study or Subgroup	Post PCI Mean	SD	Total	Pre PCI Mean	SD	Total	Mean Difference IV, Random, 95% CI	Year
Danchin	62	13	38	55	14	38	7.00 [0.93, 13.07]	1996
Sirnes	67	11	87	62	13	87	5.00 [1.42, 8.58]	1998
Chung	57.3	20.1	75	53.2	16.3	75	4.10 [-1.76, 9.96]	2003
Baks	62	11	27	61	9	27	1.00 [-4.36, 6.36]	2006
Kirschbaum	63	11	21	60	9	21	3.00 [-3.08, 9.08]	2008
Locca	59	16	12	54	15	12	5.00 [-7.41, 17.41]	2008
Pavlovic	54	13	13	51	11	13	3.00 [-6.26, 12.26]	2009
Fiocchi	54	17	14	50	16	14	4.00 [-8.23, 16.23]	2009
Paul	54	11	19	50	13	19	4.00 [-3.66, 11.66]	2011
Kirschbaum'	54	12	43	50	11	43	4.00 [-0.87, 8.87]	2012
Sun	52.9	7	40	47.7	8	40	5.20 [1.91, 8.49]	2012
Yue	59.1	7.1	32	54.1	6.4	32	5.00 [1.69, 8.31]	2012
Galiuto	55.6	8.3	24	47.5	8.7	24	8.10 [3.29, 12.91]	2013
Roifman	54	11	19	50	13	19	4.00 [-3.66, 11.66]	2013
Pujadas	65	11.5	33	62	12.2	33	3.00 [-2.72, 8.72]	2013
Erdogan	58.3	10.2	118	56.3	9.8	118	2.00 [-0.55, 4.55]	2013
Total (95% CI)			**615**			**615**	**4.09 [2.91, 5.28]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.72$, df = 15 (P = 0.89); $I^2 = 0\%$
Test for overall effect: Z = 6.75 (P < 0.00001)

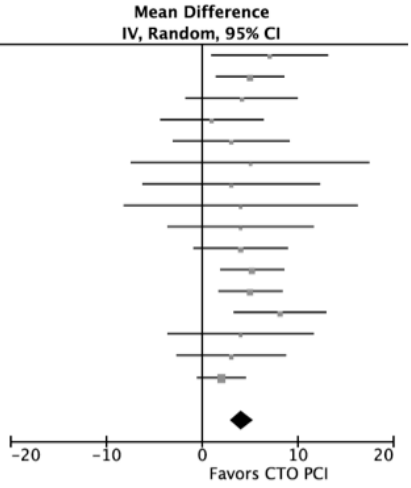

Figure 1. Changes in left Ventricular Ejection Fraction Following Percutaneous Intervention of Coronary Chronic Total Occlusion

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UTILITY OF A NOVEL CORONARY ARTERY DISEASE BIOMARKER ALGORITHM IN MODIFYING PHYSICIAN ADHERENCE TO GUIDELINE-BASED THERAPY

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Background: Initial coronary artery disease (CAD) presentation for most patients is acute coronary syndrome (ACS) from rupture of non-obstructive plaque. Screening for ACS risk remains a challenge; traditional risk factors and standard noninvasive testing predict only 60-65% of events. In this study, we examined whether providing physicians with a novel CAD predictive algorithm would impact their management of patients to conform more appropriately to established guidelines.
Methods: We studied 22 physician practices including cardiology, internal medicine, family practice, obstetrics and gynecology, and endocrinology. Participating physicians developed a treatment plan per their usual standard of care. In patients at intermediate risk based on established risk factors, a novel CAD predictive algorithm (CADPA) using biomarkers (CTACK, Eotaxin, Fas Ligand, HGF, IL-16, MCP-3, sFas, Hba1c, HDL-C) and key risk factors (age, sex, diabetes, and family history) was then applied, providing revised CAD risk estimates (low <3.5%, intermediate 3.5-7.49%, and high >7.49% CAD risk in 5 years). Physicians then had the opportunity to revise their treatment plan. All treatment plans were documented and recorded by an independent trial monitor.
Results: A total of 583 patients were evaluated using traditional risk assessment and 144 (25%) were initially classified as intermediate risk; 10 patients were lost to follow-up. The remaining 134 intermediate-risk patients (mean age 61.6 years, 36% female), based on CADPA results, were reclassified as low (8.2%), intermediate (30.6%), or high (61.2%) risk and new treatment plans were developed at the discretion of the treating physicians. Lifestyle or drug treatment plans were changed in 57% of the cases (P<0.001), conforming more appropriately to ATPIII/AHA guidelines (85%). Most physicians (96%) agreed that CADPA provided information that would impact their current treatment decisions.
Conclusion: Implementation of a novel CAD predictive algorithm provides additional actionable clinical information that results in more appropriate therapy and alignment with current guidelines.

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CYP2D6 GENETIC INFORMATION-GUIDED METOPROLOL USE IN A CARDIOLOGY CLINIC – A PROSPECTIVE STUDY

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Background: The CYP2D6 enzyme is a major determinant of metoprolol plasma clearance. It has close to 100 genetic polymorphisms, which give rise to four phenotypic: Extensive-Metabolizers (EM, normal capacity), Intermediate-Metabolizers (IM, reduced capacity), Poor-Metabolizers (PM, diminished capacity) and Ultra-extensive-Metabolizers (UM, higher than average capacity). Peak plasma metoprolol concentrations can be 2.1-4.6 fold greater in the IM/PM groups as compared with the EM group.
Objectives: To evaluate CYP2D6 genetic variations in patients and assess the clinical outcomes of this genetic information-guided metoprolol dosing.
Methods: DNA sequences of CYP2D6 are analyzed in 479 patients. Individual metoprolol recommendations are made based on their phenotype and are then followed up at the clinic.
Results: Distribution of CYP2D6 phenotypes in our patients are (expressed as phenotype: patient number): EM: 251, IM: 158, PM: 64 and UM: 6. Distribution of the 306 (63.8%) patients who are on metoprolol are: EM: 159, IM: 102, PM: 39 and UM: 6. Metoprolol was decreased in dose in 26 patients and switched to atenolol in 125 patients. Dose is unchanged in 192 patients who are either already on a low dose or tolerating current dose. Doses are increased in UM patients. For those who're not on metoprolol but phenotypically abnormal (IM: 59 and PM: 25), "metoprolol caution" is documented. All patients are then followed up for one year with primary endpoints of 1) ACS-or-CHF-related hospitalization, 2) cardiac death and 3) symptomatic bradycardia, hypotension or syncope.
Conclusions/Discussion: Metoprolol should be used with caution in patients with CYP2D6 variants due to the marked pharmacokinetics effect. Prevalence of IM, PM and RM phenotypes are substantial (combined 48%). Lowing dose or switching to beta-blocker that is not metabolized by CYP2D6 in IM/PM patient should decrease major side effects, whereas increasing dose in RM patients should increase clinical efficacy.

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SERUM CYSTATIN C, AN INDEX OF RENAL DYSFUNCTION, AS A MARKER IN ISCHEMIC HEART DISEASE

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Objectives. To investigate whether patients with ischemic heart disease display altered serum cystatin C as a possible biomarker of acute ischemia.
Background. Cystatin C, a well-known index of renal dysfunction, more efficient than creatinine, was recently suggested as a candidate biomarker in cardiovascular pathology. However, the precise role of cystatin C in acute ischemia and myocardial infarction is not studied enough. The aim: to evaluate serum cystatin C in patients with ischemic heart disease in dynamics of myocardial infarction development.
Methods. 42 male patients (62 ± 5.0 years) were enrolled in a study; the control group consisted of 60 healthy persons of the appropriate age. Serum hs-CRP, D-dimer, cystatin C, creatinine, urea, lipid profile, LDH, CPK, CPK-MB were measured with help of Architect 8000 (Abbott, USA) and with Access-2 (Beckman Coulter, USA), pro-BNP by ELISA method.
Results. In healthy persons, aged 50-60, an elevation of serum cystatin C was shown vs healthy persons, aged 20-40 years. In patients with ischemic heart disease, there was a significant ($p < 0.001$) increase in serum CPK-MD, hs-CRP, D-dimer and elevated ($p < 0.01$) CPK, cystatin C vs the control. Positive correlation was shown between serum pro-BNP and cystatin C ($r = 0.57$, $p< 0.05$), pro-BNP and urea ($r = 0.49$, $p< 0.05$) indicating on cardio-renal syndrome development.
Conclusions. In patients with myocardial infarction serum pro-BNP, cystatin C were elevated more significantly as compared with hs-CRP and D-dimer levels, indicating that these indexes can be used as predictors of increased risk of acute ischemia.

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CORONARY SINUS FILLING TIME IN PATIENTS HAVING ANGINA WITH NORMAL EPICARDIAL CORONARY ARTERIES

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Objective: We evaluated Coronary sinus filling time (CSFT) in patients having angina with normal epicardial coronary arteries and compared it with control population.
Background: Patients having angina with normal epicardial coronary arteries are often considered to have coronary microvascular dysfunction that results in coronary slow flow. CSFT may represent transit time through coronary microcirculation.
Method: We enrolled 31 patients having definite angina or probable angina with positive exercise tolerance test with normal epicardial coronary arteries in coronary angiogram (CAG) in study group and 31 patients having normal epicardial coronary arteries in CAG during preoperative evaluation before surgical treatment for valvular and congenital heart diseases in control group. CSFT, TIMI (Thrombolysis In Myocardial Infarction) frame count, cTIMI (Corrected TIMI) frame count and TMP (TIMI Myocardial Perfusion) score were assessed in CAG of both groups and compared between groups.
Results: Patients' Mean±SD of age in study and control group were 48.84±9.50years and 46.71±5.53years respectively with no significant difference (p=0.569). There was female preponderance (55% and 65%) in both groups. CSFT was significantly prolonged in study group (4.22±0.71sec vs. 3.65±0.25sec, P value 0.001) but TIMI frame count, cTIMI and TMP showed no significant difference between two groups (25.71±5.74 vs. 26.74±3.81, p= 0.552; 14.76±3.6 vs. 15.4±2.56, p=0.449; 2.54±0.5 vs. 2.61±0.49, p=0.326; respectively).
Conclusion: We concluded that CSFT was significantly prolonged in patients having angina with normal epicardial coronary arteries which might be a surrogate marker for diagnosis for coronary microvascular disease.

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INCREASED LV MASS IS RELATED WITH ATYPICAL CHEST PAIN IN WOMEN

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Background: Chest pain in women seems to have different features from that in men with chest pain. Korean Women's Registry was established to elucidate unique features of chest pain in women in 2011. We evaluated demographic characteristics including obstetric history as well as echocardiographic and coronary angiographic data and treadmill exercise test (TMT).
Methods: 880 women patients with chest pain in Korean Women's Registry, which is a multicenter registry, were enrolled. The findings of TMT and echocardiography and clinical data were analyzed. 197 patients were performed dobutamine stress echocardiography (DSE). Among them, 102 patients were finally enrolled for the DSE analysis according to exclusion criteria.
Results: Patients who showed left ventricular (LV) outflow tract obstruction during DSE have higher LV mass index and LV relative wall thickness and diastolic dysfunction. Typical angina is not a good diagnostic indicator of coronary arterial disease (CAD) in women. After age 55, classic angina classification is moderately predictive of CAD. Patients with positive TMT showed lower LV mass index and higher pulmonary artery systolic pressure. Conventional predictors of CAD such as age, DM and hypertension were not different in prevalence between patients with negative or positive TMT. After multivariate adjustment, significant CAD seems to be only predicted by duration of TMT, indicator of exercise capacity.
Conclusion: DSE-provoked LV outflow tract obstruction is related to LV concentric remodeling and LV diastolic dysfunction and may be associated to the limited exercise tolerance in Korean women with chest pain regardless of coronary artery disease. Duration of TMT was an independent predictive factor of the presence of CAD by multivariate analysis. Increased LV mass and diastolic dysfunction were related with atypical chest pain in women.

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HEART ATTACKS IN YOUNG ADULTS OF CENTRAL CALIFORNIA

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Patients admitted over a ten-year time period were included in this case-controlled retrospective study. Using ICD 9 codes, patients admitted with diagnosis of acute coronary syndrome (ACS), STEMI and NSTEMI, were identified. Random sample of 100 patients was selected from each of the four groups (young ACS, old ACS, young non-ACS, and old non-ACS). Young was defined as between age 18 and 50, while old was defined as 50 and older. Lipid profiles were significantly different in the comparison groups. Young ACS patients had higher mean TG when compared to old ACS patients; (P=0.001). Young ACS patients experienced significantly more metabolic syndrome as defined by TG/HDL ratio greater than 3.5 (P = 0.02). Hypertension was more prevalent in older ACS patients (71%) followed by older non ACS patients adults (64%) (P=0.001). History of cardiac disease (41%) was more common in older ACS patients as well (P=0.024). BMI, race, illicit drug use, and prevalence of diabetes mellitus did not differ significantly between young and old ACS adults or the non ACS groups. On multivariate logistic regression analysis, male sex (OR 2.73, 95% CI 1.38-5.39, P=0.001), smoking (OR 2.74, 95% CI 1.47-5.09, P=0.005), and metabolic syndrome (OR 2.91, 95% CI 1.52-5.5, P=0.006) were independently associated with young patients presenting with ACS. Young ACS adults are more likely to be males, smokers, and have propensity for single vessel disease, specifically the LAD. Metabolic syndrome is associated with ACS in young adults, potentially requiring additional risk stratification and control beyond traditional risk factors.

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COLCHICINE FOR PREVENTION OF PERICARDITIS RECURRENCE: META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Objectives: To evaluate the efficacy and safety of colchicine use in the treatment of acute pericarditis and prevention of pericarditis recurrences.
Background: Recurrent pericarditis is the most common complication of acute pericarditis. Colchicine has been used for several centuries as an anti-inflammatory treatment for arthritis and acute gout attacks. There have been studies that suggest colchicine as a first-line treatment for acute pericarditis and for prevention of recurrent episodes. Recently studies have shown that it is superior to conventional therapy, which includes nonsteroidal anti-inflammatory drugs (NSAIDs).
Methods and results: Electronic databases were searched to identify randomized control trials that evaluated the effects of colchicine vs. NSAIDs or placebo for treatment of acute or recurrent pericarditis. The primary endpoint was recurrent pericarditis. The safety end point was any side effects. Odds ratios (OR) and 95% confidence intervals (CI) computed using fixed-effect model. Eight randomized controlled trials were included in the meta-analysis, enrolling a total of 1635 patients. Colchicine significantly reduced the rate of recurrent pericarditis (OR 0.382; 95% CI, 0.300-0.486, P = 0.000, NNT = 6, I2 = 0.000) but when compared with conventional treatments, the risk of side effects were higher with colchicine (OR 1.457, 95% CI, 1.038-2.045, P = 0.029, NNH = 29, I2 = 0.000)
Conclusions: Colchicine is an effective treatment for acute pericarditis and superior to NSAIDs for prevention of pericarditis recurrences without a significant risk of serious side effects.

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PATTERN OF CARDIAC SURVEILLANCE AMONG LYMPHOMA PATIENTS RECEIVING ANTHRACYCLINE-BASED CHEMOTHERAPY

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Background: Anthracyclines are potent anti-neoplastic agents in the treatment of lymphoid malignancies but their therapeutic benefit is limited by cardiotoxicity. The American Heart Association (AHA) recommends routine surveillance, early diagnosis and treatment of anthracycline-based chemotherapy (AC) induced cardiomyopathy (AC-CMP). We aimed to assess the prevalence of AC-CMP in lymphoma patients, surveillance patterns of left ventricular ejection fraction (LVEF) in those receiving AC and management of AC-CMP patients at an academic medical center prior to the development of a comprehensive cardio-oncology program.
Methods: We performed a retrospective cohort study examining 218 patients with aggressive B-cell Non-Hodgkin lymphomas (B-NHL) who received AC 1992-2012 and had serial follow-up. AC-CMP was defined as LVEF decrease >=10% with final LVEF =<50% or LVEF reduction >=15% regardless of final LVEF.
Results: Of 218 patients treated with AC, 73 (34%) had LVEF assessment both prior to and after receiving AC. Of these 73 patients, 24 developed AC-CMP and had higher cumulative all-cause mortality than those without AC-CMP (HR 2.35, p=0.03). Coronary artery disease (CAD) was an independent predictor of AC-CMP (p=0.048). Mean post-AC LVEF was lower in CAD patients compared to those without CAD when their baseline LVEF was 45% (p=0.0009) or 55% (p=0.001) but was similar at 65% (p=0.33). Less than half of AC-CMP patients received recommended heart failure medication therapy.
Conclusions: Historically, one third of B-NHL patients treated with AC underwent surveillance according to AHA guidelines. There is substantial opportunity for collaboration between oncologists and cardiologists to improve the care of lymphoma patients receiving AC.

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LEFT VENTRICULAR ASSIST DEVICE (LVAD) REVERSES INHIBITION ON BETA-ADRENERGIC RECEPTOR RESENSITIZATION

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Traditionally left ventricular assist device (LVAD) is used for mechanical unloading of the heart in conditions of chronic heart failure. Post-LVAD there is significant preservation of cardiac function in part, due to recovery in beta-adrenergic receptor (betaAR) function. BetaAR function is regulated by phosphorylation (desensitization/shutting off) and dephosphorylation (resensitization/re-activation) of the receptor. Increased betaAR desensitization is a classical hallmark of heart failure but not much is known about betaAR resensitization. In order to test whether resensitization plays a role in recovery of betaAR function post-LVAD, we used pre- and post-LVAD human heart samples to assess PI3K activity, PP2A activity, beta2AR phosphorylation and adenylyl cyclase (AC) activity as a measure of G-protein coupling. Significant PI3Kgamma activity was observed in pre-LVAD samples compared post-LVAD and non-failing human heart samples. Similarly, AC activity was markedly reduced in pre-LVAD samples compared to post-LVAD and non-failing showing reduced ability of receptors to couple to G-proteins indicating reduced recovery of receptor function in post-LVAD heart samples. Consistent with the reduced recovery in betaAR function in pre-LVAD samples, significant betaAR phosphorylation was observed in pre-LVAD compared to post-LVAD and non-failing. Correspondingly, we observed significant reduction in endosomal PP2A activity in the pre-LVAD samples which was remarkably reversed in post-LVAD samples similar to the activity in non-failing. These studies suggest that resensitization is inhibited in end-stage human heart failure and may critically contribute to cardiac remodeling and hypertrophic response upon cardiac stress.

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THE IMPACT OF LIVER TRANSPLANTATION ON MYOCARDIAL FUNCTION IN PATIENTS WITH FAMILIAL AMYLOID POLYNEUROPATHY

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Introduction: familial amyloid polyneuropathy (FAP) is a genetic disorder characterized by amyloid deposits in multiple organs. Myocardial amyloid infiltration results in diastolic dysfunction and subclinical changes in systolic function, better assessed by myocardial deformation parameters. Liver transplantation (LT) inhibit liver production of abnormal protein and prevent disease progression. However, its impact on myocardial deformation has never been assessed.
Objective: To evaluate the impact of LT in global myocardial deformation parameters depicted by speckle-tracking echocardiography in patients with FAP.
Methods: Prospective study of patients with FAP undergoing LT. Global longitudinal strain (GLS) and global longitudinal systolic (GLSR-S), protodiastolic (GLSR-E) and end-diastolic (GLSR-A) strain rate were evaluated prior to surgery and repeated at least 1 year thereafter.
Results: Eighteen patients (66.7% female; 39 ± 7 years) with FAP undergoing LT were included. At baseline the neurophysiological median score was 5 [Interquartile range (IQR): 0-14]. All patients had mild neurological symptoms, but none exhibited cardiovascular symptoms. The severity of neurological involvement correlated with the GLSR-S impairment (Pearson R: 0.49, P=0.042). Sixty seven percent of patients had significantly improvement of GLS 3.5 years (median) after LT (post-LT: -18.9 ± 3.0% vs. pre-LT: -17.4 ± 2.4%; p = 0.05). There was consistency between GLS variation and the improvement of the other deformation parameters (GLSR-S variation: Pearson r=0.66, P=0.003; GLSR-E variation: Pearson R=-0.55, P=0.019; GLSR-A variation: Pearson R=-0.55, P=0.017). Variation of myocardial deformation did not depend on age, duration of symptoms or severity of neurological involvement.
Conclusion: Patients with FAP have subclinical changes in systolic function assessed by myocardial deformation analysis, which correlates with the neurological involvement of the disease. After LT, changes in myocardial deformation tend to be reversed.

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RESOLUTION OF THE S WAVE IN LEAD I: A CRITERION OF SUCCESSFUL THROMBOLYSIS IN ACUTE PULMONARY EMBOLISM

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Objective: To determine whether a simple, readily applicable electrocardiographic (ECG) criterion such as rapid reduction of the S wave in lead I(SI),will allow early prediction of successful thrombolysis in patients with acute massive pulmonary embolism(PE).
Background: In contrast to myocardial infarction, there are no strict ECG criteria for assessing the efficacy of thrombolysis in acute pulmonary embolism.
Methods: Our study enrolled two hundred patients admitted in our Department with the diagnosis of massive PE (confirmed by computed tomography scan) during a period of thirteen years (from July 2001 to May 2014). Thrombolysis involved the use of alteplase at a dose of 100 milligram over a 2-hour period followed by unfractioned heparin as a bridge to anticoagulation with warfarin. A baseline(pre-thrombolysis)12-lead ECG was recorded immediately before initiation of alteplase and at 60 minutes,120 minutes and 24 hours thereafter(post-thrombolysis ECG).The ECG marker studied was the S wave in lead I >1 millimeter. Patients with either contraindication to fibrinolysis and previously intraventricular conduction defects were excluded from the study.
Results: Two group were created: group A including 136(68%) patients with successful thrombolysis and group B including 64(32%) subjects with unsuccessful thrombolysis. We observed a newly emerged deep SI in 114(84%) of the patients in group A and SI was present in 51(80%) of the subjects in group B. Rapid reduction of SI in the post-thrombolysis ECG in the first 24 hours was detected in 102(90%) of the patients in group A. There was no resolution of the SI in any of the patients in group B after completion of the fibrinolysis in the first 24 hours.
Conclusions: Resolution of the S wave in lead I can be used as an ECG marker and a simple bedside tool for predicting of successful reperfusion after thrombolysis in acute pulmonary embolism.

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EXERCISE HEMODYNAMICS AMONG PATIENTS WITH DYSPNEA ON EXERTION

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Background: Among patients with shortness of breath, whose echocardiogram suggests pulmonary arterial hypertension, the next step is a right heart catheterization. Patients symptoms are at exercise thus, we elect to measure exercise hemodynamics. We present series of patients whose hemodynamics suggest diastolic dysfunction causing pulmonary venous hypertension on exercise.
Methods: After informed consent, patients had right heart catheterizations and had normal hemodynamics at rest. We exercised these patients for 3 minutes with a 2.5 pound weight with repeat hemodynamics. Patients were also subjected to a cardiopulmonary stress test (CPET).

Results:

Mean PA Pressure	Patient Number	Mean PA pressure with exercise
Lesser than 25 mm at baseline (normal)	53	unchanged
Greater than 25 mm at baseline	30	NA
Lesser than 25 mm at baseline (normal)	49	increased (15 of 19 had elevation of PCWP above 18 mm)

Among 49 patients out of 102 who had normal mean PA pressure at baseline, 19 showed a rise above 25 mm with 3 minutes of exercise and 15 of these had their PCWP rise above 18 mm Hg. Thus a third of patients who have shortness of breath had normal resting hemodynamics with evidence of diastolic dysfunction with 3 minutes of exercise. These patients had a low VO2 max on CPET along with a blunted rate of rise of stroke volume curve on Wasserman Curve.
Discussion: We propose that symptomatic patients who undergo right heart catheterization should be assessed with exercise.

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PERICARDIAL DECOMPRESSION SYNDROME: AN ENTITY IN NEED OF URGENT ATTENTION

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Background: Pericardial decompression syndrome (PDS), defined as paradoxicalhemodynamic deterioration and/or pulmonary edema, frequently associated with left (LV), right (RV), or bi-ventricular dilation and systolic dysfunction following pericardiocentesis, has been reported uncommonly. Pathophysiology of PDS is poorly understood. However, it has been associated with increased periprocedural mortality.
Methods & Results: We encountered a cluster of 3 cases and a systematic literature search identified 40 reported cases of PDS [n=43, age 16-91 (mean 48±18) years, 28 (65%) female]. Pre-procedural echocardiogram showed normal LV ejection fraction in 92% and evidence of tamponade in 60%. Overall, 23 had percutaneous, 17 had surgical drainage and 3 had both. Volume of drained pericardial fluid ranged from 450 to 2100 (914±431) ml. Fluid was hemorrhagic in 68% and underlying etiology was malignancy in 45%. Post-procedurally, ventricular dilation and systolic dysfunction was noted in LV (57%), RV (43%) or both (29%) ventricles. Peri-procedural recovery of ventricular function was documented in 96% (27/28), (within days to months) and mortality was 26% (11/43). Rapid drainage of large pericardial effusion appeared to correlate with presence and severity of PDS and occurrence of poor outcome.
Conclusions: PDS is being recognized as an important complication of pericardiocentesis with increasing frequency. Understanding of pathophysiology of this potentially fatal condition requires a focused approach. Meanwhile, a caution approach to large, chronic pericardial effusion with stepwise or slow drainage (beyond relief of tamponade) appears warranted for prevention of PDS.

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BIOMARKERS IN THE RESPITE TRIAL INVESTIGATING RIOCIGUAT IN PAH PATIENTS WITH INSUFFICIENT RESPONSE TO PDE-5I

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Rationale: A significant proportion of pulmonary arterial hypertension (PAH) patients fail to reach or maintain treatment goals with phosphodiesterase-5 inhibitors (PDE-5i). Because PDE-5i effect depends on endogenous bioavailability of nitric oxide (NO), NO deficiency may be a key feature in patients failing PDE-5i treatment. The RESPITE study will investigate whether replacement of PDE-5i therapy with riociguat, a soluble guanylate-cyclase (sGC) stimulator, can improve clinical outcome in PAH patients demonstrating insufficient response to PDE-5 inhibition.
Methods: Riociguat directly stimulates sGC independently of NO, potentially restoring the NO-sGC- cyclic guanosine monophosphate (cGMP) pathway. The RESPITE study is a prospective, international, multicenter, open-label, single-arm, phase IIIb trial in PAH patients with WHO Functional Class (FC) III, 6 minute walk distance (6MWD) of 165-440 m, and cardiac index < 3.0 L/min/m2 despite stable doses of sildenafil or tadalafil for at least 90 days. Patients will undergo a PDE-5i wash-out phase and will then receive therapy with riociguat for 24 weeks. In addition to clinical endpoints including invasive hemodynamic measurements, echocardiogram, 6MWD, and WHO FC, a number of biomarkers will be explored. These include N-terminal pro-brain natriuretic peptide, cGMP (from blood and urine), asymmetric dimethyl arginine, growth differentiation factor 15, and suppression of tumorigenicity 2. These biomarkers will be analyzed at a central lab prior to initiation of riociguat, at 12 weeks and 24 weeks of treatment.
Conclusion: The characterization of biomarkers relevant to the NO Pathway in PAH patients enrolled in RESPITE could help elucidate the concept of "NO deficiency" in PAH patients.

NEW DIAGNOSTIC METHODS AND IMAGING TECHNIQUES / ECHOCARDIOGRAPHY

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DOBUTAMINE STRESS ECHOCARDIOGRAPHY FOR CARDIOVASCULAR RISK STRATIFICATION PRIOR TO RENAL TRANSPLANT

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Background: Coronary artery disease (CAD) is a major cause of death in renal transplant (RT) candidates with end-stage renal disease (ESRD). Dobutamine stress echocardiography (DSE) has been used for CAD screening in this setting, however, data on its prognostic significance is limited.
Methods: Electronic databases (PubMed, ScienceDirect, and COCHRANE) were searched with the MESH terms RT, DSE, ESRD, and prognosis. Studies were included if they reported on cardiovascular events in patients with ESRD evaluated for RT.
Results: 7 studies (n=643, 1486 patient years of follow up) met selection criteria (age 52 years, 64% men, 58% diabetics, 91% hypertensive, 32% smokers and 25% prior CAD). Using pooled data (figure 1a-c), abnormal DSE was associated with significant increase in MACE [odds ratio (OR)=3.94 (95% confidence interval (CI) 2.27-6.84, p<0.00001]. Risk of cardiac death (CD) and myocardial infarction (MI) was increased with abnormal compared to normal DSE [OR=4.77 (95% CI 2.13-10.7), p=0.0001]. Abnormal DSE was associated with higher risk of all-cause mortality [OR=5.16 (95% CI 1.79 to 14.85), p=0.002].
Conclusions: Patients with abnormal DSE had increased risk of MACE, all-cause mortality and combined CD and MI during follow up. DSE can be effectively used for risk stratification of patients with ESRD awaiting RT.

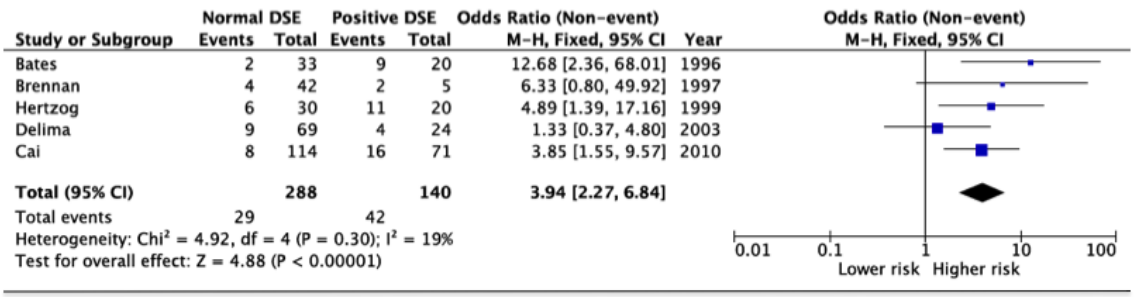

Figure 1a: Meta-analysis of the risk of major adverse cardiovascular events (MACE) in patients with abnormal Dobutamine stress echocardiography (DSE) compared to normal DSE.

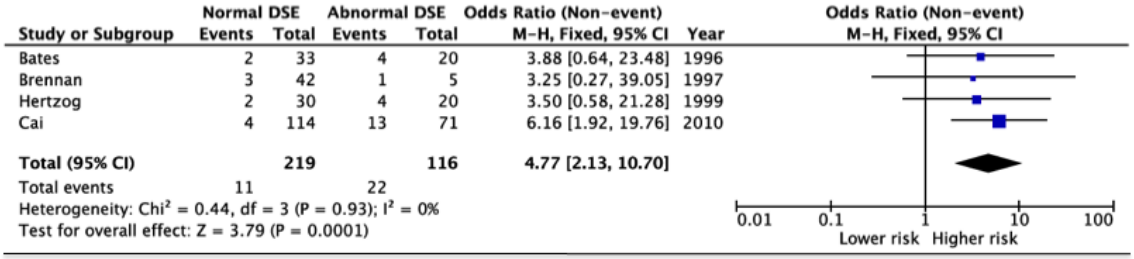

Figure 1b: Meta-analysis of the risk of combined cardiac death (CD) and myocardial infarction (MI) in patients with abnormal Dobutamine stress echocardiography (DSE) compared to normal DSE.

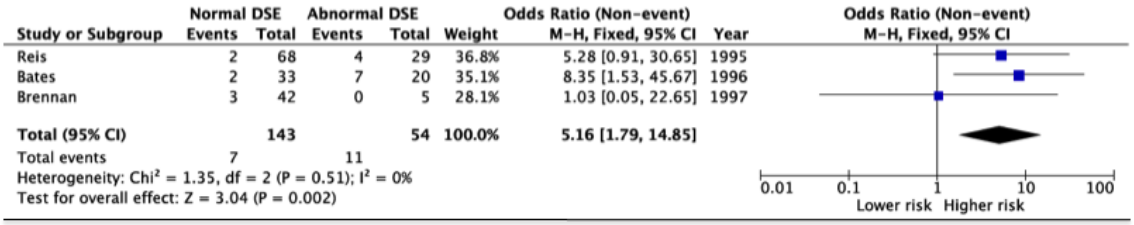

Figure 1c: Meta-analysis of the risk of all cardiac death (ACD) in patients with abnormal Dobutamine stress echocardiography (DSE) compared to normal DSE.

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UTILITY OF HAND HELD ECHO FOR ASSESSMENT OF LEFT ATRIAL VOLUME IN CLINICAL SETTINGS

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Background: Echocardiography (echo) is an essential imaging modality, but in many regions demand has outpaced the capacity to provide timely results. Current hand-held echo (HHE) systems have high imaging and computational processing capabilities. While HHE is not equivalent to a full clinical echo system, it may provide useful point-of-care data in certain scenarios, enabling treatment decision to be made quickly. We compared the accuracy of HHE (VScan, GE Medical) versus clinical echo systems for evaluation of left atrial volume (LAV), an established marker of adverse cardiac outcomes.
Methods: We aimed to assess the concordance between left atrial parameters obtained with a full clinical echo system and the HHE system. Adults (age >18 yrs) presenting for an outpatient comprehensive clinical echo were invited to undergo a brief assessment with the HHE system immediately after the clinical echo. Subjects with congenital heart disorders, prosthetic valves, left ventricular assist devices or in atrial fibrillation were excluded. We obtained 2D 4-chamber and 2-chamber views using the HHE, and images were downloaded for offline LAV assessment using standard biplane area length methods without knowledge of the clinical echo findings.
Results: Clinical echo and HHE images were obtained for 74 subjects (median age 68.5, range 32-88 years; 39 women). Analysis of calculated LA volume from HHE versus clinical echo showed a good correlation overall (0.84), without any significant gender effect, but with a marked operator experience effect; correlations based on the first 20 subjects examined were substantially lower than for later enrolled subjects (0.81 versus 0.96).
Conclusions: In the hands of a trained and experienced operator, HHE assessment of LAV shows a high correlation (0.96) with results from a standard clinical echo system. There was a clear cut learning curve for proficient use of HHE. Point of care utilization of HHE for risk stratification appeared eminently feasible.

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3D ECHO CAN BE USED TO OPTIMIZE PACING ALONG THE LONGITUDINAL LEFT VENTRICULAR AXIS WHEN USING A MULTIPOLAR LEAD

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During biventricular device placement optimal lead position along the longitudinal axis of the lateral left ventricular (LV) wall remains a subject of debate. Using the St. Jude Quartet lead, which features four electrodes and ten pacing vectors, we set out to determine if pacing different sites along the longitudinal LV axis leads to differences in improved LV dyssynchrony (LVD) as measured by the systolic dyssynchrony index (SDI). Six veterans underwent implantation of a biventricular device using the Quartet lead from January to September 2012. Each patient underwent post-procedure LV volumetric analysis with 3D echocardiography. Mean SDI with biventricular pacing turned off was compared with LV pacing at different sites along the lateral LV longitudinal axis. All patients had significant LVD during native conduction, with a mean SDI of 14.7 +/- 3.2% (5.6% = upper limit of normal). Mean SDI when using the optimal LV pacing vector for each subject was 4.8 +/- 2.7%, an improvement of nearly 10% (14.7 vs. 4.8, P = 0.006). When pacing locations along the LV longitudinal axis were compared, only pacing along the mid LV cavity as opposed to the base and apex provided a statistically significant improvement in dyssynchrony when compared to native conduction (14.7 vs 5.3, P=0.007).Using 3D echocardiography following biventricular device implantation with quadripolar LV pacing, we were able to demonstrate that LVD acutely improves when pacing the lateral left ventricle. Ventricular dyssynchrony improved the most when pacing the mid lateral LV cavity as opposed to the base or apex.

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DIASTOLIC MYOCARDIAL STIFFNESS ESTIMATED BY ECHOCARDIOGRAPHY IN PATIENTS WITH AORTIC STENOSIS

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Background and Aims: The speed of wave transmission of myocardial stretch has been validated as a direct measure of myocardial elasticity. We hypothesize this wave speed (Vp) may be increased in the left ventricular (LV) myocardium of patients with LV pressure-overload (e.g., aortic stenosis, AS) due to high LV afterload and its long-term consequences. Our aim was to determine Vp values in the LV myocardium of patients with severe AS.
Methods: We studied 46 patients with diagnosed severe AS (aortic valve area 0.9±0.2 cm2, mean pressure gradient 51±14 mmHg, age 72±11 years) and 20 normal controls (age 58±14 years). Regional Vp (along each LV wall) and global Vp were measured from 3 standard apical views using customized ultra-high frame rate tissue Doppler. All subjects had comprehensive echocardiographic exams.
Results: Global Vp was higher in AS compared to controls (1.9±5.8 vs. 1.4±0.2 m/s respectively, $p<0.001$). Abnormal Vp (>1.8 m/s, upper value in controls) was found in 52% of patients, despite normal LV ejection fraction (EF, 65±6%) and nearly normal global longitudinal strain (GLS, -18.2±2.9%) by speckle tracking. In patients with normal GLS (<-18%), an abnormal Vp was still found in 10 (22%) patients. Higher Vp was associated with smaller aortic valve areas ($p<0.001$), more reduced GLS ($p=0.02$) and higher filling pressures (E/e', $p=0.002$), but not with age ($p=0.107$) or EF. A regional heterogeneity in Vp was observed.
Conclusions: Patients with severe AS have increased LV diastolic myocardial stiffness as estimated by the intrinsic wave method. This increase could be the result of abnormal filling pressures and tissue properties (e.g., due to fibrosis deposition) that occur with chronically elevated LV afterload. Noninvasive measurement of myocardial stiffness may be a new imaging biomarker that may facilitate early identification of structural abnormalities in the LV of patients with severe AS.

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EXERCISE STRESS ECHOCARDIOGRAPHY BETTER PREDICTS MYOCARDIAL ISCHEMIA THAN EXERCISE ECG IN FEMALE PATIENTS WITH CHEST PAIN

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Objective: The purposes of this study were 1) to determine the diagnostic accuracy of Exercise stress echocardiography (ESEcho) in female patients with chest pain, and 2) to evaluate the clinical outcomes of coronary angiography, revascularization, and cardiac events in Korean female patients undergoing ESEcho.
Background: ESEcho is sufficiently sensitive and has high enough specificity for the clinical detection of coronary artery disease (CAD) in women. However, the ability of ESEcho to predict clinical outcomes in female patients with chest pain remains unknown.
Methods: Over a period of 15 years, 3,396 patients (57±10 yrs) among 3,930 female patients with chest pain undergoing ESEcho and exercise stress electrocardiography (ESECG) were assessed.
Results: Positive results for ESEcho (newly developed regional wall motion abnormality) were seen in 134 patients (3.9%). Conventional coronary angiograms or coronary computed tomography angiograms were obtained for 325 patients (9.6%). Significant coronary artery disease (CAD) was diagnosed in 30 patients (10 of 260 patients with negative ESEcho results and 20 of 65 patients with positive ESEcho results). The sensitivity and specificity of ESEcho were 66.7% and 84.8% respectively. Among 2022 patients with available clinical outcomes, myocardial infarction (MI) and revascularization occurred more frequently in patients with positive ESEcho results (6.7% vs. 0.1%, $p < 0.01$). Positive ESEcho was an independent predictor of major adverse cardiac events (composite of cardiac death, MI, and revascularization) in multivariate analyses.
Conclusions: ESEcho is effective for diagnosing CAD in female Korean patients with chest pain. Negative ESEcho results were associated with favorable cardiac outcomes, but its prognostic value needs to be validated in a large-scale prospective study.

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CENTRAL OBESITY: AN INDEPENDENT ROLE OR SYNERGISTIC EFFECT TO METABOLIC SYNDROME ON RIGHT VENTRICULAR STRUCTURE AND FUNCTION?

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Background: The metabolic syndrome (MS) has been shown to affect the right ventricle (RV). Whether the impact of central obesity (CO) on RV function is independent of the MS is uncertain.
Objective: To assess the impact of CO with or without MS diagnosis on RV structure and function.
Methods: Cross-sectional study of 100 patients (56 women) with CO defined as a waist circumference (WC) >102 cm in men, >88 cm in women. MS was defined by the presence of ≥ 3 ATP-NCEP-III criteria. All patients were subjected to conventional and tissue Doppler (TD) echocardiography.
Results: MS was diagnosed in only 57 patients. The RV wall thickness (RVWT), and RV outflow tract proximal dimension (RVOTPD) were significantly higher (p= 0.008, and p=0.003) in MS compared to non-MS patients. Tricuspid flow E/A ratio was significantly lower in MS compared to non-MS patients (p = 0.001). TD derived RV myocardial performance index (MPI) was significantly higher (p= 0.000) in MS compared to non-MS patients. The tricuspid annular plane systolic excursion and the RV fractional area change were however similar in MS and non-MS patients. The independent predictors for RVWT, RVOTPD were WC (ß=0.004, p=0.000 and ß= 0.008, p=0.005 respectively) and systolic blood pressure (SBP) (ß=0.001, p=0.037 and ß=0.004, p=0.016 respectively), for RV MPI was SBP (ß = 0.003, p= 0.000) and for tricuspid E/A ratio was age (ß = -0.008, p= 0.000) after multivariable adjustment for WC, age and different components of MS.
Conclusion: CO in the presence of MS has a greater synergistic impact on RV structure and function than CO alone. WC and SBP had a significant impact on RV dimensions while SBP alone had a significant impact on RV function independent of the other components of the MS.

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VALUE OF RESTING MYOCARDIAL DEFORMATION ASSESSMENT BY TWO DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY IN DETECTING THE PRESENCE, AND PREDICTING THE EXTENT AND LOCALIZATION OF CORONARY ARTERY AFFECTION IN PATIENTS WITH SUSPECTED STABLE CORONARY ARTERY DISEASE

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Background: Myocardial deformation assessed by 2D speckle tracking echocardiography (STE) can accurately evaluate regional and global left ventricular (LV) function. Aim: Examine the value of peak systolic LV strain (S) and strain rate (SR) assessed by STE in detecting, stratifying and localizing coronary artery disease in stable coronary artery disease (SCAD).
Methods: 81 suspected SCAD patients, normal resting echocardiography, were examined by 2D-STE and coronary angiography. The global longitudinal strain (GLS)/SR=GLSR; global radial strain (GRS)/SR=GRSR were calculated as the mean of the sum of S/SR in the 18 segments from apical views. Mid circumferential strain (MCS)/SR=MCSR were calculated as the mean of S/SR of the 6 LV segments of the mid cavity short axis view. Significant CAD definition was >50% diameter stenosis.
Results: Twenty patients had normal coronaries, 27 patients had one/two vessel-CAD (stratified low risk LR) and 34 patients had three vessel/left main-CAD (stratified high risk HR). GLS, GLSR, GRS, GRSR, MCS and MCSR were significantly lower in CAD compared to normal coronaries (p=0.000). By receiver operating characteristic (ROC) curve analysis, GLSR showed the highest sensitivity (90 %) and specificity (96.7%; AUC=0.98, 95% CI: 0.95-1.0; p=0.000) for predicting CAD (cut-off value -1.55 1/s). GLS, GLSR, GRSR, MCS and MCSR were significantly lower in HR compared LR (p=0.03, p=0.009, p=0.000, p=0.000, and p=0.004 respectively); whilst MCS best differentiated LR from HR (cutoff value -20.87%, sensitivity: 88.9 %, specificity: 76.5%, AUC=0.83, 95% CI: 0.73-0.94; p=0.000). ROC curve analysis showed the mean of longitudinal strains of the anterior wall and septum to best predict LAD disease (sensitivity=90%, specificity=91.1%). Mean longitudinal strain of posterior and lateral wall segments best predicted LCX disease (sensitivity=95%, specificity=80%). Mean circumferential strain of mid inferior wall best predicted right coronary disease (sensitivity=83.3%, specificity=78.8%).
Conclusion: STE calculated myocardial deformation diagnoses, stratifies and localizes CAD in SCAD.

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IMPROVEMENTS IN LEFT ATRIAL APPENDAGE VELOCITIES FOLLOWING TRANSCATHETER AORTIC VALVE REPLACEMENT

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Objectives: We aimed to assess the effect of transcatheter aortic valve replacement (TAVR) on LAA emptying and filling velocities.
Background: Left atrial appendage (LAA) is a common source of systemic thromboembolism. LAA velocity predicts future thromboembolism risk.
Methods: Medical records of patients who underwent TAVR at a single center were retrospectively reviewed. LAA velocities were recorded before and after TAVR by transesophageal echocardiography. Low flow-low gradient severe aortic stenosis (LFLG-SAS) patients were defined as stroke volume index < 35 ml/m2 and mean aortic pressure < 40 mmHg. Patients with persistent atrial fibrillation were excluded.
Results: Forty-five patients were included. Mean age was 79±9, male was 51%. There were 12 (27%) LFLG-SAS patients. LAA emptying and filling velocity pre and post TAVR for LFLG-SAS patients were 30.8 (21.6-50.9) cm/sec vs 42.4 (38.8-55.4) (p<0.01) cm/sec and 31.5 (22.2-36.5) cm/s vs 39.6 (31.8-53.4) (p<0.01) cm/s, respectively (Figure 1) whereas for non-LFLG-SAS patients it was 29.5 (19.7-37.3) cm/s vs 30.3 (21.0-42.7) (p=0.42) and 29.5 (19.7-37.3) vs 25.7 (21.2-39.7) (p=0.86), respectively.
Conclusions: Our study showed improved LAA velocities in LFLG-SAS patients shortly after TAVR but not in non-LFLG-SAS patients. Whether these improvements translates into future fewer thromboembolic events needs further study.

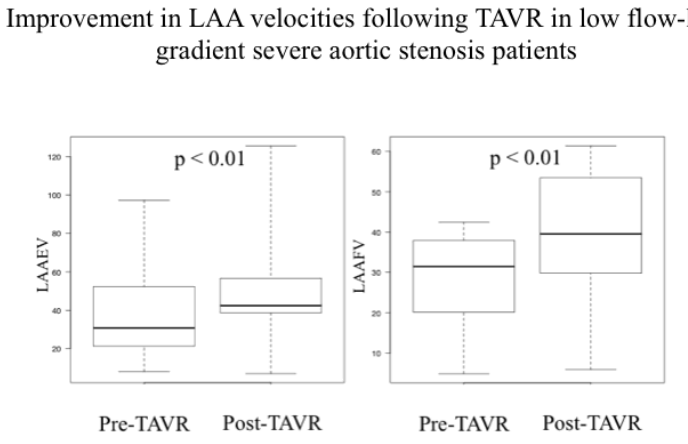

Figure 1

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INVESTIGATION OF GRAVITY OF THORACIC AORTIC ATHEROSCLEROSIS COMPARED TO AGE, SEX AND PRESENCE OF THROMBOUS IN LEFT ATRIAL APPENDAGE

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Aim: The purpose of this study is to investigate the existence or non-correlation between the severity of atherosclerosis of the thoracic aorta with age, gender and the presence of thrombus in the left atrial appendage
Methods: 39 adults (15 women, 24 men) who underwent transesophageal ultrasound this year in our clinic were used to collect the data. The parameters studied were the thickness of the plaque at the level of thoracic aorta mm xo, 1, the presence of contrast media, the presence of thrombus in the left atrial appendage and the flow rate of the flap of the left atrium.
Results: From the analysis of the data showed correlation between the severity of the atherosclerotic thoracic aorta with increasing age ($r=0.567$, $p<0.01$). It was also shown that the incidence of atherosclerosis of the thoracic aorta is greater in men ($r=0.595$, $p<0.01$) than women ($r=0.530$, $p=0.02$). Further analysis of the data revealed the presence of echo contrast at 33.3% of the total examined, the presence of thrombus in the left atrial appendage at a rate of 33.3% and in the presence of low flow velocity in patients they brought thrombus in left atrial appendage. The percentage of women with thrombus in the left atrial appendage was 46% (7 out of 15) and the percentage of men with thrombus in the left atrial appendage was 25% (6 out of 24).
Conclusions: There is positive correlation between the severity of atherosclerosis of the thoracic aorta with increasing age with greater incidence observed among men compared with women. Presence of thrombus in the left atrial appendage appeared more frequent in women rather than men in patients with atherosclerotic thoracic aorta.

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PROFILES AND PROGNOSIS OF PATIENTS WITH SEVERE CAROTID ARTERIOSCLEROSIS

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There have been few reports on prognosis of severe carotid sclerosis in association with other cardiovascular disease.

Methods: Severe carotid sclerosis was diagnosed by carotid ultrasonography, and plaque score (PS) was calculated by summation of max thickness of each plaque. 242 patients with severe carotid sclerosis • iSCS: PS more than 10 • jwere studied and compared those with mild carotid sclerosis • iMCS: PS less than 5 • j. Patients with significant carotid stenosis (more than 50% in diameter) were excluded. The 262 patients with MCS were compared.

Results: In patients with SCS, mean age was 72.7, and mean PS was13.8. Cerebral infraction (CI) was observed in 76 patients(31.4%). Cardiovascular disease was observed in 95(39.2%), and coronary artery disease (CAD) only was observed in 71 (29.3%). Antiplatelet therapy had been done in 46% of patients with SCS and in 12% of MCS. In patients with MCS, mean age was 69.5, and mean PS was 3.82. CI was observed in 28 patients(10.69%) • iP=0.0001 vs SCS • jCardiovascular disease was observed in 26 patients(9.92%),and coronary artery disease(CAD) only was observed in 20(7.63%)(P=0001 vs SCS). In 3 year follow up, CI developed in 8 out of 242 with SCS, and in 4 out of 262 patients with MCS. All patients who developed CI had other cardiovascular disease. Mean number of risk factor was 2.2 • 1.1 in patients who developed CI and 1.8 •

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SERUM CYSTATIN C IN PATIENTS WITH CORONARY STENTS AND RISK OF RESTENOSIS

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Objectives: To investigate whether patients with atherosclerosis after coronary stenting display altered serum cystatin C as a possible biomarker of acute ischemia.
Background: The incidence of coronary restenosis after stent placement is high, especially in the 1-year follow-up. Inflammation plays an important role in the pathogenesis of in-stent restenosis, causing neointimal proliferation through the stent meshes. Subsequent in-stent restenosis may affect the long-term safety and efficacy of angioplasty and stenting. Cystatin C was recently suggested as a candidate biomarker in cardiovascular pathology.
Methods: 34 male patients (61.8 ± 7.3 years) treated by anticoagulant therapy were enrolled in a study from the Outpatient Clinic N 1 of Novosibirsk (6 mos - 1 year after coronary stenting). The control group consisted of 25 healthy persons (50-65 years old). Serum CRP-hs, D-dimer (Architect C-8000, USA) and Cystatin C by ELISA kit for humans (BioVendor, Czechia) were measured in all groups. Results. In healthy persons, aged 50-65, an elevation of serum cystatin C (1.11± 0.23 mg/L, $p< 0.01$) was shown vs. healthy persons, aged 20-40 years. In patients with coronary stents, there was a significant increase in serum CRP-hs ($p < 0.001$), D-dimer ($p < 0.001$) and cystatin C (2.05 ± 0.21 mg/L, $p < 0.001$) vs the control (aged 50-65). Positive correlation was shown between cystatin C and d-Dimer in stenting patients ($r = 0.45$; $p < 0.05$).
Conclusions: Serum cystatin C is elevated in patients with coronary stenting, as well as CRP-hs, indicating on inflammation, increased risk of in-stent restenosis and ischemia.

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IS THERE ANY CORRELATION BETWEEN PLATELET INDICES WITH EXTENT OF CORONARY ARTERY INVOLVEMENT AMONG PATIENTS WITH ISCHEMIC HEART DISEASES?

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Objective: Ischemic heart diseases (IHD) is the most common form of heart disease and death across the world. Nowadays Platelet counts (PC) and volumetric platelet indices using automatic counters are available routinely in most laboratories and reflect the level of mobility and the production of platelets. It seems that the excessive flexibility of the platelets and their local activation have a major role in acute coronary events. So, our objective is the study of platelet indices in ischemic heart disease and trying to find out a clinical-pathological correlation.
Materials and methods: This non-randomized prospective study was performed on 247 patients with ischemic heart disease, who underwent the coronary angiography. The patients were divided into four groups: stable angina, unstable angina, acute myocardial infarction and control group; and then platelet indices, including the platelet counts (PC), the average platelet volume (MPV), the Platelet Distribution Width and plateletcrit (PCT) in each group with the extent of coronary disease were compared based on an Syntax Score System.
Results: The average ages of the patients were 57 years and 65% of them were male and the rest were female. A significant difference existed between indexes in all three groups compared to the control that this difference was related to gender and the type of the disease however, only in infarction group, PDW in different disease intensities was significantly different.
Conclusion: In this study, unlike many of the previous studies no relationship was found between the MPV with the extent of coronary disease.

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THE DIAGNOSTIC VALUE OF THE NEUTROPHIL-LYMPHOCYTE RATIO IN STROKE RECOGNITION

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Background: The role of the neutrophil-lymphocyte ratio (NLR) in stroke diagnosis has not been thoroughly evaluated. The NLR has been recognized as a marker of inflammation. Since a stroke causes local inflammation, the NLR should be influenced. However, since this inflammation is the result of aseptic damage of the relatively small affected area of the brain, an NLR that is excessively divergent from the average value decreases the likelihood of a stroke's presence. The NLR can be calculated using a routine blood test.
Objective: This study determined the diagnostic value of the NLR in stroke recognition.
Methods: Data of all incoming patients with suspected stroke from Raritan Bay Medical Center over the period of 3 years (2010-2013) was collected. The significance of age, sex, smoking, presence of diabetes, abnormal renal function, and dyslipidemia was ruled out using the t-test and chi-squared test. The Receiver Operating Characteristic (ROC) for different NLR values was compared by constructing ROC space, ROC inverse charts, and ROC contingency tables.
Results: The study revealed the inverse correlation between the NLR and stroke presence. An NLR above 4.0 decreases the likelihood of the presence of a stroke, while an NLR lower than 4.0 makes the diagnosis of a stroke more probable in patients with stroke-like symptoms.
Conclusion: The NLR has diagnostic value in stroke recognition. It can be used as a tool in ruling out the presence of a stroke.

PREVENTION OF CARDIOVASCULAR DISEASE: ASSESSMENT AND MANAGEMENT OF CARDIOVASCULAR RISK

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CLINICAL IMPACT AND COST-EFFECTIVENESS OF TREADMILL TEST IN ASYMPTOMATIC INDIVIDUALS

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Objectives: The purpose of this study was to investigate the clinical impact and cost-effectiveness of treadmill test in asymptomatic individuals.

Methods and Results: We analyzed 8,694 propensity-score matched asymptomatic individuals aged 18 years and older with no prior history of cardiovascular disease who underwent self-referral treadmill test evaluation as part of a general health examination (treadmill test [n=2,898] versus control [n=5,796]). Clinical outcome was defined as a composite of all-cause death, myocardial infarction, and stroke in 1 year after the index test. Subsequent use of cardiac tests, total medical costs, and coronary artery disease (CAD)-related medical costs were investigated within 6 months of the index test. Compared with the matched control group, the treadmill test group underwent further cardiac tests (3.90% versus 2.43%, p<0.001). However, coronary revascularizations were less frequently performed in the treadmill test group (0.03% versus 0.21%, p<0.001) and the primary composite clinical outcome was not statistically different between the two groups (0.14% versus 0.28%, p=0.157). Total medical costs were higher in the treadmill test group ($544 versus $492, p=0.045), but CAD-related costs were not different between the two groups ($12 versus $15, p=0.611) for 6 months. However, considering the baseline cost of a treadmill test ($42), the treadmill test group had higher 6-month CAD-related medical costs (p<0.001)

Conclusions: In asymptomatic individuals, screening with treadmill test was associated with higher subsequent cardiac tests and medical costs, but did not decrease the 1-year risk of death, myocardial infarction, and stroke.

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MODEL FOR ASSESSING CARDIOVASCULAR RISK IN A KOREAN POPULATION

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Background: A model for predicting cardiovascular disease in Asian populations is limited.
Methods and Results: In total, 57,393 consecutive asymptomatic Korean individuals aged 30 to 80 years without a prior history of cardiovascular disease who underwent a general health examination were enrolled. Subjects were randomly divided into the train (n=45,914) and validation (n=11,479) cohorts. Thirty-one possible risk factors were assessed. The cardiovascular event was a composite of cardiovascular death, myocardial infarction, and stroke. In the train cohort, the C-index (95% confidence interval) and Akaike Information Criterion were used to develop the best-fitting prediction model. In the validation cohort, the predicted versus the observed cardiovascular event rates were compared by the C-index and Nam and D'Agostino X2 statistics. Over a median follow-up period of 3.1 (interquartile range, 1.9–4.3) years, 458 subjects had 474 cardiovascular events. In the train cohort, the best-fitting model consisted of age, diabetes mellitus, hypertension, current smoking, family history of coronary heart disease, white blood cell, creatinine, glycated hemoglobin, atrial fibrillation, blood pressure, and cholesterol (C-index=0.757 [0.726–0.788] and Akaike Information Criterion=7,207). When this model was tested in the validation cohort, it performed well in terms of discrimination and calibration abilities (C-index=0.760 [0.693–0.828] and Nam and D'Agostino X2 statistic=0.001 for 3 years; C-index=0.782 [0.719–0.846] and Nam and D'Agostino X2 statistic=1.037 for 5 years).
Conclusion: A risk model based on traditional clinical and biomarkers has a feasible model performance in predicting cardiovascular events in an asymptomatic Korean population.

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CARDIOVASCULAR RISK AND HEALTH-RELATED QUALITY OF LIFE (HRQOL) AMONG HIV-POSITIVE PATIENTS IN US HOUSEHOLD POPULATION: THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) 1999-2012

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Cardiovascular disease has emerged as a problem among HIV-infected population and may have a profound impact on quality of life. Although previous studies found a higher cardiovascular risk linked to worse health-related quality of life (HrQoL) among general population, limited studies have been conducted for HIV patients. This study is to characterize HIV-positive adults in household population in terms of cardiovascular risk and HrQoL using large national survey datasets.
Methods: The analyses utilized the data of NHANES 1999-2012 which included a valid sample of 119 HIV-positive cases and 357 HIV-negative controls matched by age, gender, race, and survey year. Cardiovascular risk was measured by using Framingham 10-year risk scores. HrQoL was measured by using the CDC 4-item HrQoL. A series of conditional logistic regression analyses was conducted to determine the difference of cardiovascular risk and HrQoL between HIV-positive and –negative adults.
Results: Among 119 HIV-positive patients, 72.4% were male and 66.4% were African Americans. Their mean age was 39.1(±8.6). A lower level of HDL ($p<0.0001$), Framingham 10-year cardiovascular risk ($p=0.0659$), waist circumference ($p=0.0074$), and BMI ($p=0.0016$) was observed among cases. Controls reported a lower level of number of days mental health was not good ($p=0.0581$), inactive days due to mental and physical health ($p=0.0002$), LDL ($p=0.0314$), and times received healthcare in past year (<0.0001). Cases were more likely to have at least one disease history ($p=0.0338$) and a higher prevalence of chronic kidney disease (6.3% for cases and 1.3% for controls; $p=0.0275$).
Conclusion: Our study found that although HIV-positive cases had favorable anthropometric measurement and cardiovascular risk, they had worse health-related quality of life and received healthcare more frequently. However, it was not clear that worse HrQoL was caused by cardiovascular risk heightened by HIV infection. Further study is needed to examine the cause of worse health status of HIV-positive patients, controlling for anti-retroviral therapy and stage of HIV.

PREVENTION OF CARDIOVASCULAR DISEASE: ASSESSMENT AND MANAGEMENT OF CARDIOVASCULAR RISK

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THE DEVELOPMENT OF A LIFESTYLE INTERVENTION PROGRAM FOR PEOPLE WITH METABOLIC SYNDROME: BASED ON THE HEALTH BELIEF MODEL

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Background: Lifestyle intervention is advocated for people with metabolic syndrome (MS). However, interventions delivered across reviewed studies were inconsistent and insufficient to meet the needs of a Chinese population. Moreover, the lack of conceptual guidance limited the study's ability to explain the corresponding outcomes. In regard to the high prevalence of MS, an effective lifestyle intervention program by scientific approach is important for people with MS. This study aimed to develop a lifestyle intervention program by identifying needs from the targeted population as guided by the extended Health Belief Model (eHBM).
Methods: A cross-sectional survey based on eHBM was conducted to assess health behaviors and health beliefs on 132 Chinese with two or more MS components. Hierarchical regression approach was used to analyze the survey data. Synthesizing the survey results with current recommendations, a lifestyle intervention program (LIPMS) was developed.
Results: Self-efficacy and perceived barriers were found to have high predictive values to health behavior. These results provided directions for the development of LIPMS. LIPMS is a twelve-week program containing three components: two weekly group educational sessions, one brief individual counselling, and two telephone calls. The effects of LIPMS was tested in another RCT study and regarded as effective in terms of improving health outcomes and health behavior.
Conclusions: The use of the eHBM provides a conceptual framework to guide the development of LIPMS for people with MS. Lifestyle intervention program should include practical strategies to increase participant's self-efficacy for overcoming barriers perceived.

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INFLUENCE OF ALBUMINURIA ON AMBULATORY BLOOD PRESSURE REGULATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE: THE HYGIA PROYECT

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Objectives: Sleep-time hypertension and the non-dipper blood pressure (BP) profile determined by ambulatory BP monitoring (ABPM) are highly prevalent in chronic kidney disease (CKD). Although presence of kidney damage is intrinsic to the current definition of CKD, stratification of patients according to disease stages has been frequently based on estimated glomerular filtration rate (eGFR) alone, independent of presence or absence of albuminuria. We evaluated the potential influence of albuminuria on ambulatory BP in patients with stage 3-5 CKD participants in the Hygia Project, designed to evaluate prospectively cardiovascular, metabolic, and renal disease risk by ABPM in primary care centers of Northwest Spain.
Methods: This study involved 3339 patients with stage 3-5 CKD (eGFR <60 ml/min/1.73 m2 at least twice within 3 months), 1816 men/1523 women, 69.1±11.9 years of age. Among them, 1073 had albuminuria (albumin/creatinine ratio >30 mg/gCr). BP was measured at 20-min intervals from 07:00 to 23:00h and at 30-min intervals at night for 48h.
Results: Ambulatory BP was significantly higher in patients with than without albuminuria, mainly during the nighttime sleep span (awake/asleep BP means of systolic BP 137.0/129.0 vs. 131.1/122.2 mmHg, respectively, P<0.001). The sleep-time relative BP decline was significantly attenuated (5.6 vs. 6.7%, P<0.001) and, accordingly, the prevalence of the non-dipper/riser BP pattern significantly greater (67.8 vs. 63.2, P=0.002) in patients with albuminuria. Prevalence of sleep-time hypertension (asleep BP >120/70 mmHg) was also significantly larger in patients with albuminuria (70.3 vs. 56.2, P<0.001).
Conclusions: Our findings document the extremely high prevalence of altered circadian BP patterning in patients with CKD. Prevalence of sleep-time hypertension and/or non-dipper BP patterning, documented relevant prognostic markers of increased cardiovascular risk, was significantly greater in the presence of albuminuria. These findings corroborate the need to use both eGFR and albuminuria for proper stratification of patients according to CKD stage severity.

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THE RISK FACTORS THAT PREDICTING THE OCCURRENCE OR PROGRESSION OF CHRONIC HYPERTENSION IN POSTPARTUM PERIOD IN WOMEN WITH A HISTORY OF PREECLAMPSIA

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Purpose: Preeclampsia (PE) was one of the most important pregnancy complications to bring about the lethal effects to mothers, in addition this is associated with the subsequent development of future chronic hypertension. The purpose of this study was to identify the clinical risk factors progressing to the chronic hypertension in postpartum period in the women diagnosed with PE.
Methods: We included the 659 patients who were delivered as diagnosed with PE in index pregnancy. According to the subsequent development of chronic hypertension, we divided two groups as case group (n=73), presenting the chronic hypertension and normal control group (n=586). The clinical and demographic factors were evaluated. The duration of median follow-up was 51.2±31.8 months.
Results: By multiple regression analysis, high blood pressure in first trimester, comorbidities as renal disease, systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APLS), vascular disease, and higher body mass index (BMI) at previous pregnancy were associated with the progression of chronic hypertension in postpartum period. The incremental pattern of area under receiver operating characteristics (AUROC) for seven models, from 0.619 to 0.818, showed that the prediction of progression on the chronic hypertension improved to add the significant risk factors by multivariate analysis stepwise.
Conclusions: This retrospective registry demonstrated that the clinical risk factors as high blood pressure in first trimester, higher BMI, and comorbidities (renal disease, SLE or APLS, and vascular disease) were significantly independent predictors, which can identify the women at a risk of developing future chronic hypertension after delivery. Through identifying these risk factors for evaluating the capacity of progression, we could decide the particular women for monitoring and managing the high blood pressure in postpartum period.

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DIAGNOSTIC ACCURACY OF OFFICE BLOOD PRESSURE MEASUREMENT ACCORDING TO SEX AND AGE

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Objectives: To evaluated the diagnostic accuracy of office blood pressure (OBP) measurement.
Background: The OBP measurement is subject to many biases. Women have higher office BP, and older patients higher pulse pressure, so that the diagnostic accuracy of OBP may be lower in those patients.
Methods: We evaluated the diagnostic accuracy of OBP compared with 24-hour ambulatory BP (ABP) as reference BP in 1.028 patients. Hypertension was defined as systolic BP>140mmHg, and/or diastolic BP>90mmHg.
Results: The mean age was 58 years, 49% were male. The mean office systolic and diastolic BP was ±17mmHg and 84±12mmHg, respectively, and they were higher than those of ABP (SBP, 123±13mmHg; DBP, 78±11mmHg) (paired T-test P<0.001). There was only a week correlation between the OBP and ABP (r=0.180, P<0.001). Overall 44% showed discordance; 23% had false positive and 21% had false negative results. Women had twice higher false positive results than men (29% vs. 15.7%, p < 0.001), while men had higher false-negative results (25.9% vs. 17.3, P < 0.001). As for the age, the concordance rate was highest among patients <20 years (87.5%) and >80 years (78.8%), whereas in middle aged group it was around 55%.
Conclusions: The diagnostic accuracy of OBP is low. Women have higher false-positive, men higher false-negative results. High discordance between OBP and ABP indicates suboptimal management of hypertensive patients in both men and women. The use of ABP should be considered in all hypertensive patients.

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ABNORMAL CAROTID ARTERIAL MECHANICS DESPITE NORMAL INTIMA-MEDIA THICKNESS IN PATIENTS WITH DIABETES MELLITUS OR HYPERTENSION

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Background: Carotid intima-media thickness (cIMT) is an established surrogate marker of atherosclerosis. However, cIMT may not reflect the whole arterial changes occurring in various pathologic conditions, such as diabetes or hypertension.
Objective: The aim of this study was to evaluate whether vascular properties of CA differed in patients with hypertension or diabetes who have normal cIMT.
Methods: Vascular properties of CA were assessed in 402 consecutive asymptomatic subjects who have normal cIMT (151 patients with diabetes mellitus, 131 with hypertension, and 120 age- and gender-matched controls). Conventional carotid stiffness indices, including beta stiffness, distensibility coefficients and elastic modulus calculated from vessel diameter and blood pressure, and parameters from velocity-vector imaging (VVI), including vessel area, fractional area change (FAC), radial velocity, circumferential strain, and strain rate of CA were measured to assess the differences between the groups.
Results: Both patients with hypertension and diabetes showed higher elastic modulus, lower distensibility coefficients and FAC by VVI when compared to those of controls. However, when adjusting for baseline covariates, there was no more differences of mechanical properties of CA between patients with diabetes and controls. Only patients with hypertension showed lower FAC than controls and larger vessel area than both controls and diabetes, independent of baseline covariates.
Conclusion: Despite normal cIMT, the CA of hypertensive patients was stiffer and positive remodeling preceded the wall thickening independent of baseline covariates, whereas vascular properties of patients with diabetes were not different from that of controls after adjustments.

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EFFECT OF TREATMENT OF HYPERURICEMIA WITH FEBUXOSTAT IN HYPERTENSIVE PATIENTS WITH CHRONIC HEART FAILURE AND CHRONIC KIDNEY DISEASE

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Background: Febuxostat, a non-purine xanthine oxidase inhibitor, has been reported to have a stronger effect and more safety on hyperuricemia than allopurinol. However, there is not available on the effect of febuxostat in hypertensive patients with chronic heart failure (CHF) and chronic kidney disease (CKD).
Methods: The aim of this study is to examine the efficacy and safety of febuxostat in hypertensive patients with CHF and CKD for treating hyperuricemia. Twenty hyperuricemic patients with hypertension (HT), CHF and CKD were enrolled and treated with febuxostat (10-20mg/day). Serum uric acid concentrations and serum estimated GFR levels in the 3 months before and after the start of febuxostat treatment were collected for HT, CHF and CKD patients switched from allopurinol after failing to achieve serum uric acid concentrations <6.0mg/dL.
Results: Evaluable data were available for 20 patients, 20% of whom had advanced CKD (eGFR<30mL/min/1.73m2). Mean dose of febuxostat was 11 (±3.7) mg/day. By using febuxostat, mean serum uric acid concentration decreased from 7.6 (±1.2) mg/dL at baseline to 6.2 (±0.9) mg/dL at 3 months ($p<0.001$); 35% of patients achieved a level <6.0mg/dL. No serious adverse reactions were noted with febuxostat, and there were no significant changes in blood pressure, heart rate, total cholesterol, triglyceride, hemoglobin A1c, and hepatic and renal function.
Conclusions: Febuxostat was effective for hyperuricemia in patients with HT, CHF and CKD without severe side effects.

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EARLY DETECTION OF UNSTABLE CARDIAC LESIONS IN ASYMPTOMATIC INDIVIDUALS AT RISK OF ACUTE CORONARY SYNDROME

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Coronary artery disease (CAD) remains the world's leading cause of death (7 million annually). Initial CAD presentation for most patients is acute coronary syndrome (ACS) from rupture of non-obstructive unstable plaque. Screening for ACS risk remains a challenge; traditional risk factors, multi-factorial absolute risk methods, and standard noninvasive testing predict only 60-65% of cardiovascular risk. Plaque rupture results from an inflammatory injury/repair process underlying the formation, progression, and eventual rupture of unstable thin-cap atheromas. Although active inflammation is increased in ACS patient plaques, smoldering inflammation characterizes unstable silent plaque. We undertook clinical trials to identify predictive biomarkers constant in atheroma progression to unstable lesions as a result of inflammatory pathway activation, and developed a 9-protein/4 clinical risk factor algorithm for identification of at-risk patients frequently missed by current methods (CTACK, Eotaxin, Fas Ligand, HGF, IL-16, MCP-3, sFas, Hba1c, HDL; age, sex, diabetic status, and family history). Longitudinal outcome-based cohorts, disease free at baseline, represented 31,569 individuals; Cases/Controls totaled 1,634/4,474. Measuring baseline serum samples from 1,084 CAD-free individuals, 362 of which subsequently developed CAD, optimized biomarker assay panels. Using an optimum size model predicted by the drop-in-deviance approach, a multivariate Cox proportional hazard regression model was fit using the most powerful predictors within the clinical and protein variables. A multi-ethnic case-cohort sample (MESA) was used for external validation. The Biomarker Algorithm detected 46% of ACS patients missed by current methods in the Intermediate Risk group (clinical Net Reclassification Index 43% from initial FRS), and, when combined with lipids, correctly identified 61% of ACS patients. We conclude that the algorithm demonstrates clinical utility in identifying patients with unstable cardiac lesions frequently missed by current evaluations, and predicts how likely these apparently healthy individuals are to experience an ACS, enabling preventative therapies to be initiated in individuals who might benefit most.

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INTRACRANIAL HEMORRHAGE FOLLOWING FIBRINOLYSIS FOR ACUTE ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Background: Intracranial hemorrhage (ICH) is a recognized complication of fibrinolysis for ST elevation myocardial infarction (STEMI). Data on predictors and outcome of ICH in this setting is limited.
Methods: Adult STEMI patients treated with fibrinolysis were identified from the National Inpatient Sample (NIS) database from 2003-2011 using ICD9 codes. A retrospective analysis of baseline demographics, clinical characteristics, comorbidities and outcomes was performed.
Results: ICH was reported in 738 (0.9%) of 85,187 acute STEMI patients treated with fibrinolysis. ICH was associated with significantly higher in-hospital mortality [54.7% vs. 4.5%, adjusted odds ratio (OR) = 20.54, p<0.001]. When compared to those without ICH, patients with ICH were older (71-vs-61.3 years, p <0.001) and were more often women (50.8%-vs-29.9%, p<0.001) No significant racial differences were identified. ICH patients were more likely to have pre-existing coagulopathy (3.8%-vs-2.2%; p=0.003), renal failure (11-vs-4.8%; p<0.001) and hypertension (65.9%-vs-55.3%; p<0.001). Stepwise logistic regression analysis identified older age (≥65yrs) (OR 2.51, p <0.001); female sex (OR 1.72, p<0.001);); hypertension (OR 1.31, p=0.04) and alcohol abuse (OR 2.3, p<0.001) as independent predictors of ICH. White race (OR 0.80, p=0.044) and obesity (OR 0.21, p<0.001) were independent negative predictors. Diabetes mellitus, renal failure, coagulopathy and treatment at either rural or non-teaching hospitals were not found to be independent predictors of ICH.
Conclusions: ICH following fibrinolysis for STEMI is relatively uncommon. It occurs more commonly in older women and those with hypertension and alcohol abuse, and is associated with greatly increased in-hospital mortality.

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PROGNOSTIC VALUE OF ST-SEGMENT MORPHOLOGY IN FIRST ANTERIOR ST-SEGMENT MYOCARDIAL INFARCTION

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Background: The morphology of ST-segment elevation has been mainly investigated regarding its diagnostic value for acute myocardial infarction. We aimed to clarify the prognostic value of the morphology of ST-segment in patients with ST-segment elevation myocardial infarction (STEMI).
Methods: We carried out a retrospective analysis of 167 consecutive first anterior STEMI patients who underwent coronary angiography. Patients with prior myocardial infarction, bundle branch block or ventricular paced rhythm were excluded. ST-segment morphology was classified into concave or non-concave (straight or convex) patterns based on the shape of the ST-segment in the lead with maximal ST-segment elevation. Baseline characteristics, echocardiographic and angiographic findings, as well as in-hospital and 1-year all-cause mortalities were compared between the two groups.
Results: Of the 167 patients, 84 patients (50%) had concave pattern. Patients with concave pattern had a lower prevalence of diabetes than those with non-concave pattern. Patients with concave pattern had a significantly lower rate of Killip class 3 or 4 on presentation (6% vs. 16%, p=0.04). There was no statistically significant difference between the two groups in peak creatine kinase value (median; 2641 IU/L vs. 2391 IU/L, p=0.82) or left ventricular ejection fraction (median; 38% vs. 38%, p=0.99). There was a trend toward shorter duration from symptom onset to presentation in patients with concave pattern (median; 2-hour vs. 3-hour, p=0.32). Patients with concave pattern had a significantly lower rate of in-hospital mortality (0% vs. 6%, p=0.03). Similarly, at 1-year follow-up, patients with concave pattern had significantly lower all-cause mortality (0% vs. 12%, p=0.001).
Conclusion: Concave pattern ST-segment elevation was significantly associated with lower in-hospital and 1-year mortalities in patients with first anterior STEMI.

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MYOCARDIAL VIABILITY ASSESSMENT PRIOR TO PERCUTANEOUS CORONARY INTERVENTION FOR CORONARY CHRONIC TOTAL OCCLUSION: A SYSTEMATIC REVIEW

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Background: Patient selection for percutaneous coronary intervention (PCI) of coronary chronic total occlusion (CTO) has focused on symptoms, lesion characteristics and state of collateral circulation. Value of myocardial viability assessment has not been well studied in these anatomically complex lesions.
Methods: Review of literature identified 11 observational (8 prospective, 3 retrospective) studies that assessed viability before PCI of CTO (n=640) [Table]. These studies were analyzed for viability parameters and imaging modalities.
Results: Mean age was 63.7 years and 76% were men. Patients were followed up to 12 months. In earlier studies collateral grade by coronary angiography (CA) (5 studies, n= 157) was used as a marker of viability with good sensitivity (> 75%) but poor specificity (21% to 65.7%). Transmural extent of infarction was the primary marker of viability by cardiac magnetic resonance (CMR) imaging in 6 studies (n=222). Other viability markers included systolic wall thickening, myocardial blood flow, and contractile reserve. Myocardial perfusion imaging (MPI) was used for viability assessment in 2 studies (n=321) and an ischemic threshold of >12.5% identified those with most benefit from CTO PCI.
Conclusion: In absence of prospective studies, demonstration of viability may identify those who would most benefit from PCI of CTO.

Author Year	No.	Viability Parameters	Results in Relation to Viability
Studies Utilizing Collateral Grade and microvascular integrity by Coronary Angiography			
Di Carli 1994	42	Collateral grade & perfusion defects	Angiographically visible collaterals sensitive (84%) not specific (21%)
Petronio, 1998	18	Micro vascular integrity & RWT	Microvascular integrity correlated with viability
Muehling 2007	30	Collateral grades & perfusion	TEI <50%=preserved contractile function in collateral-dependent myocardium
Kumbasar 2007	47	Collateral grades & contractile reserve	Collateral grades 2-3 predicts viability (sensitivity 75%, specificity 65.7%)
Chammas 2008	20	Collateral grades & perfusion	Collaterals indicative of viability
Studies Utilizing Cardiac Magnetic Resonance imaging			
Muehling 2007	30	Collateral grades & perfusion	TEI <50%=preserved contractile function in collateral-dependent myocardium
Baks 2006	27	SWT & TEI	TEI <25%=likelihood of ↑ SWT on follow up (p<0.001)
Cheng 2008	17	Hyperemic and resting MBF	Hyperemic MBF ↑within 24 hours of CTO PCI and persisted at 6 months (p<0.01)
Fiocchi 2009	23	Diastolic & systolic wall thickness	Functional recovery correlated with SWT (p=0.015)
Kirschbaum 2012	72	EDWT, TEI, contractile reserve, SWTur	Contractile reserve+SWTur+TEI better predictive than TEI alone for recovery of function (p<0.001)
Pujadas 2013	43	Perfusion & TEI	Ischemia and DE<50% predicted recovery of segmental perfusion (p,0.001) and function (p=0.01)
Studies Utilizing Perfusion imaging for viability assessment			
Chammas 2008	20	Collateral grades & perfusion	Collaterals not protective of inducible ischemia but could preserve viability
Safely 2011	301	Perfusion	Ischemia threshold >12.5% of myocardium identified those with most benefit from CTO PCI

CTO=Chronic total occlusion; DE=Delayed enhancement; EDWT=End diastolic wall thickness); MBF=Myocardial blood flow; PCI=Percutaneous coronary intervention; RWT=Regional wall thickening; SWT=Systolic wall thickening; SWTur=Systolic wall thickness of unenhanced rim; TEI=Transmural extent of infarction (by late gadolinium enhancement)

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ROLE OF GALECTIN-3 IN ISCHEMIA/REPERFUSION INJURY

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Myocardial reperfusion has the potential to salvage the ischemic myocardium after a period of coronary occlusion. Reperfusion, however, can cause a wide spectrum of deleterious effects. Galectin-3 (GAL-3), a beta galactoside binding lectin, is closely associated with myocardial fibrosis and heart failure. We investigated its role in ischemia-reperfusion injuries (IR). C57B6/J wild type (WT) mice and GAL-3 knockout (KO) mice were used for murine model of Ischemia-reperfusion in the heart where a period of 30 min ischemia was followed by 24 hours of reperfusion. There was a significant increase in GAL-3 levels in the left ventricle after IR injury which signifies an important role for GAL-3 in IR in the heart. Troponin I levels were found to be significantly higher in GAL-3 KO group than the GAL-3 WT group depicting that GAL-3 is regulating troponin I levels in the IR model. Antioxidant enzymes Superoxide dismutase, Glutathione and catalase were found to be significantly raised in the GAL-3 WT IR group as compared to the GAL-3 KO IR group. We also noticed a more anti-apoptotic bcl-2 and less pro-apoptotic cleaved caspase-3 and cytochrome c protein expression in GAL-3 WT IR group than in GAL-3 KO IR group. Our study shows that GAL-3 is associated with an increase in the anti-oxidant activity in the IR injured myocardium. We can conclude that GAL-3 can interfere with redox pathways controlling cell survival and death and plays a protective a role in the pathogenesis of ischemia reperfusion injury in the heart.

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NOT ALL ST-SEGMENT CHANGES ARE MYOCARDIAL INJURY: HYPERCALCEMIA-INDUCED ST-SEGMENT ELEVATION

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Objectives/Background: While other causes of ST-segment elevation on electrocardiogram (EKG) than ischemia have been described, hypercalcemia is an etiology that has been rarely documented.
Description: We describe the case of an 83 year old man with coronary artery disease, ischemic cardiomyopathy with left ventricular ejection fraction of 15%, newly diagnosed multiple myeloma and other comorbidities who presented with shortness of breath and increased leg swelling, denying any chest pain. Thorough workup revealed new ST segment elevation in anterior leads (V1-3) and ST segment depression in lateral leads with subsequent labs showing hypercalcemia and negative cardiac enzymes. It was thought that the EKG changes were not indicative of cardiac ischemia and he was treated with fluids, diuretics and zolendronic acid with subsequent resolution of ST segment changes.
Results/Discussion: ST-segment changes mimicking myocardial ischemia must be taken into consideration if physical exam and history do not lend itself towards myocardial injury as unnecessary invasive revascularization procedures have inherent risks. In medical literature, EKG features of hypercalcemia are described as: absent or shortened ST segment, shortened QT segment, and lengthened T wave duration. In addition, there have been approximately 26 reported cases of hypercalcemia leading to ST-elevation, mostly localized to anterior leads (V1-3). The physiologic mechanism of these changes is unknown. Many of these cases note the ST-elevation due to hypercalcemia is likely more common than currently documented in medical literature.
Conclusion: Our patient's ST segment changes mimicking myocardial injury on EKG were due to hypercalcemia. Further vigilance is required to determine if this really is a relatively common cause of ST-elevation mimicking ischemia.

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PRIMARY PERCUTANEOUS CORONARY INTERVENTION (PPCI) IN OCTOGENERIANS: CLINICAL CHARACTERISTICS AND OUTCOMES IN AN AUSTRALIAN REGIONAL SETTING

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Background: The Sunshine Coast Hospital and Health Service (SCHHS), Queensland, Australia began a PPCI service in 2012. The region has a large elderly population with proportions of >65 year old residents projected to increase from 18% in 2011 to 21.8% by 2026 with >85 year olds trebling over this period.
Aim: To compare PPCI characteristics and outcomes in the elderly (>80yrs) verses non-elderly (<80yrs) STEMI population treated within SCHHS.
Methods & Results: Data on all PPCI patients since commencement to January 2015 were collected prospectively. Of 405 PPCI, 61(15%) were elderly. Compared to the younger cohort, the elderly were more likely to be female (38%v22%, p=0.01), had previous CABG (10%v3%, p=0.002), and have hypertension (67%v44%, p=0.002). Elderly patients had marginally longer (non-significant) median [interquartile range] door-to-balloon times (DTBT) (50 [63] v 45 [50] mins, p=0.27), were less likely to receive ticagrelor (48%v62%, p=0.13) or IIb/IIIa inhibitor (38%v56%, p=0.013) and more likely to receive bare metal stents (36%v20%) or no stent (26%v23%). Thirty-day mortality in the elderly cohort was higher (18%v3%, p<0.001). Of the eleven elderly deaths, four had cardiac arrest, three arrived intubated and ventilated, three had LMCA culprit and only five received PCI. For those receiving PCI who subsequently died, median DTBT was 106 [99] mins.
Conclusion: Octogenarians represent a substantial proportion of referrals for primary PCI and is expected to increase. Timely PPCI is feasible in this inherently high-risk group however mortality is higher compared to a younger cohort.

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LARGEST REPORTED SINGLE OPERATOR PERCLOSE CLOSURE DEVICE EXPERIENCE WITH VERY LOW COMPLICATIONS

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Background: Femoral artery is the most common access site in cardiovascular procedures in US. Radial access is recommended as an option for both early patient ambulation and lower complication risk. However, the need for a switch in practice to radial access may not be necessary for physicians with large experience with femoral access who always do their own access stick and closure rather than have a trainee attempt it.
Methods: Our hospital participates in the American College of Cardiology National Cardiovascular Data Registry (ACC NCDR) and we analyzed the data on patients who underwent procedures from 01/01/2006 to 12/31/2014 by a single operator. Ambulation time is ordered as 2 hours for Perclose patients. Data were recorded by independent hospital staff. All the definitions of complications are ACC NCDR based.
Results: The single operator who is American Board of Internal Medicine Interventional Cardiology certified, performed procedures on 6,726 total patients and of these 6,218 were femoral access with Perclose device used on 4,995 (80.3%) patients. No patients are excluded from this analysis of patients with Perclose and the results are as below. Mortality 0.4%, Bleeding 0.4%, Dissection 0.1%, Thrombosis 0.5%, Occlusion 0%, Pseudoaneurysm 0%, Embolism 0% and Fistula 0%. No infection was noted. The total data on 6,726 patients also showed the above complications to be below 1% for each category.
Conclusions: Femoral Access with Perclose is extremely safe in the hands of experienced operators who do their own initial stick and closure device placement. Hence, experienced physicians with excellent femoral outcomes using the Perclose Closure Device may not switch their practice to radial access approach.

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MORBIDLY OBESE PATIENTS GET EXCELLENT OUTCOMES WITH FEMORAL ACCESS WHEN ACCESS IS OBTAINED BY EXPERIENCED OPERATORS

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Objectives: During vascular procedures, radial access is preferred over the femoral access in the morbidly obese patients per American College of Cardiology (ACC) guidelines but the guidelines do not acknowledge operator experience. We hypothesize that experienced operators get excellent femoral outcomes in high-risk groups like the morbidly obese. *Background:* Only American Board of Internal Medicine (ABIM) Interventional Board certified operators attempt arterial access in our hospital. We defined an "experienced operator" as certified in ABIM. Excellent outcomes are defined as access site complication rates of less than or equal to 1% based on outcomes considered favorable in prior radial access studies. In prior studies favoring radial access, it was not required for access attempts to be made only by an experienced operator. Femoral artery being an end-artery be less forgiving than radial artery when thrombosed.
Methods: All patients presenting between 01/01/2006 and 10/31/2014 that had femoral access and a BMI greater than 40 were included in our study. The total number of patients was 3179. All data reported in this study are taken from the ACC/National Cardiovascular Data Registry (ACC/NCDR). ACC defined the variables evaluated by us, which are available at http://www.ncdr.com.
Results: Our results reveal that there was low overall mortality (<0.6%) and no access site infection. Vascular complications included bleeding (0.5%), thrombosis (0.3%), dissections (0.1%), occlusions (0.0%), pseudo-aneurysms (0.1%), emboli (0.0%) and fistulae (0.0%).
Conclusions: Experienced operators obtain excellent outcomes in morbidly obese patients from the femoral approach and uniform preference of radial access may not be necessary.

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TRANSCATHETER REPAIR OF A RADIAL ARTERIOVENOUS FISTULA AFTER CARDIAC CATHETERIZATION USING A COVERED STENT

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Introduction: Arteriovenous fistulas after cardiac catheterization using radial approach are extremely rare. We report a case of arteriovenous fistula following transradial access which was repaired successfully using a covered stent.
Case Report: A 55-year old female underwent coronary angiography for non-ST elevation MI. Patient had a normal Allen's test prior to procedure. The right radial artery was cannulated for access using a 5F radial sheath which was removed after completion of procedure. A radial band was applied for hemostasis and removed 2 hours later with no evidence of bleeding or hematoma. On follow-up visit, patient complained of pain in her right upper extremity (RUE) and had a palpable thrill on examination. MRA of RUE revealed radial AV fistula with rapid filling and opacification of the veins near the radial artery. RUE angiogram was performed in the cardiac catheterization lab using impulse diagnostic catheter. It demonstrated arteriovenous fistula involving distal radial artery. A 110 cm 7F Shuttle sheath was then advanced over a supracore wire, followed by a 125cm Vertebral catheter, advanced distally across the fistula origin. Superselective angiogram was performed confirming flow into the radial artery distal to the AV fistula. A Viabahn 6mm x 5cm covered stent was advanced over the Supracore wire and deployed across the fistula origin. Post-dilation with a 5mm x 40mm FoxCross balloon was performed. Final angiography demonstrated excellent flow through the stent with no residual fistulous communication. Patient tolerated the procedure well and experienced complete resolution of symptoms.
Conclusion: Transcatheter repair of radialarteriovenous fistulas using covered stents is a safe and effective method. In a select patient population, endovascular covered stents provide a less invasive treatment modality compared to surgery.

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COMPARISON OF MANUAL COMPRESSION AND ARTERIAL CLOSURE DEVICE FOLLOWING PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH STEMI USING BARC CLASSIFICATION

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Background: Bleeding complications are associated with increased risk of adverse outcomes following percutaneous coronary intervention (PCI). A meta-analysis of 16 studies had suggested a reduction in vascular complications with the use of Angio-Seal closure device compared to manual compression (MC). However, safety comparison between studies was difficult due to substantial heterogeneity in defining significant bleeding. We compared bleeding complications after PCI between Angio-seal and MC in the setting of primary PCI for STEMI, using the BARC (Bleeding Academic Research Consortium) bleeding definitions.
Methods: Retrospective chart review and data collection was performed on consecutive patients who underwent primary PCI through femoral approach for STEMI between September 2011 and June 2013. The bleeding complications were compared between MC and vascular closure device (VCD) using BARC classification.
Results: Data was obtained in 190 patients (age 64±13 years); 124 (66%) men. Two patients were excluded due to insertion of an intra-aortic balloon pump. Of the remaining 188 patients, 50 (26.5%) had MC, 108 (57.3%) had Angio-Seal and 30 (14%) had Perclose proglide VCDs. Bleeding complications were compared between the Angio-Seal group (n=108) and MC (n=50) group based on the BARC classification. There were 10 patients with type 1 bleeding and 15 patients with type 2 bleeding in total and 133 had no bleeding. Statistical analysis indicated no relationship between the technique of hemostasis used and the presence or severity of bleeding complications (p =0.56).
Conclusions: When BARC classification is used to define vascular access site bleeding complications, MC is as effective as Angio-Seal in providing hemostasis following femoral approach to primary PCI in the setting of acute STEMI.

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QUALITY AT THE CATHLAB: CORONARY REINTERVENTION RATE AT 30 DAYS

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Introduction: Post coronary angioplasty readmissions counts from 9 - 48%, many of them being avoidable.
Objective: To evaluate coronary reintervention rates in patients admitted with chest pain within 30 days after coronary angioplasty (PTCA)
Materials and methods: Among January 2005 to December 2014, 2022 PTCA were performed. Patients (pts) deceased during index hospitalization and those with acute coronary syndrome as an epiphenomenon were excluded, leaving the final number at 1931 pts. Within 30 days, 160 of them required hospitalization after PTCA (8.2%) to evaluate symptomatic recurrence. 54 (34%) pts underwent new angiography while 106 (66%) pts went through medical treatment optimization. Of those pts with renewed angiography, 20 pts (group A) had new PTCA, whereas 34 pts (group B) had no new angiographic findings. Baseline characteristics from group A and B n(%) respectively: mean age 63.23±11 vs 61.1±10.8 years; diabetes 11(55) vs 10(29) p=0.06; ACS 15(75) vs 23(67); LVF average 58.7±5.6 vs 63.2±17.9; bifurcation lesions 3(15) vs 4(12); chronic coronary occlusion 2(10) vs 0; more than 33 mm of stent 16(80) vs 20(59); re-angina and new changes in ECG 6(30) vs 0 p=<0.001; re-angina and positive troponin 2(10) vs 9(26); re-angina with new changes in ECG and troponin positive 5(25) vs 1(3) p=0.02; intracoronary thrombosis 6(30) vs 0 p=<0.001.
Results: From 1931 angioplasties performed, global reintervention rate was 1.03%. Then, 2(10) vs 1(3) pts had clinically relevant myocardial infarction (p=0.5); and 1 (5) vs 0 (p=0.3) had cardiovascular death. Reinterventions were because of: 1) subacute coronary occlusion in 6 (30) vs 0; 2) another lesion or another vessel in 14 (70) vs 0.
Conclusion: The rate of coronary reinterventions within 30 days post-angioplasty in patients with new episode of chest pain was low. The dyad of chest pain and new ECG changes was the best determined of intracoronary thrombosis.

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USE OF IMPELLA CP AS AN ADJUNCT TO BALLOON AORTIC VALVULOPLASTY AND STENTING OF UNPROTECTED LM

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Background: In an aging population, the occurrence of co-existent aortic stenosis and left main (LM) or equivalent coronary disease poses a major challenge to patients and clinicians, especially when these patients are not surgical candidates due to multiple co-morbid conditions. Alternative options need to be considered.
Case: 86 year old female admitted with chest pain. She was ruled in for non-ST elevation MI based on dynamic EKG changes with ST depressions in V4-V6 and peak troponin-I level of 4.47. Echocardiogram revealed severe biventricular dysfunction with LVEF of 30% and severe aortic stenosis with AVA of 0.6cm2. Due to co-morbidities she was deemed not to be a surgical candidate and a percutaneous approach was offered. Catheterization Findings & Intervention: The left main and right coronary artery revealed >90% disease. An Impella CP device was retrogradely advanced into the left ventricle over the 0.035”-280 cm Amplatz stiff wire. The left main lesion was crossed using 0.014”-180cm whisper wire. Laser atherectomy and stenting was performed with 4.0 x12 mm Promus stent. Stenting of the distal and proximal segment of the RCA was performed using a 6 French guide liner; a 3.0 x 24 mm and 4.0 x 12 mm Promus stents were deployed respectively. Percutaneous aortic balloon valvuloplasty was performed successfully under rapid pacing by using a 16 x 5 cm Z-Med balloon.
Conclusion: Unprotected left main coronary artery stenting and sequential balloon aortic valvuloplasty for critical aortic stenosis with Impella device support is a viable option in high risk patients for surgery. The combined procedure serves as a bridge to TAVR or palliation.

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REDUCTION IN THE USE OF DRUG ELUTING STENTS AFTER INTIAL INCREASING TREND IN THE SETTING OF STEMI IN THE UNITED STATES

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Background: Drug eluting stents are increasingly utilized during intervention. The goal of this study was to evaluate this trend in in the United States using inpatients data. *Method*: The Nationwide Inpatient Sample (NIS) database was utilized to calculate the age-adjusted rate for drug eluting stent use from 2003-2007 in the setting of STEMI in the United State using ICD-9 coding.
Results: We found that age adjusted rate for the use of drug eluting stents in the United States initially increased from 2003 to highest level in 2006 with gradual reduction in 2007. (Age adjusted rate for the use of drug eluting stent was 8.9 per 100,000 in 2003. It increased to highest trend of 34.6 per 100.000 in 2006 with reduction to 20.3 per 100,000 in 2007).
Conclusion: Initial higher utilization rate of drug eluting stent in the setting of STEMI did not persist. The cause of this lower trend in 2007 is not known but is probably related to the fear of higher stent thrombosis rate.

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PRDX II DEFICIENCY INSTIGATES THE DEVELOPMENT OF ANGIOTENSIN II-INDUCED ABDOMINAL AORTIC ANEURYSMS

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With population aging, abdominal aortic aneurysms are becoming common vascular disorders. AAAs exhibit progressive dilations of the abdominal aorta, and rupture of it is often a lethal event. Although it is well documented that inflammation and oxidative stress are pathogenic mediators of AAA, the molecules that could be therapeutic targets are not well characterized. Peroxiredoxin II is one of major isoforms of peroxiredoxin, a critical antioxidant enzyme, and exhibit higher affinity toward low concentrations of hydrogen peroxide. The purpose of this study is to determine whether PrdxII contributed to the development of AAA. In aortas from aortic aneurysm patients, there was a marked increase in expression level of PrdxII. We confirmed it in mouse AAA model, infusing angiotensin II via subcutaneous os motic pumps. To further investigate the role of PrdxII in AAA formation, we established Prdx II KO mice. Compared with wild type control, subcutaneous infusion of Ang II markedly increased the incidence of AAA in PrdxII KO mice. PrdxII deficiency enhanced AngII induced changes in overall abdominal aorta morphology and the increase in aorta diameter. High frequency ultrasound images of abdominal aorta, which is taken at the level of the suprarenal aorta in every week after AngII infusion, also showed more advanced dilations of abdominal aorta at earlier time point in PrdxII KO mice. Correspondingly, SMA positive cells and elastic lamina degradations are elevated in aneurysm sections from PrdxII KO mice. In addition, when comparing AngII treated WT mice, aortas from AngII infused PrdxII KO mice displayed increased immune cell infiltration and significantly upexpression of proinflammoty cytokines in AAA. These results indicate that PrdxII has a pivotal role in modulating of AngII induced AAA. With mechanistic further studies, our research might suggest PrdxII as a potential therapeutic target for prevention of AAA.

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CO2-ENRICHED WATER BATH AS A NOVEL THERAPY FOR PERIPHERAL VASCULAR DISEASE

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Peripheral artery disease (PAD) is a major health problem whereby narrowed arteries reduce blood flow to the ischemic limbs. We investigated the effects of CO2-enriched water bath (CEWB) therapy on blood flow in the ischemic hind limb. The femoral artery was occluded in rats to induce PAD and the animals were treated with or without CEWB at 37°C for 4 weeks (20 min/day; 5 days/week) starting one week after artery occlusion. CEWB was prepared by using Carbothera (Mitsubishi Rayon Engineering, Tokyo). Peaks, mean and minimal blood flows, as measured by Pulse Wave Doppler Ultrasound technique, were not detected in the untreated ischemic hind limb of animals due to arterial ligation. However, blood flow values were about 50% of the control upon treatment with CEWB; 67% of the ligated animals showed positive blood flow by CO2 treatment. Morphological examination of the treated ischemic skeletal muscle revealed a 3-fold increase in small artery numbers indicating the formation of new blood vessels. Although plasma triglycerides decreased and plasma NO concentration increased in ischemic animals, CEWB treatment produced no effects on these parameters. It is suggested that beneficial action of CO2 therapy on blood flow to hind limb may be due to the development of angiogenesis in the ischemic skeletal muscle. (Infrastructure support for this study was provided by the St. Boniface Hospital Foundation)

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WHOLE EXOME SEQUENCING FOR THORACIC AORTIC ANEURYSM: THE FUTURE IS HERE

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Background: Convincing evidence is accumulating that genetics play an important etiologic role in thoracic aortic aneurysm and dissection (TAAD). Multiple genes have been found to cause syndromic and familial TAAD. The current study evaluates the impact of genetic testing via whole exome sequencing (WES) for a panel of genes associated with TAAD as a clinical test performed at a specialized aortic center.
Methods: WES was offered as an ongoing clinical test to 188 patients (mean age 59.2±14.8 years, range 13-85, 131 males (69.7%)) with TAAD. Thirty-four patients were declined testing for insurance reasons. DNA was extracted from saliva samples collected in Oragene kits. DNA exonic fragments were sequenced on the Illumina HiSeq platform. The resulting sequence was analyzed for single nucleotide variants and small insertions and deletions differing from the reference genome (Human Genome 19, HG19). To date, genetic results were available for 102 patients (66.2%).
Results: The panel of tested genes is presented in Figure 1. Three patients (2.9%) had a deleterious mutation identified in the FBN1, COL5A1, and MYLK genes. Twenty patients (19.6%) had suspicious variants of unknown significance (previously unreported) in one or more of these genes: FBN1 (n=5), MYH11 (n=4), ACTA2 (n=2), COL1A1 (n=2), FLNA (n=2), TGFBR1 (n=2), COL3A1 (n=1), COL5A1 (n=1), COL5A2 (n=1), NOTCH1 (n=1), PRKG1 (n= 1), and TGFBR3 (n=1). Identified mutations had implications for clinical management. Seventy-three patients (71.6%) had no medically important genetic alterations.
Conclusion: Routine genetic screening of patients with TAAD provides important information that enables genetically personalized care and permits identification of novel mutations responsible for aortic pathology.

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WHAT DIABETES MELLITUS HAS TAUGHT US ABOUT POTENTIAL TREATMENTS FOR SMALL ABDOMINAL AORTIC ANEURYSMS

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Increased detection of abdominal aortic aneurysm (AAA) at early stages of growth (more than 80% of those diagnosed now are less than 3.5 cm maximum diameter), and the high rate of severe complications of urgent, open abdomen or endovascular surgical treatment have emphasized the need for less invasive strategies that target the pathogenetic mechanisms of progression and rupture. In sharp contrast to hypercholesterolemia, diabetes mellitus (DM) is negatively associated with AAA in experimental animal models and in epidemiological studies in humans. Whereas hypercholesterolemia favors an increased proteolytic state in the arterial wall, diabetes, through increased glycation of protein precursors and increased advanced glycation end products, facilitates matrix protein synthesis and increases covalent bonding of matrix proteins, rendering the wall less prone to proteolysis, decreasing the likelihood of aneurysmal dilatation and rupture. Recent studies from our laboratory have shown that Low Level laser (LLL) photobiomodulation, in the visible to near infrared range [780 nm] of the electromagnetic spectrum, used widely clinically for reducing pain and increasing wound healing, inhibits the development and progression of AAA in the angiotensin-II-infused, apolipoprotein-E-deficient mouse. The mechanism for this effect involves upregulation of collagen-rich fibrous matrix repair of transmedial defects in the aortic wall in the vicinity of aortic branch orifices. Reinforcement of the extracellular matrix in the aortic wall also explains the negative association between DM and AAA even though the underlying cellular mechanisms are different. In this talk, we discuss the use of minimally invasive photobiomodulation, and other options, for mechanism-based targeting and management of small, progressing aneurysms that are refractory to risk factor modification and pharmacological therapy in order to save the patient from the frequently severe consequences of urgent, obligatory, surgical or endovascular intervention.

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STRATEGIES FOR PREVENTION OF CARDIOVASCULAR EVENTS IN PATIENTS WITH POLYVASCULAR DISEASE

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Patients with severe carotid arterial sclerosis or those with polyvascular disease (PVD) are at high risk for cardiovascular events.
Ultrasonography(US) is very useful for detection of PVD and we investigated usefulness of US and prognosis of patients with PVD or those with severe carotid arteriosclerosis. Carotid arterial sclerosis was evaluated by carotid US and plaque score (PS) was calculated. PS was summation of maximum thickness of each plaque and graded as follows: severe (10≤PS), moderate (5≤PS <10) and mild (PS<5). Out of 2428 patients who underwent US in 2010, severe arteriosclerosis was observed in 602 patients. 102 of them had PVD. In most of patients with PVD, treatment of diseased major vessels was done. Diagnosis of PVD was based on exercise test, US, coronary angiography. MRI. In 380 patients with severe carotid sclerosis, antiplatelet drug was administered. Most of patients had more than 2 risk factors for arteriosclerosis. During 3 year follow up of patients with severe carotid sclerosis without significant carotid stenosis, cerebral infarction (CI) occurred in 10 (4 with antiplatelet) and acute myocardial infarction (AMI) occurred in 6 (3 with antiplatelet). In 1258 patients with mild carotid arteriosclerosis, CI occurred in 12 and AMI occurred in 7 patients. In 24 cases with severe stenosis, CEA was done and restenosis was not observed. There was no significant difference in development of CI or AMI between severe and mild carotid arteriosclerosis. In 78 cases with PAD, PTA with stenting was done in 32 and restenosis was observed in 5. If severe carotid, coronary or peripheral arterial stenosis is treated, cardiovascular events in patients with PVD can be prevented in most of patients of our hospital. Diagnosis of carotid arterial sclerosis by US and treatment with antiplatelet drug are useful for prevention of cardiovascular event in high risk patients.

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DIAGNOSTIC TRICKS AND TIMELY TREATMENT OF AORTIC INTRAMURAL HEMATOMA

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Aortic intramural hematoma is a variant of acute aortic syndrome with a presentation similar to that of acute aortic dissection but difficult to make a timely diagnosis. This entity may be easily missed because of the absence of the intimal flap often seen in classical dissection. An intramural hematoma is formed from medial hemorrhage from rupture of the vasa vasorum and the subsequent weakening of the aortic wall. In spite of the subtlety of this condition, it is critical to make a prompt diagnosis because of the high mortality rate of 21% associated with it. Some specific CT findings on the unenhanced and contrast-enhanced CT axial images are listed below 1. Intimal areas of calcification in a curvilinear configuration.2. An enlarged aortic diameter and crescentic, eccentric hyperattenuating area of the thickened aortic wall (60-70 HU) Conventional aortic angiogram may not detect intramural hematoma since the appearance of intimal flap and double lumen is absent. CT and TEE show circumferential or crescentic aortic wall thickening of more than 7mm.Therefore, prompt and accurate detection of aortic intramural hematomas is critical to providing appropriate therapy. Timely surgical repair of ascending aortic intramural hematoma is needed whereas medical therapy with a good control of blood pressure may be pursued in patients with descending aortic intramural hematoma.

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PATIENT QUALITY OF LIFE FOR TISSUE AND MECHANICAL VALVES AFTER COMPOSITE AORTIC ROOT REPLACEMENT

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Objective: To assess whether postoperative quality of life for composite aortic root replacement patients differs based on the use of mechanical valves or tissue valves. *Background:* It is presumed that biological valves provide higher quality of life than mechanical. We examined this preconception in the specific setting of aortic root replacement.
Methods: 146 consecutive patients who underwent composite aortic root replacement at our institution from January 2010 to April 2014 with a tissue valve (34.9%, n=51) or a mechanical valve conduit (65.1%, n=95). Patient perceived quality of life was measured using the Short Form 36v2 Health Survey augmented by a series of supplemental questions to further evaluate valve specific differences. Survey participation included 76.5% (39/51) of patients with tissue valves, and 86.3% (82/95) of patients with mechanical valves.
Results: No significant differences were found between the tissue and mechanical valve groups for any quality of life aspects scored by the SF-36v2 survey. All 8 domains and 2 summary scales comprising the evaluation were above national norms calculated using gender and age matched, norm-based scoring. The supplemental questions indicated patient satisfaction with each valve type. In the mechanical valve group, 90.2% (74/82) reported the audible valve click was not troublesome, 85.4% (70/82) reported taking a blood thinner regularly did not affect daily life, and 81.7% (67/82) of patients reported blood testing for anticoagulation therapy was not troublesome.
Conclusions: Receiving a tissue or mechanical valve does not directly affect postoperative quality of life in composite graft aortic root replacement. Answers to supplemental questions suggest previous concerns with mechanical valves do not affect patients in the commonly accepted negative manner. The preconception of heavy quality of life burden for mechanical composite grafts is contradicted by this study.

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LONG-TERM SURVIVAL IN PATIENTS WITH CONTRALATERAL CAROTID OCCLUSION AFTER ENDARTERECTOMY. A COMPARATIVE STUDY

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Severe carotid stenosis is typically treated by carotid endarterectomy , (CEA), but there's no agreement about the safety of this procedure in patients with contralateral carotid occlusion (CCO).
Objective: The aim of the present work is to assess how the CCO affect 30-day outcome and the long-term survival and to compare to those without CCO.
Methods: We reviewed medical records of 434 patients who underwent CEA, 394 as group I and 40 with CCO (group II).
Results: The mean age was 72 and 71,35 years respectively. The mortality following all CEA was 1,6% (1,7% vs 0%; p=0,395). The overall stroke rate was 3,5% (3,8% vs 0%; p=0,209). The transitory ischemic attack rate was 1,38% (1,26% vs 2,5%; p=0,370). At mean follow-up of 75,49±47,5 months (group I) and 72,72±49,9 months (group II), 157 additional deaths were identified in group I and 13 deaths in group II (p=NS). Long-term survival curves did not show statistical difference for both groups (p = 0,514). Overall 1, 5, 10 and 15 -year survivals were for group I 92.2%, 78.8%, 49.8% ,34.8% and for group II were 97.5%, 79%, 50.8% ,42.3% respectively.
Conclusion: Patients who have to undergo CEA with CCO seem not to have an increased risk for perioperative incidence of stroke and death. These patients have an excellent cumulative 15-year survival.

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MITOCHONDRIAL QUALITY CONTROL IN TYPE 1 DIABETIC HEART

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Mitochondrial dysfunction and reactive oxygen species (ROS) are critical to diabetic heart damage. However, antioxidant therapies have failed to reduce heart failure in clinical trials, underscoring the need to develop new therapeutic strategies. A healthy pool of mitochondria is maintained through a number of quality control mechanisms including mitochondrial autophagy known as mitophagy which degrades dysfunctional mitochondrial fragments that are segregated by the fission process. The present study investigated the functional roles of mitophagy and mitochondrial fission in high glucose (HG)-treated cardiomyocytes and in type 1 diabetic heart. Mitochondria in the diabetic heart appeared small and spherical, suggesting increased mitochondrial fragmentation. Meanwhile, mitophagy flux was markedly diminished in the diabetic heart as determined by a novel dual fluorescent mitophagy reporter in the absence and presence of the lysosomal protease inhibitors E64d and Pepstatin A. Human diabetic hearts also showed reduced markers for mitophagy. Similarly, HG increased mitochondrial fragmentation and inhibited mitophagy in cultured cardiomyocytes, which was accompanied by increased cell death. These observations demonstrate a mismatch or uncoupling between mitochondrial fission and mitophagy in the diabetic heart and in HG-treated cardiomyocytes, which may contribute to diabetic cardiac injury. Indeed, overexpression of the E3 ligase Parkin increased mitophagy flux and diminished HG toxicity; while parkin knockdown had the opposite effects as measured by the levels of ROS generation, oxidative injury and cardiomyocyte death. Further, overexpression of the fission factor Drp1 increased mitochondrial fragmentation and reduced HG-induced cardiomyocyte injury, while Drp1 knockdown inhibited fission, predisposing cells to high glucose toxicity. Together, these findings suggested that whereas the HG-induced inhibition of mitophagy is detrimental, the increased mitochondrial fragmentation appears to be adaptive that limits HG cardiotoxicity. Studies are underway to determine if these results also hold true in the hearts of type 1 diabetic mice.

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TARGETING MOLECULAR PATHWAYS IN DIABETES ASSOCIATED CARDIOVASCULAR DISEASE

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Background: Mechanisms underlying the ability of glucagon-like peptide-1 (GLP-1) to prevent myocardial ischemic injury, and reduce cardiovascular event rates in short-term studies of diabetic subjects receiving GLP-1-targeted therapies are not known.
Methods and Results: Here we show that cardioprotective effects of a metabolite of GLP-1, namely GLP-1(28-36), are mediated by soluble adenylyl cyclase Adcy10 (sAC) expressed in mouse coronary artery smooth muscle cells (caSMC). Ex vivo and in vivo mouse models of ischemia-reperfusion injury and myocardial infarction respectively revealed that GLP-1(28-36) was as cardioprotective as GLP-1, with its effect abolished by scrambling its amino-acid sequence. Pharmacological inhibitors, siRNA and sAC-null mice demonstrated that GLP-1(28-36) acts directly on human and mouse caSMC, resulting in sAC-dependent cytoprotection from oxidative stress injury. Next, we cloned full-length GLP-1 receptor (GLP-1R) mRNA from a human megakaryocyte cell line (MEG-01), and found expression levels of GLP-1R in MEG-01 to be less than pancreas but more than lung. GLP-1 and the GLP-1R agonist exenatide elicited a cAMP response in MEG-01 cells, and an inhibitory effect on thrombin-stimulated aggregation of human and mouse platelets. Incubation with exenatide also inhibited thrombus formation in perfusion chamber experiments with whole blood. In a cremaster artery laser injury model, exenatide inhibited thrombus formation in normoglycemic and hyperglycemic mice in vivo. Thrombus formation was greater in mice transplanted with bone marrow lacking a functional GLP-1R (Glp1r-/-), as compared to wild-type bone marrow. However, anti-thrombotic effects of exenatide were only partly lost in mice transplanted with bone marrow from Glp1r-/- mice.
Conclusions: GLP-1(28-36) represents a new small peptide that targets a novel molecular (sAC) and cellular (caSMC) pathway for the treatment of myocardial ischemic injury. Inhibition of platelet aggregation and thrombus formation by GLP-1R agonists represent a potential mechanism for reduced atherothrombotic events in subjects treated with these agents.

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INHIBITION OF PYRUVATE DEHYDROGENASE KINASE DECREASES THE SEVERITY OF HEART FAILURE

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In heart failure, changes in cardiac mitochondrial energy metabolism contribute to this contractile dysfunction and to a decrease in cardiac efficiency. The failing heart has defects in energy metabolic processes that compromise ATP production necessary to maintain contractile function. Normal oxidative phosphorylation is impaired in the failing heart, oxygen consumption is depressed, and the heart has compromised ATP production. With reduced oxidative phosphorylation, the heart increases its reliance on the highly inefficient process of ATP generation via glycolysis (glucose metabolism occurring outside of the mitochondria). Alterations in energy substrate metabolism accompanying heart failure are complex, and are partly dependent on the stage/severity of the syndrome. However, an elevation in glycolytic rates in relation to glucose oxidation in the failing heart is a consistent finding. We showed an increased uncoupling of glycolysis from glucose oxidation, accompanied by an enhanced H+ production and decreased efficiency in mouse and rat hearts subjected to permanent myocardial infarction. Studies involving heart failure secondary to pressure overload also show a depressed overall oxidative metabolism, as well as a decrease in glucose oxidation. We have shown that heart failure secondary to an abdominal aortic constriction, a transverse aortic constriction, or Ang II infusion in mice inhibits cardiac glucose oxidation. Pharmacological stimulation of glucose oxidation in both rat and mouse hearts improves overall cardiac energetic and cardiac function. In the failing heart, a decrease in pyruvate dehydrogenase (PDH) activity (the rate-limiting enzyme involved in glucose oxidation), and an increase in PDH kinase (PDK) expression (which phosphorylates and inhibits PDH) occurs. Genetic deletion of PDK can prevent this decrease in glucose oxidation in the failing heart, and is associated with improved cardiac function. This supports the concept that inhibition of cardiac glucose oxidation may be a promising approach to treat heart failure.

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ROLE OF MITOCHONDRIAL OXIDATIVE STRESS IN GLUCOSE TOLERANCE, INSULIN RESISTANCE, AND CARDIAC DIASTOLIC DYSFUNCTION

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Background: Diabetes is associated with mitochondrial oxidative stress. We have shown that myocardial oxidative stress leads to diastolic dysfunction in the hypertensive mouse model. Therefore, we hypothesized that diabetes could cause diastolic dysfunction through mitochondrial oxidative stress and that mitochondria-targeted antioxidant (MitoTEMPO) could prevent diastolic dysfunction in a diabetic mouse model.

Methods and Results: C57BL/6J mice were fed either 60 kcal% fat diet (HFD) or normal chow (control) for eight weeks with or without concurrent MitoTEMPO administration, followed by *in vivo* assessment of diastolic function and *ex vivo* studies. HFD mice developed impaired glucose tolerance compared with the control (serum glucose = 495 ± 45 mg/dL vs. 236 ± 30 mg/dL at 60 min after intraperitoneal glucose injection, $p<0.05$). Myocardial tagged cardiac magnetic resonance imaging (CMR) showed significantly reduced diastolic circumferential strain (Ecc) rate in the HFD mice compared with controls (5.0 ± 0.3 1/s vs. 7.4 ± 0.5 1/s, $p<0.05$), indicating diastolic dysfunction in the HFD mice. Systolic function was comparable in both groups (LVEF= 66.4 ± 1.4% vs. 66.7 ± 1.2%, $p>0.05$). MitoTEMPO-treated HFD mice showed significant reduction in mitochondria reactive oxygen species, S-glutathionylation of cardiac myosin binding protein C (cMyBP-C), and diastolic dysfunction, comparable to the control. The fasting insulin levels of MitoTEMPO-treated HFD mice were also comparable to the controls ($p>0.05$).

Conclusions: MitoTEMPO treatment prevented insulin resistance and diastolic dysfunction, suggesting mitochondrial oxidative stress may be involved in the pathophysiology of both conditions.

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PRO-INFLAMMATORY AND ANTI-INFLAMMATORY MAST CELLS IN OBESITY AND DIABETES

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Mast cells contribute to the pathogenesis of obesity and diabetes. Deficiency or pharmacological inactivation of mast cells protects mice from these metabolic diseases. This study demonstrates that leptin deficiency slants otherwise pro-inflammatory mast cells toward anti-inflammatory functions. Mast cells in the white adipose tissues of lean humans and mice are leptin-deficient. Adoptive transfer of leptin-deficient mast cells expanded *ex vivo* mitigates diet-induced and pre-established obesity and diabetes in diet-induced and genetic obese mice. Mechanistic studies show that leptin-deficient mast cells polarize macrophages from M1 to M2 functions because of an altered balance between pro- and anti-inflammatory cytokines, but do not affect T-cell differentiation. Rampant body weight gain in *ob/ob* mice, a strain that lacks leptin, associates with reduced mast cell content in the white adipose tissues. In *ob/ob* mice, genetic depletion of mast cells exacerbates obesity and diabetes, and repopulation of bone marrow *in vitro* differentiated mast cells ameliorates obesity and diabetes.

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ROLE OF REACTIVE OXYGEN SPECIES IN THE ADDED SUGAR-INDUCED CARDIOVASCULAR DISEASE

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Consumption of high amount of sugars has been implicated in the pathophysiology of cardiovascular diseases.
The objectives of this presentation are to determine if sugars generate reactive oxygen species (ROS) and if cardiovascular diseases are associated with enhanced production of ROS. Various mechanisms are involved in sugar-induced generation of ROS. Glucose metabolism increases the formation of reduced nicotinamide -adenine –dinucleotide, and flavin adenine dinucleotide which would increase the generation of superoxide anion in the mitochondria. High glucose concentrations activate nicotinamide adenine dinucleotide phosphate-oxidase, and increase the production of advanced glycation end products, insulin and uric acid which would increase the generation of ROS. High consumption of sugars is reported to be associated with the development of atherosclerosis, hypertension, coronary artery disease, cardiac arrhythmias, cardiomyopathy, and peripheral vascular diseases. ROS also have been implicated in the pathophysiology of all of the above mention diseases. In conclusion the data suggest that added sugar-induced cardiovascular diseases are mediated through sugar- induced generation of ROS.

CARDIOVASCULAR DISEASE AND CARDIOPROTECTION IN DIABETES AND METABOLIC SYNDROME

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EXERCISE IMPROVES VASCULAR INSULIN SENSITIVITY: ROLE OF MITOCHONDRIAL ROS

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Vascular insulin resistance contributes to elevated peripheral vascular dysfunction and subsequent hypertension. Excessive production of oxidants, decreased NO bioavailability, and decreased local antioxidant capacity in the vasculature are central causes of vascular insulin resistance. We found that reactive oxygen species (ROS) production was increased in the mesenteric arterioles of spontaneously hypertensive rats (SHRs). Among many sources of increased vascular ROS production in hypertension, mitochondrial ROS overproduction plays an important role. Treatment with the mitochondria-targeted antioxidant decreased mitochondrial superoxide level which has therapeutic benefits in endothelial insulin resistance-related vascular dysfunction and hypertension. Exercise training that can improve vascular insulin sensitivity may have significant value in prevention and treatment of hypertension. Our findings suggest that exercise training beginning at the early hypertensive stage in young SHRs ameliorates hypertension via improving vascular insulin sensitivity. However, the beneficial effects of exercise training on vascular function have not been fully elucidated. Recent evidence has suggested that chronic aerobic exercise training in old rats preserved aortic mitochondrial function as evidenced by reduced ROS formation, increased ATP formation and restored activities of electron-coupling capacity. Regular exercise training reduces vascular expression of NAD(P)H oxidase resulting in decreased local ROS generation. Our study also indicates that exercise ameliorates myocardial insulin resistance by rescuing mitochondrial response to insulin via an eNOS-dependent manner. Furthermore, targeting mitochondria to restore mitochondria-ROS homeostasis is a promising intervention to reduce vascular insulin resistance. Taken together, our results demonstrate that exercise improves cardiovascular insulin sensitivity and vascular function through enhancing mitochondrial function and restoring mitochondria-ROS homeostasis.

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ASLEEP, BUT NOT DAYTIME CLINIC OR AWAKE MEAN, BLOOD PRESSURE IS AN INDEPENDENT PREDICTOR OF CARDIOVASCULAR EVENTS IN PATIENTS WITH DIABETES: THE HYGIA PROJECT

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Objectives: Recent guidelines suggest relying on the ambulatory blood pressure (BP) monitoring (ABPM) derived awake mean to corroborate the diagnosis of hypertension suspected by elevated clinic BP measurement. However, several prospective ABPM studies have found elevated sleep-time BP is a better predictor of cardiovascular (CVD) risk than awake BP mean, also in diabetes. We evaluated the combined contribution to CVD risk of clinic, awake, and asleep BP among patients with diabetes participants in the Hygia Project, designed to evaluate prospectively CVD risk by ABPM.
Methods: This study involved 2632 patients with type 2 diabetes, 1589 men/1043 women, 65.1±11.6 years of age, prospectively evaluated throughout a 4.1-year median follow-up. BP was measured at 20-min intervals from 07:00 to 23:00h and at 30-min intervals at night for 48h.
Results: The hazard ratios (HR) of total CVD events for each 1-SD elevation in clinic, awake, and asleep systolic BP (SBP) analyzed separately (adjusted for the significant influential characteristics of age, sex, chronic kidney disease, cigarette smoking, waist perimeter, and history of previous CVD event) were 1.25 [95%CI: 1.17-1.35]; 1.39 [1.30-1.50], and 1.51 [1.41-1.62], respectively (always P<0.001). Exploration of the combined contribution of all three BP measurements revealed elevation in asleep SBP (HR=1.55 [1.38-1.75], P<0.001) but not in clinic BP (1.08 [0.99-1.18], P=0.082) or awake BP (0.93 [0.82-1.06], P=0.270) was the only independent BP parameter significantly associated with increased CVD risk.
Conclusions: In patients with diabetes, sleep-time SBP mean, but not daytime clinic BP measurement or ABPM-derived awake BP mean, is the only significant and independent prognostic marker of CVD morbidity and mortality. These findings indicate ABPM, but not conventional clinic BP so far mistakenly used to diagnose hypertension and establish therapeutic targets, is a clinical necessity to accurately detect abnormal sleep-time BP and assess CVD risk in diabetes.

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RISK OF DIABETES INCIDENCE WITH STATIN TREATMENT: STUDY USING NATIONWIDE DATABASE FOR HEALTHCARE RESEARCH

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Introduction: Statins are one of the few drugs that have a dramatic effect on health outcome. Some recently published studies have shown increased trends towards incidence of diabetes (DM) in statin-users. We used MarketScan® database that captures claims data from a selection of large employers and health plans, including commercial insurance companies with information on over 85 million covered lives.
Method: A matched case control study sample is selected with predefined inclusion & exclusion criterion using the ICD-9 codes during first year of enrollment period. Then cases were selected based on statin exposure (index date) and matched with controls (unexposed) based on their age, gender and geographic location. They were then followed from the index date till the end of study for a minimum of two years for DM incidence. Data on hypertension, coronary artery disease, peripheral vascular disease, stroke, and hyperlipidemia is collected as dependent variables. Cox proportional hazard model is used to perform the analyses.
Results: Study population includes 231,478 matched pairs of cases & controls with mean age of 51.3(±7.5) years. Statins have shown an increase in DM incidence (adjusted HR 2.33, 95%CI 2.28, 2.39). A linearly increasing trend in hazard ratio has been noticed with every 10 years age increase. Compared to males, females are more likely (adjusted HR 1.08; 95% CI 1.06, 1.10) to develop DM while on statins.
Conclusion: Statins raise the risk of diabetes development that increases with age. Females, with generally smaller body sizes, have higher risk of DM incidence compared to males.

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FEMORAL AND AORTIC INTIMA-MEDIA THICKNESS BUT NOT CAROTID OR BRACHIAL INTIMA-MEDIA THICKNESS ARE ABNORMAL IN CHILDREN WITH TYPE 1 DIABETES

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Objective: To investigate feasibility and sensitivity of Intima-Media Thickness (IMT) analysis at the level of the brachial artery, femoral artery and abdominal aorta compared to the carotid artery in children with type 1 diabetes mellitus (T1DM).

Background: T1DM patients are at risk for cardiovascular disease. IMT – commonly measured as carotid IMT – is an established marker for early cardiovascular risk in adults but rarely used in children. However, autopsy studies have shown atherosclerotic changes even in early childhood and most prominently in the abdominal aorta.

Methods: Using high-resolution external ultrasound, IMT was analyzed as carotid, brachial, femoral, and aortic IMT in established pediatric T1DM patients (group I) and healthy controls (group II). Excluded were individuals with other cardiovascular risk factors (smoking, obesity, dyslipidemia, hypertension).

Results: 63 subjects were studied (group I=25; group II=38). Groups were matched regarding age (13.6±3.6 vs. 13.2±4.3y, p=ns), sex, and BMI. Carotid, brachial, femoral and aortic IMT analyses were feasible in 100%, 83%, 91% and 94% of subjects, respectively. Reproducibility was excellent. IMT was increased in T1DM patients if analyzed at the level of the femoral artery (0.40±0.06 vs. 0.36±0.06mm, p=0.002) or aorta (0.58±0.11 vs. 0.52±0.10mm, p=0.011). IMT was not different between groups if analyzed at the level of the carotid or brachial artery.

Conclusion: IMT analysis at the level of the femoral artery and aorta was feasible in the vast majority of children. Femoral and aortic IMT analyses detected early vascular changes in teenage T1DM patients while carotid and brachial IMT analyses did not.

CARDIOVASCULAR DISEASE AND CARDIOPROTECTION IN DIABETES AND METABOLIC SYNDROME

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THE EFFECTS OF A LIFESTYLE INTERVENTION PROGRAM ON CENTRAL OBESITY OF PEOPLE WITH METABOLIC SYNDROME

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Purpose of the study: The purpose of this study is to examine the effects of a lifestyle intervention program (LIPMS), on central obesity and other health outcomes of people with metabolic syndrome (MS), guided by the extended Health Belief Model (eHBM).
Methods: This cluster-randomized controlled trial invited participants with two or more MS components by the American Heart Association definition. Participants in the intervention group received a 3-month LIPMS program while participants in the control group received an attention placebo. The mixed effects model was adopted to evaluate outcomes included body weight, waist circumference, blood pressure, fasting glucose, and fasting lipid profiles. These measures were further evaluated to indicate the presence of MS.
Results: The final sample consisted of 183 adults (19.1% male) with the mean age of 54.0 years (SD 7.8). More than one-third had one or more chronic diseases and half had MS. At 3 months, the outcomes of both groups exhibited a favorable trend from baseline to the end of intervention. Overall MS prevalence reduced for 13.8%. After controlling for age, gender, education level and total number of chronic diseases, statistical differences were found in the change of total cholesterol (standardized coefficients=0.065, p=0.035) and waist circumference (standardized coefficients=0.146, p=0.008) between the intervention and control group after participation in LIPMS.
Conclusions: A lifestyle intervention program based on the eHBM was effective in improving health of people with MS. The current findings provide empirical information under a theoretical framework for improving health services targeting MS.

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EFFECTIVELY SCREENING FOR CORONARY ARTERY DISEASE IN PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANT EVALUATION

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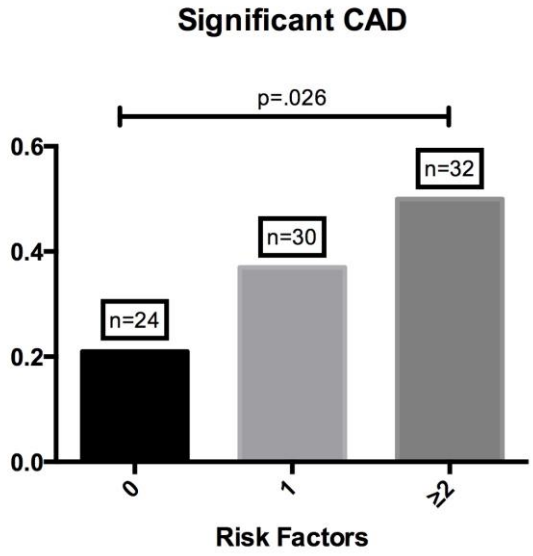
Coronary artery disease (CAD) is prevalent in patients with end-stage liver disease and associated with poor outcomes among those undergoing orthotopic liver transplant (OLT). Non-invasive screening for CAD in this population is less sensitive than in the general population. We describe our institutional experience among patients undergoing CAD screening in the course of OLT evaluation.

Methods: We retrospectively identified all patients that underwent CAD screening in the course of OLT evaluation between May 2009 and February 2014. Demographic, clinical and procedural characteristics were collated and analyzed.

Results: Within the patient cohort (n = 135), the mean age was 56 (range 32 – 71), and 92 (70%) were male. Among those undergoing angiography, obstructive CAD was common (n = 38; 28%). The number of traditional risk factors was linearly associated with CAD, and those with two or more risk factors were found to have CAD by angiography 50% of the time (OR 1.92; CI 1.07 – 3.44, p=0.026, Fig. 1).

Conclusion: Obstructive CAD is common among patients with advanced liver disease. Our data supports coronary angiography in pre-OLT patients with two or more risk factors. Whether or not this affects outcomes awaits ongoing prospective reports.



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NON-INVASIVE RISK STRATIFICATION WITH STRESS SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY IN PATIENTS WITH MYOCARDIAL INJURY FOLLOWING NON-CARDIAC SURGERY

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Myocardial injury following non-cardiac surgery (MINS), as measured by postoperative troponin elevation, is the most common major vascular complication after non-cardiac surgery. Myocardial infarction (MI) is the most common vascular complication following major surgery, and many patients with evidence of MINS will have had a perioperative MI. Risk stratification and the selective revascularization has been shown to reduce cardiovascular events in the non-perioperative MI setting, however, its utility in the perioperative setting is not established, and only a minority with MINS undergo such a strategy.
Methods: This study has consisted of a retrospective chart review of 567 patients conducted at McMaster University. We have screened patients between 2009-2014 who underwent a SPECT myocardial perfusion study within 2 months following hospital admission for surgery. Patients were included in this analysis if 1) there was evidence of MINS, defined as an abnormal troponin value in the post-operative period during the index admission, and 2) the nuclear study was performed for the purpose of risk stratification for the postoperative event. Our primary objective determined the association between the degree of ischemia identified on SPECT and the composite outcome of death, MI at 6 months. Secondary analyses evaluated the feasibility of the test in this patient population.
Results: Of the patients analyzed 120 patients were with MINS. The patients who experienced MINS were older, more likely to have diabetes, and have hypertension. The 6-month mortality rate was 2.3% (93% CI, 1.5%-1.9%). SPECT predict major cardiovascular events in individuals with MINS (92% CI, 1.27-2.23).
Conclusion: SPECT is a promising tool for providing better care for patients with MINS. The study has shown that the use of SPECT permitted early detection of major cardiovascular events in individuals with MINS. The peak troponin values were associated with higher 6-month mortality myocardial infarction as well as revascularization.

RISK STRATIFICATION AND SECONDARY PREVENTION OF CVD

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DO WE KEEP CARDIAC PATIENTS OUT OF HOSPITAL BY ADDING TELEREHABILITATION TO STANDARD REHABILITATION?

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Background: Standard in-hospital cardiac rehabilitation (CR) has been proven to be effective. Cardiac patients however often do not attend these rehabilitation sessions leading to non-compliance with lifestyle and risk factor recommendations, which is associated with increased adverse outcomes.

Objectives: We investigated whether the addition of an internet-based rehabilitation program to standard CR can reduce the number of cardiovascular rehospitalisations.

Methods: The Telerehab III study is a multi-centric randomized controlled trial, that runs from February 2013-2015. Coronary artery disease or heart failure patients were eligible. Intervention patients (n=70) were, at study start, stratified in different subgroups based on their cardiovascular risk factor profile and cardiopulmonary exercise testing. This stratification enabled the caregiver to provide each patient with a personalised diet and exercise protocol. The intervention patients were asked to wear a motion sensor continuously for a total study period of 6 months. Each week, they received feedback messages (via e-mail and/or SMS) to gradually increase their activity level and to inform them about healthy diets. Control patients (n=70) wore taped motion sensor three times for 9 days (week 1, 6 and 24) for measurement purposes only. They did not receive feedback regarding their physical activities via SMS or e-mail, nor did they receive dietary advice.

Results: The Kaplan-Meier curve showed a significant lower rehospitalisation rate in the intervention group (P=0.01055) (13 rehospitalisations), when compared to the control group (29 rehospitalisations).

Conclusions: The addition of an internet-based telerehabilitation program to standard CR can impact favorably on cardiovascular rehospitalisation rate.

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HEART ATTACK ANXIETY: THE IRONY BEHIND PHYSICAL ACTIVITY RECOMMENDATIONS FOR POST-MI PATIENTS

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Background: The American Heart Association (AHA) recommends 30 minutes of moderate-to-vigorous exercise five or more times a week for most patients surviving a myocardial infarction (MI). The characteristics of those who will maintain this lifestyle recommendation are currently unknown.
Methods: We conducted a nationally representative survey of 1500 U.S. adults previously diagnosed with an MI. Patients reported their demographics, usual physical activity pattern, and nominated their single most important current health concern. Patients were categorized into those who did and did not meet the AHA exercise recommendation, using the validated, single-item question assessing days per week of moderate or vigorous physical activity >30 minutes.
Results: 38% of respondents were female and the average age was 60.9 years (+ 11.9 SD). 18% of patients reported that "worsening of heart problems" was their single most important health concern. 24% reported regular exercise at the level recommended by the AHA. Ironically, those who reported worsening heart problems as their single most important health concern were significantly more likely to not meet the exercise recommendation in multivariable analysis, (adjusted odds ratio [aOR] 1.40, 95% CI 1.01-1.94), as were women (aOR 1.40, 95% CI 1.09-1.81) and those over 65 years of age (aOR 1.34, 95% CI 1.03-1.75).
Discussion: For patients surviving a MI, adherence to exercise guidelines was worse among those who were most concerned about a decline in their heart health. Appropriately tailoring an exercise message to those surviving, and worrying about heart disease, may require interventions derived from fear and avoidance science.

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OPIUM ADDICTION AND EARLY AND 6-MONTH OUTCOMES OF PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION

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Background: Myocardial infarction is one of the most important causes of mortality worldwide. To date multiple risk factors have been described but still the role of opium addiction is not clarified yet and there are many unproved believes about it.
Objectives: This study is performed to evaluate if opium addiction has any effect on early and 6 month outcomes of ST elevation myocardial infarction (STEMI).
Methods: This cohort study was performed on 334 patients with STEMI in Shahroud, Iran, during years 2009-2012. There were 117 patients with opium addiction and 217controls. Patients were followed up during hospitalization and for 6 months and the primary endpoint of the study was a composite of death, heart failure, recurrent chest pain and recurrent STEMI.
Results: The primary end point of the study was not significantly different neither during in-hospital nor 6–month follow up ($P>0.05$). Some risk factors of coronary artery disease (CAD), including hypertension, diabetes and hyperlipidemia were seen less in opium addiction group ($P<0.05$), but family history of CAD was not significantly different.
Conclusion: The present study showed that although opium addicted patients had less risk factors of CAD, in-hospital and 6-month adverse outcomes were not significantly different in STEMI patients with or without opium addiction.

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CORONARY ARTERY DISEASE AND SERUM APELIN LEVELS: A META-ANALYSIS

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Background: Apelin is peptide produced by adipose tissue that appears to function as an endogenous ligand for the orphaned G-protein-coupled receptor (APJ). The Apelin/APJ system plays a role in regulating cardiovascular system physiology and homeostasis. It is suggested that apelin/APJ system may possess an anti- atherogenic effect via endothelium-dependent vasodilation and down regulating expression of adhesion molecules and chemokines leading to reduced vascular inflammation. The association between serum apelin and coronary artery disease (CAD) is obscure.
Objective: The aim of the present study is to conduct a meta-analysis to evaluate the relationship between circulating apelin levels and CAD.
Methods: We searched MEDLINE, CINHAL and COCHRANE databases for studies reporting serum apelin levels in the CAD and non CAD study population. We included case controls, cohort and cross-sectional studies. We calculated the weighted standardized mean difference (SMD) in serum apelin levels between the CAD and control groups.
Results: Our search strategy yielded 160 articles and we included 7 studies enrolling 1266 participants. The median age of the CAD group was 58.9yrs (IQR 55.7 – 63.4) compared to 56.1yrs (IQR 43-56.1) in the control group. The median body mass index in the CAD group was 24.9 kg/m2 (IQR 24.9-25.1) compared to 24.2 kg/m2 (IQR 23.7-24.7) in the control group. The unweighted median serum apelin levels in the CAD group were 0.54 ng/ml (IQR 0.05-0.66) compared to 1.98 ng/ml (IQR 0.07-3.11) in the control group. The SMD of serum apelin level was -2.53 (95% CI -3.50, -1.56) $p<0.001$ comparing those in the CAD and control group.
Conclusion: Serum apelin levels are significantly and negatively associated with CAD. Further studies are needed to clarify the role of apelin in the development of CAD and its potential to serve as a novel biomarker.

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ST DEPRESSION IN LEAD AVL AS A POTENTIAL PREDICTOR OF POOR OUTCOME AND PROGNOSIS FOR NSTEMI PATIENTS

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Introduction: ST depression in lead aVL has been postulated to predict poor outcome after acute myocardial infarction (AMI). The objective of this study is to investigate the correlation between ST depression in lead aVL and multi-vessel coronary disease in patients with Non-ST elevation MI (NSTEMI) and the outcome of these patients.
Methods: Charts of all patients that underwent diagnostic coronary angiography for NSTEMI at an urban community hospital were retrospectively reviewed. The ECGs of all patients were reviewed for changes in lead aVL. ECGs were recorded in 12-lead format and reviewed by two independent physicians (one cardiologist and one emergency department physician). ST-segment depressions in lead aVL were noted. Coronary angiogram results were studied and the correlation between the ST segment depression and the number of vessels affected examined. In addition, in-hospital mortality, length of hospital and intensive care unit stay, readmission rate as well as the need for coronary artery bypass graft (CABG) was studied.
Results: 218 patients underwent percutaneous coronary intervention (PCI) for NSTEMI. 42 patients (19.3%) were found to have ST segment depression in lead. Of these 42 patients who had STD in lead aVL, 12 patients (29%) had triple vessel disease (TVD) and 3 patients (7.1%) had left main disease (LMD). Seven patients (16.7%) underwent coronary artery bypass graft (CABG) of which two patients (28.6%) had LMD. All seven of the patients (100%) had TVD. Five patients (71.4%) were male and two patients (28.6%) were female. The average age for these patient groups was 75 years.
Conclusion: ST depression in lead aVL was increasingly associated with TVD and LMD and may predict significant coronary artery disease. This study can help identify patients with NSTEMI that require aggressive management and early coronary catheterization. Further studies with patients who have NSTEMI are required to verify these findings.

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DYNAMIC LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION: ECHOCARDIOGRAPHY GUIDED CLINICAL RISK PREDICTION IN CRITICAL CARE SETTINGS

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Introduction: Dynamic left ventricular outflow tract obstruction (LVOTO) is increasingly recognized in critically ill patients. The aim of this study is to identify clinical risk predictors that may identify high risk patients as predicted by echocardiographic features. *Methods:* Clinical and demographic data of all patients diagnosed with acute LVOTO were matched with a randomly derived control group to develop a clinical scoring model. Subsequently, consecutive patients (n=167) admitted to intensive care units (July 2007 - November 2009) and underwent echocardiography were screened to identify 143 patients. Using pre-determined echocardiographic criteria, a blinded observer classified all patients as either high or low risk for developing LVOTO. *Results*: The cross sectional study could not validate the clinical score because it did not differentiate between different LVOTO risk groups (p=0.54). Univariate analysis suggested female sex (high vs low risk, 64% vs 32%; p=0.009), advanced age (74.8 ± 14.1 vs 57.8 ± 18.4; p=0.0004) and lack of inotrope use (35% vs 61%; p=0.03) to be significantly associated with high risk LVOTO group. All other variables were insignificant. Based on the multiple logistic regression, age (p= 0.003) was found to be the only independent predictor of high risk for developing LVOTO, with the estimated area under the ROC curve (AUC) being 0.81.
Conclusion: Elderly patients are at high risk of developing dynamic LVOTO. Other clinical and demographic parameters did not reliably predict risk in our study. Larger studies are warranted to validate clinical risk prediction models to better manage this potentially life threatening cardiac condition.

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POSTINFARCTION VENTRICULAR DEFECT: OPERATE OR WAIT?

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Objectives: The objective of this paper was to study the clinical application of our decision algorithm in the treatment of post-infarction VSD at the Montreal Heart Institute.
Methods: Between April 2004 and August 2014, 35 consecutive patients with post-infarction VSD were treated. Twenty-three patients underwent surgery, and twelve patients were treated with percutaneous closure of VSD during the same period.
Results: The mean age was 67.9 ± 10.1 years and 70% of patients were male. Before surgery, 78% of patients were in cardiogenic shock and 87% were supported had IABP pump. The preoperative EuroSCORE II was 21.9 ± 14.5%.. 74% of patients were in New York Heart Association functional class III or IV preoperatively. The mean time between acute myocardial infarction and the VSD diagnosis was 6.7 ± 4.1 days and between VSD diagnosis and surgery was 1 day. The average VSD size was 19.4 ± 9.7 mm and 74% were located in apical position. 2 patients had failed Amplatzer before surgery. 65% of patients underwent concomitant coronary bypass surgery with an average of 1 ± 1.1 grafts, and 26% patients underwent other concomitant procedures. 52% of patients developed acute renal failure with 35% requiring temporary dialysis. Mild to moderate residual VSD was present in 35% of cases and dehiscence of the patch was found in 13% of cases, requiring reoperation. The overall mortality was 22% at 30 days. In the percutaneous occlusion treatment group (n = 12), the 30-day mortality was 58% and mild to moderate residual VSD persisted in 42% of cases.
Conclusion: The early management of stable VSD is associated with acceptable mortality rates. The emergence of new technologies (ventricular assistance device, percutaneous Amplatzer) could stabilize critical patients, but their role is not yet well defined.

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THE ROLE OF PHARMACOLOGICAL THERAPY IN CHRONIC HEART VALVE DISEASES

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Valvular heart diseases (VHDs) are progressive. When they are "primary", i.e., due to intrinsic abnormality of valve structure and not secondary to comorbid conditions (e.g., ischemia), they generally are characterized by long asymptomatic phases during which cardiac functional and hemodynamic debility progresses. Ultimately, these developments lead to symptoms, other morbidities and, finally, death. Treatment depends on VHD type and severity. However, when VHDs are hemodynamically/functionally severe and symptomatic, therapy generally requires mechanical intervention (replacement or repair). Asymptomatic patients, and those who lack objective descriptors that predict high imminent risk, are managed by close clinical observation and efforts to minimize associated cardiovascular risk factors until surgical indications develop. In this setting, drugs often are prescribed based on theoretical concerns or preclinical studies or small clinical studies involving "surrogate" rather than clinical endpoints. However, no rigorous evidence supports pharmacological therapy in most chronic situations. For Aortic Stenosis, multiple drugs (statins, ACE inhibitors, bisphosphonates, etc.) have been tested. Rigorous randomized controlled trials are available only with statins and these generally have shown no benefit. For Aortic Regurgitation, multiple direct and indirect vasodilators have been studied, generally for effect on surrogate, rather than clinical, outcomes; the only drug shown in randomized controlled trials to benefit outcome has been long-acting nifedipine, and that benefit seems to have been largely related to effect on the comorbidity of hypertension. For Mitral Stenosis, no drugs have been rigorously studied for clinical outcome. For Mitral Regurgitation, few studies are available and all have been neutral or negative (i.e., potentially harmful). Based on these findings, hemodynamically active drugs generally should be avoided in asymptomatic patients with primary valve disease.

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FIRST-IN-HUMAN TRANSCATHETER MITRAL VALVE REPLACEMENT FOR NATIVE MITRAL VALVE REGURGITATION

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Mitral regurgitation is a common valvular heart disease. The prevalence increases with age. Therefore, with the aging of the population, a continuing increase in the prevalence of mitral regurgitation is expected in the coming years. Surgical mitral valve repair or replacement is the standard treatment of mitral regurgitation. However, a study has demonstrated that 49% of patients with severe mitral regurgitation were declined for mitral valve surgery due to impaired left ventricular systolic function, older age, and significant comorbidity. Moreover, the benefit of surgical treatment of functional or ischemic mitral regurgitation remains controversial. As transcatheter aortic valve implantation, developing transcatheter mitral valve replacement would benefit the patients with severe mitral regurgitation who are declined valve surgery. In recent years transcatheter mitral valve replacement has aroused significant interest and many transcatheter valve devices have been developed. However, there were only a few first-in-human (FIH) transcatheter mitral valve replacement cases that were performed worldwide. We performed our first transapical transcatheter mitral valve replacement with the Edwards FORTIS self-expandable transcatheter mitral valve in an 81 years old patient with symptomatic severe functional mitral regurgitation and left ventricular dysfunction, who was not a surgical candidate for open-heart surgery. The FORTIS valve was successfully implanted under the guidance of echocardiography and fluoroscopy. No contrast or rapid ventricular pacing was required. At 6-month follow-up, the patient heart failure symptom was improved significantly. The follow-up echocardiography showed normal function of the well-seated FORTIS valve with trivial paravalvular leak and no mitral regurgitation, as well as positive LV remodeling with improved left ventricular systolic function. Transcatheter mitral valve replacement is challenging, but shows tremendous promise.

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AORTIC VALVE DISEASE MANAGEMENT FOR THE 21ST CENTURY: THE UNFOLDING OF TAVR REVOLUTION

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Transcatheter aortic valve replacement (TAVR) has become the preferred therapy for the treatment of aortic stenosis compared to surgical aortic valve replacement among high-risk patients. The enthusiasm from the success of TAVR in high risk patients is affecting management decisions for all patients with aortic valve disease and application of TAVR is being used for patients not included in the landmark studies done for regulatory approval.

In addition to inoperable or high surgical risk patients with native aortic stenosis, TAVR has demonstrated promising medium term results for treatment of failed aortic and mitral bioprosthesis. At present, clinical trials are also underway to examine the role of TAVR as the initial management strategy compared to surgical aortic valve replacement for low to moderate surgical risk patients. With the advent of new technology and evolution of existing devices, an even greater number of patients with aortic valve disease may benefit from TAVR therapy.

This presentation will review the epidemiology of aortic stenosis; describe recent trends in the surgical management of aortic valve disease and discuss implications for TAVR therapy in the next decade. Furthermore, the promise offered by the 2nd generation transcatheter heart valves, recent data for long term durability and TAVR trends across countries will be presented.

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LIPID LOWERING IN PATIENTS WITH MILD AORTIC STENOSIS AND ELEVATED LOW DENSITY LIPOPROTEIN: THE SEAS STUDY

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Aims: To examine if pretreatment low density lipoprotein cholesterol (LDL) levels and aortic stenosis (AS) severity alter the efficacy of lipid-lowering therapy in AS patients.
Methods and Results: Asymptomatic patients with AS randomized (1:1) to 40 mg Simvastatin + 10 mg Ezetimibe combination vs. placebo and ≥2 echocardiograms in the SEAS trial. The main endpoint in this substudy was impact of randomization on the association between pretreatment LDL levels and progression in AS severity, as determined by peak aortic jet velocity and a composite cardiovascular endpoint. Treatment effect was analyzed by separating patients into quartiles of LDL levels in mild and moderate-to-severe AS (>3.0 m/sec). A total of 1,682 patients were followed for a mean of 4.4 years (7,373 patient-years of follow-up). Among patients in the highest quartile of LDL with mild AS at baseline (p=0.03 for interaction), Simvastatin-Ezetimibe was associated with lesser end of study progression in peak jet velocity (OR 0.85, 95% CI: 0.74 – 0.98, p=0.03). In a parallel analysis, Simvastatin-Ezetimibe also reduced composite endpoints in the highest quartile of LDL with mild AS at baseline (HR 0.46, 95% CI: 0.23 – 0.90, p=0.02). Conversely, there was no detectable effect of Simvastatin-Ezetimibe combination on AS progression in the other LDL quartiles with mild AS baseline (p=0.75). No effect of lipid lowering was noted in patients with moderate to severe aortic stenosis irrespective of pretreatment LDL levels (p=0.87).
Conclusion: In a non-prespecified post-hoc analysis, asymptomatic patients with mild AS and elevated LDL benefited from lipid-lowering therapy (SEAS study: NCT00092677).

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MISCONCEPTIONS AND DIAGNOSTIC CHALLENGES IN BIOPROSTHETIC VALVE THROMBOSIS

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Bioprosthetic valve thrombosis (BPVT) is a rare, but potentially life-threatening complication. In a review of the Mayo Clinic experience we found that BPVT was systematically under-reported on TTE, and that most cases occurred late post-implantation. Furthermore, oral anticoagulation with vitamin K antagonists resulted in hemodynamic and clinical improvement with minimal risk, and should be considered first line therapy in hemodynamically stable patients. Echocardiographic criteria for improving BPVT diagnosis are proposed.

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MANAGEMENT OF ASYMPTOMATIC AORTIC STENOSIS: WHAT IS NEW IN 2015?

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Calcific aortic stenosis is now the primary etiology of aortic stenosis in the majority of patients. Risk factors such as hyperlipidemia play an important role in the progression of aortic stenosis. According to the most recent American College of Cardiology/American Heart Association guidelines, peak velocity greater than 4 m/sec, or a mean gradient of more than 40 mmHg and a valve area of less than 1.0 cm2 is considered hemodynamically severe aortic stenosis. Aortic valve surgery promptly should be done in symptomatic patients due to dismal prognosis without operation. Features such as reduced left ventricular ejection fraction (<50%), very high velocity (>5 m/sec) or a high mean gradient (>60 mm Hg) or a positive exercise test identify high risk asymptomatic patients who would benefit from early aortic valve surgery. Recently, it was recognized that up to 25% of severe aortic stenosis patients may have low trans-valvular gradient despite preserved left ventricular ejection fraction due to concentric remodeling and high vascular resistance. Although challenging, identification of this subgroup is important due to reduced long term survival without surgery. Currently percutaneous aortic valves are used only in very high-risk patients with severe symptomatic aortic stenosis. Their role may expand in the future, depending on the technological advances and operator experience.

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ROLE OF CILIA IN CONGENITAL HEART DISEASE

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Motile cilia at the embryonic node and in the respiratory tract are required for left-right patterning and for muco-ciliary clearance from the respiratory tract, respectively. The heart is one of the most asymmetric organs in the body in order to support two separate circulatory systems, the pulmonic and systemic circulations, in parallel. Hence defects in ciliary function could contribute to abnormal heart development resulting in congenital heart disease (CHD) as well as increased respiratory complications. This dual role is exemplified by patients with primary ciliary dyskinesia (PCD) in which patients have abnormal respiratory ciliary function leading to severe respiratory complications over time as well as ~50% of patients having complete reversal of visceral organ situs or situs inversus totalis.

Laterality defects are characterized by randomization of left-right patterning in thoraco-abdominal visceral situs. We have shown that patients with complex CHD with heterotaxy have a high prevalence of ciliary motion (CM) abnormalities as demonstrated by abnormally low nasal nitric oxide (nNO) levels as well as high-speed video-microscopy of ciliated nasal epithelial tissue. These CHD patients with CM abnormalities had increased respiratory symptoms reminiscent of PCD patients and were enriched for mutations in genes typically associated with PCD. We have also extended this work with studies on patients with transposition of the great arteries (TGA), both D- and L-TGA, and show that these patients, similar to heterotaxy patients, have a high prevalence of abnormal CM, borderline or PCD level abnormal nNO levels, increased respiratory symptoms as compared to TGA patients without CM abnormalities, and are enriched for novel or rare coding variants in the genes typically associated with PCD. In addition we have shown that a wide variety of CHD patients have CM abnormalities along with low nNO level and these are associated with increased respiratory symptoms as well as adverse post-operative outcomes.

Our studies support a possible underlying mechanism leading to development of CHD involving mutations in genes relating to cilia structure or function. Screening patient with CHD for ciliary dysfunction might allow for prophylactic treatment of such patients in order to decrease their risk of post-operative infection and complications, which typically have been attributed to their CHD in the past.

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REOPERATIVE CARDIAC SURGERY IN ADULT CONGENITAL HEART DISEASE PATIENTS

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Objectives: To discuss the spectrum of anomalies which require reoperative cardiac surgery in the adult congenital heart disease (ACHD) patient.
Background: There are >1,000,000 ACHD patients in North America. Cardiac surgery in those is divided into cases involving great complexity (e.g. cyanotic lesions, single ventricle, double-outlet ventricle), moderate complexity (e.g. anomalous pulmonary venous drainage, atrioventricular septal defects, coarctation, Ebstein's, right ventricular (RV) or left ventricular (LV) outflow tract obstruction, non-secundum atrial septal defect (ASD), pulmonary regurgitation (PR) or stenosis, tetralogy of Fallot, complicated ventricular septal defect (VSD)), and simple complexity (e.g. isolated congenital valve stenosis or insufficiency, simple VSD, secundum ASD).
Results: The majority of reoperations for ACHD patients involve reoperative valve replacement, especially in the pulmonary position. Often, more than one valve is addressed at reoperation, the most common being pulmonary valve replacement and tricuspid valve repair. Pulmonary valve replacement is indicated for severe PR with symptoms, RV dysfunction/enlargement, arrhythmias, or significant tricuspid insufficiency. Indications for reoperative valve repair or replacement include worsening CHD valvar stenosis or regurgitation, which should undergo valve therapy as in patients with non-congenital valve disease. Patients may also present with subaortic stenosis, and should undergo resection if operative criteria are met. Other operations include reoperations on the RV outflow tract for obstruction from severe valvar obstruction who require surgery if percutaneous therapy is contraindicated. Subvalvar stenosis, supravalvar stenosis and double-chambered RV require surgery. Only a minority of single ventricle patients will require reoperation in adulthood, most commonly either implantation of an epicardial pacemaker/defibrillator, or heart transplantation.
Conclusions: Reoperative cardiac surgery for ACHD patients involves a wide spectrum of lesions with established indications and reasonable morbidity and mortality. As more CHD patients survive into adulthood, the variety of reoperative cardiac surgical repairs will increase in complexity.

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CHILDREN WITH CONGENITAL HEART DISEASE MAY BE AT RISK FOR PREMATURE ATHEROSCLEROSIS IN SPITE OF SUCCESSFUL BIVENTRICULAR REPAIR

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Objective: To prospectively assess the risk for premature vascular aging in asymptomatic children with congenital heart disease (CHD at least 5 years after successful surgical repair.
Background: Autopsy studies have shown that atherosclerotic changes can be found in early childhood. Oxidative stress, endothelial dysfunction, and vessel wall proliferation have been associated with key initiating events in developing vascular disease. Little is known about the vascular status of children with congenital heart disease CHD years after successful biventricular repair in infancy.
Probands and methods: 32 pediatric patients with CHD and 33 controls (11 age-matched children and 22 young adults), matched for sex, race, and BMI. The CHD group comprised Ventricular Septal Defects (5), Tetralogy of Fallot (10), and Transposition of the Great Arteries (17). Plasma markers for pro-/antioxidative balance included homocystein, malondialdehyde, vitamin C, TRAP assay, and sulfhydryl groups. Brachial flow mediated vasodilation (FMD) and Intima-Media Thickness (IMT) were analyzed using high-resolution external ultrasound. Excluded were individuals with standard atherosclerosis risk factors such as smoking, diabetes, hypertension, obesity, and dyslipidemia.
Results: Compared to pediatric controls, CHD patients – like adult controls – had higher homocystein levels, lower vitamin C levels, and impaired FMD. IMT was only increased in adult controls.
Conclusion: In teenage patients with biventricular CHD, successfully repaired in infancy, evidence was found for oxidative stress endothelial dysfunction. This population may be at risk for premature vascular aging.

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AGING, EXTRACELLULAR MATRIX AND HEART FAILURE: 2015

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The aging population with heart failure (HF) is increasing worldwide. Hypertension (HTN) and myocardial infarction (MI) are the two main comorbidities leading to HF in the elderly (age ≥ 65 years). Aging is progressive and results in cardiovascular changes that lead to an aging phenotype and negatively impact disease expression and response to therapy. Aging-related changes contribute to adverse cardiac remodeling and HF with preserved ejection fraction (HF/PEF). HTN also leads to HF/PEF whereas MI leads to HF reduced EF (HF/Low-EF). Aging and concomitant HTN or MI accelerates the march to HF. The cardiac extracellular matrix (ECM) is critical for maintaining cardiac shape/function. A key mechanism in the development and progression of HF due MI and HTN involves adverse cardiac ECM remodeling. Disruption of the ECM network and dysregulation of ECM homeostasis and metabolism result in adverse cardiac remodeling with shape deformation and dysfunction that lead to HF, disability and death. Aging-related cardiac remodeling with superimposed progressive left ventricular remodeling leading to HF/PEF or HF/Low-EF in older patients is a persistent problem that has important therapeutic implications. Studies suggest that in the elderly, novel pathways can be targeted for optimizing therapy in HF/Low-EF post-MI and HF/PEF post-HTN. Therapeutic strategies that include targeting of adverse cardiac ECM remodeling could prevent/limit/reverse progression to HF in aging patients.

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THE POST-PERICARDIECTOMY SYNDROME: PREVENTION AND MANAGEMENT

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The post-pericardiotomy syndrome (PPIS) and post-operative effusions affect over one third of patients after cardiac surgery, and while they often have little impact on management, they may lead to prolonged hospital stay, readmissions, and the need for pericardial drainage. Treatment of the PPIS is similar to other types of acute pericarditis, and includes the initial use of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine, with steroids reserved for refractory or relapsing cases. Colchicine is the only therapy that has been demonstrated to significantly reduce the incidence of post-cardiac injury syndrome following cardiac surgery, but there are conflicting data suggesting that colchicine use postoperatively may be associated with an increased number of adverse medication-related side effects. Two randomized, double-blind trials have evaluated colchicine in this regard. Data from the Colchicine for the Prevention of Post-pericardiotomy Syndrome (COPPS)-1 trial of 1 month post-operative treatment with colchicine begun on postoperative day 3 significantly reduced the occurrence of the PPIS at 12 months (relative risk 0.42, 95% CI 0.24-0.73) with similar rates of side effects, primarily related to gastrointestinal intolerance in the colchicine and placebo groups. Data from the COPPS-2 trial of 1 month post-operative treatment with weight-adjusted colchicine beginning 48 to 72 hours prior to surgery significantly reduced the occurrence of the PPIS at three months (relative risk 0.66, 95% CI 0.45-0.96). However, unlike the COPPS-1 trial, treatment with colchicine was associated with significantly more gastrointestinal adverse effects. A 1-month course of colchicine to reduce the risk of developing PPIS and its potential complications should be weighed against the risk of medication-related side effects. In those who choose not to take colchicine, the early recognition and treatment of PPIS is important.

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CARDIAC FIBROSIS IN HEART FAILURE

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Myocardial fibrosis is a fundamental event in the development of cardiac failure, and is a common feature in all patients with advanced cardiac failure regardless of the aetiology of cardiomyopathy. Increasing myocardial fibrosis results in progressive deterioration of myocardial function, with more extensive myocardial fibrosis identified histologically in the hearts of patients with advanced heart failure. Regional myocardial fibrosis, whilst most commonly observed in ischaemic cardiomyopathy, is present in a broad range of non-ischaemic cardiomyopathies. With the advent of cardiac magnetic resonance (CMR) imaging, identification and quantification of regional fibrosis with late gadolinium enhancement (LGE) has stimulated research into the diagnostic and pathological role of regional cardiac fibrosis in cardiomyopathy. Whilst initially focused on its role in the identification of myocardial scar in ischaemic heart disease, the presence and distribution of LGE has improved diagnosis across a range of cardiomyopathies, including sarcoidosis and amyloidosis. Regional fibrosis is also now thought to play a significant role as a substrate for malignant ventricular arrhythmia, and its presence has been linked to pathological cardiac remodelling and adverse prognosis. Diffuse myocardial fibrosis is observed in all forms of advanced cardiomyopathy, and can now be assessed semi-quantitatively with CMR T1 mapping. Prior studies using either contrast-enhanced or non-contrast T1 mapping have demonstrated strong correlations with myocardial T1 time and the extent of diffuse fibrosis histologically. Using CMR T1 mapping, a relationship between interstitial fibrosis and cardiac stiffness has been demonstrated, where it is likely to play a significant mechanistic role in heart failure with preserved ejection fraction (HFPEF). Additional studies have demonstrated the utility of CMR T1 mapping in the differentiation of cardiomyopathy, and the extent of diffuse fibrosis identified by CMR has been shown to be a strong, independent predictor of adverse outcome in heart failure.

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GENETIC EPIDEMIOLOGY OF LEFT VENTRICULAR HYPERTROPHY

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Left ventricular (LV) hypertrophy is a strong independent predictor of increased cardiovascular morbidity and mortality in clinical and population-based samples. Clinical and hemodynamic stimuli to LV hypertrophy induce not only an increase in cardiac mass and wall thickness but also a fundamental reconfiguration of the protein, cellular and molecular components of the myocardium. Several studies have indicated that LV mass is influenced by genetic factors. The substantial heritability for LV mass in population-based samples of varying ethnicity indicates robust genetic influences on LV hypertrophy. Genome-wide linkage and association studies in diverse populations have been performed to identify genes influencing LV mass, and although several chromosomal regions have been found to be significantly associated with LV mass, the specific genes and functional variants contained in these chromosomal regions have yet to be identified. In addition, multiple studies have tried to link single-nucleotide polymorphisms (SNPs) in regulatory and pathway genes with common forms of LV hypertrophy, but there is little evidence that these genetic variations are functional. Up to this point in time, the results obtained in genetic studies are of limited clinical value. Much of the heritability remains unexplained, the identity of the underlying gene pathways, genes, and functional variants remains unknown, and the promise of genetically-based risk prediction and personalized medicine remain unfulfilled. However, molecular biological technologies continue to improve rapidly, and the long-term potential of sophisticated genetic investigations using these modern genomic technologies, coupled with smart study designs, remains intact. Genetic investigations offer much promise for future prevention, early intervention and treatment of this major public health issue.

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THE ROLE OF RIGHT VENTRICLE ON HEART FAILURE PROGRESSION

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Right ventricle (RV) has become a priority in cardiovascular research, playing a significant role in the prognosis of patients with heart failure. Both ventricles share similarities but also many differences. In the embryological origin, the shape, myocardial characteristics and architecture, physiological pump conditions and flow characteristics. The motion of tricuspid annuls plays a significant role for the filling of right ventricle; while isovolumic contraction and relaxation times are rather shortened. In high pressure conditions, those times are prolonged and the pressure-volume curve of the right ventricle becomes similar with that of the left ventricle. Beyond those morphological differences, there are also molecular differences between the left and right ventricles in response to adverse loading, with the right ventricle showing less response to a1 adrenergic stimulation, BNP infusion, compared to the left ventricle. Right ventricle pacing leads to little detectable mechanical activity (measured as developed pressure) in the left ventricle. Reducing left ventricle volume from its optimal volume to zero causes a 5.7% decrease in right ventricle developed pressure, whereas ligating the coronary supply to the left ventricle free wall results in an additional 9.3% decrease in right ventricle developed pressure; while >50% of the normal right ventricle mechanical work may be generated by left ventricle contraction and that the left ventricle free wall plays a pivotal role in right ventricle function. The prevalence of RV dysfunction in patients with reduced left ventricle left ejection fraction reaches almost 73% when assessed by Tissue Doppler. In dilated cardiomyopathy right ventricular ejection function is as complementary, independent prognostic factor, though significant correlations exist between both left and right parameters of ventricular function and has been associated with overall survival more accurately than VO2max in both severe and moderate heart failure. Right ventricular failure is a major contributor of significant morbidity and mortality after left ventricular assist devices placement. The complex pathophysiology of right ventricular failure, which could potentially be related to RV myocardial dysfunction, interventricular dependence, and right ventricular afterload, has led to inconsistencies in predicting risk factors for right ventricle dysfunction. There are several therapeutic interventions aiming to improve right ventricular performance, even in the case of heart failure with preserved ejection fraction. Among all imaging modalities, magnetic resonance and Doppler echocardiography have shown significance on visualizing right ventricular function and clinical prognosis

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EVOLVING UNDERSTANDING OF STRESS CARDIOMYOPATHY

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Stress cardiomyopathy (SC), also called Takotsubo cardiomyopathy, is increasingly diagnosed world over. ER physicians, Internists, Intensivists and anesthesiologists increasingly encounter SC patients presenting with angina, heart failure or arrhythmia. Initially, most patients were diagnosed in the catheterization lab when coronary angiograms were normal in STEMI settings. With increasing awareness among various providers and the wide proliferation of echocardiography, majority of this diagnosis is now made in critically ill hospitalized medical and surgical patients. The widely accepted Mayo criteria for diagnosis requires angiographic proof of normal coronaries. We have published a non-invasive echo based diagnostic algorithm that is applicable widely but especially suitable for the critically ill patients who are not candidates for catheterization or revascularization due to co-morbidities. Typical mental or physical stresses, ECG ischemia and subtle enzyme elevation raise the suspicion of 'possible SC'. The first test can be an echocardiogram with careful assessment of LV wall motion. Disproportional significant LV dysfunction and regional abnormalities not conforming to a single coronary territory or characteristic apical ballooning raises this diagnosis to 'probable SC' at presentation. While unstable or critical coronary disease excludes SC, in a significant portion of the people with this diagnosis, we detect coincidental mild to moderate CAD during catheterization. If symptoms or ECG suggest STEMI, catheterization and revascularization should not be delayed. In many situations, especially in critically ill medical and surgical patients, catheterization is deferred for a few days for medical stabilization. The most specific diagnostic criterion and unique feature of SC is the spontaneous complete normalization of LV function and wall motion; this typically occurs within a few days requiring only supportive care. Thus, repeat echo after 3-5 days of presentation may demonstrate this recovery of LV function, facilitating the diagnosis of 'definite SC'. Clinical suspicion and echocardiography can optimize SC care.

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MYOCARDIAL SEGMENTAL THICKNESS VARIABILITY ON CMR DISTINGUISHES ISCHEMIC AND NON-ISCHEMIC DILATED CARDIOMYOPATHY

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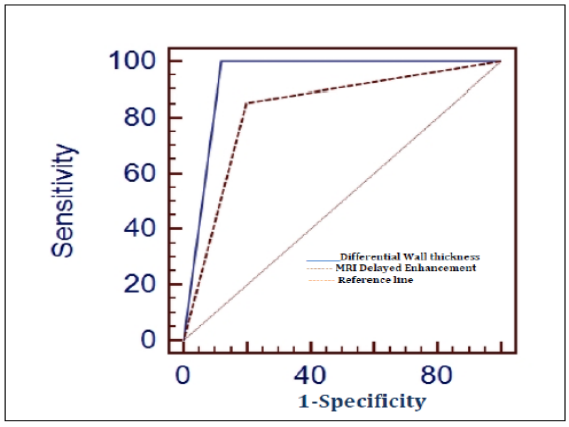
Objective: We hypothesized that in patients with dilated cardiomyopathy of unknown etiology, segmental wall thinning from infarcted or hibernating myocardium on CMR (cardiac magnetic resonance) imaging can distinguish ischemic cardiomyopathy (ICM) from non-ischemic cardiomyopathy (NICM).
Background: Distinction of dilated ICM from NICM is critical, however can be challenging by noninvasive testing.
Methods: We retrospectively identified 72 consecutive dilated cardiomyopathy patients of unknown etiology referred for CMR over a two-year period. CMR protocol included 2D steady state free precession (SSFP) cine, perfusion, delayed contrast enhancement (DE) imaging and additional sequences as required. We defined segmental wall thickness variability (differential wall thickness) as >50% difference in end systolic thickness, between the segments (a minimum of two) of any two different coronary territories. CMR characteristics of cardiac chamber morphology, differential wall thickness (DW), wall motion, valves, pericardium, myocardial perfusion and DE were compared between the ICM and NICM (as confirmed by coronary angiography) using $\chi 2$ and ANOVA. Their diagnostic value was assessed using ROC analysis.
Results: A total of 30% had NICM. Mean age, left ventricular size and ejection fraction of the study population were 58 years, 6.2 cm, and 28%, respectively. No significant difference was observed between the ICM and NICM among baseline characteristics and 13 of the 15 CMR markers. DW and DE imaging on CMR differentiated ICM from NICM. DW outperformed DE in diagnosing ICM with a sensitivity and specificity of 94% and 99% versus 89% and 74% respectively (figure).
Conclusions: DW resulting from thinning of infarcted or hibernating myocardium can accurately differentiate ICM from NICM where segmental wall thickness is uniform. As DW can be assessed by CMR with no IV contrast, it is especially useful in patients where IV Gadolinium is contraindicated.



ROC curves demonstrating the diagnostic performance of myocardial segmental thickness variability and delayed enhancement imaging on CMR in distinguishing ICM from NICM, when compared to coronary angiogram

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ASSESSMENT OF RIGHT VENTRICULAR INVOLVEMENT IN TAKOTSUBO CARDIOMYOPATHY

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Background: Although left-ventricular (LV) involvement in Takotsubo cardiomyopathy (TC) is well defined, right ventricular (RV) involvement may be under reported.
Objective: Compare co-morbidities, echocardiographic findings, and the clinical course of patients diagnosed with TC with RV involvement to those patients without RV involvement. *Methods:* A retrospective chart review identified 58 patients admitted from January 2006 to November 2011 with TC who underwent coronary angiography and had an absence of high grade coronary artery disease. LV dysfunction and RV dysfunction was defined by standard American Society of Echocardiography guidelines, and these guidelines were followed for analysis of the echo data. Both groups were compared using an unpaired student t-test.
Results: The average age of the cohort was 70 years, 80% of which were female. Further findings are reported in table 1. None of the patients died during the hospitalization.
Conclusions: Patients with TC and RV involvement were more frequently former tobacco users, had numerically lower ejection fractions, increased frequency of ST-elevation, and a longer hospital stay. None of these findings reached statistical significance; however, this may be secondary to our small cohort, which is a limitation of this study. Further exploration of RV involvement in patients with TC is warranted.

Table 1. Co-morbidities, echocardiographic findings and clinical course of TC cases in those patients with, and without, RV involvement. Values are mean (± standard deviation) unless otherwise noted. Percentages are percent of the patient population

	RV dysfunction + LV dysfunction (n=34)	**LV dysfunction only (n=24)**	**P value**
Co-Morbidities			
Hypertension	68%	71%	
Diabetes Mellitus	21%	21%	
Tobacco history	59%	42%	
Current tobacco use	9%	13%	
Echocardiography			
LV ejection fraction	.40 (±14)	.45(±.14)	.17
Wall motion score	1.8 (±.4)	1.8(±.4)	.43
Apical Left Ventricular Variant	79%	75%	
Mid-Left Ventricular Variant	21%	25%	
Basal-Left ventricular variant	0	0	
Clinical Course			
CKMB	13.5(±16.4)	22.4(±34.6)	.21
Peak Troponin	.34 (±.45)	.37 (±.4)	.76
BNP	914 (±813.5)	1412 (±1481.7)	.19
ECG ST Elevation	56 %	42 %	
Average Length of Hospitalization (days)	6.3 (±6)	5.4 (±6.5)	.59

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DETERMINANTS OF LEFT VENTRICULAR RECOVERY IN STRESS CARDIOMYOPATHY: A SINGLE CENTER EXPERIENCE

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Background: Stress cardiomyopathy (SC) has become an increasingly recognized syndrome characterized by acute, transient systolic dysfunction of different segments of the left ventricle (LV) in response to emotional or physical stress. Most patients recover LV function, however, there is insufficient evidence of what factors predict LV recovery.
Methods: We identified 46 patients (43 women, 3 men, age 68.6 ±15.8) who were admitted to our institution between 2011-2014 with a diagnosis of SC. We analyzed clinical profiles, data, and outcomes of the patients that would help predict recovery of LV function. Statistical significance was determined by the unpaired student's t-test and the Chi squared test corrected by Fisher's exact using commercially available software ($p<0.05$).
Results: Five out of 46 patients had no recovery of initial LV dysfunction with an average follow-up ejection fraction (EF) of 36.6% versus 59.2% in recovered patients. Non-recovered patients were more likely to be diabetic (40% vs 7.3%, $p = 0.02$), have greater initial creatine kinase-myocardial band isoenzyme (CK-MB) (35.62 ± 21.5 vs 16.25 ± 2.0, $p = 0.04$), and discharge troponins (0.69 ± 0.29 vs 0.32 ± 0.05, $p=0.04$). Treatment with beta blockade was also found to be associated with recovery (95.1% vs 60%, $p = 0.009$), while use of other cardio-protective drugs showed no significant difference. Factors such as mean arterial pressure, treatment with inotropes, LV hypertrophy on echocardiography, and peripheral vascular disease, did not meet statistical significance ($p<0.05$), but did demonstrate a trend that may warrant further investigation.
Conclusion: In this study, we identified a number of factors predictive of poor LV recovery in patients with SC. Knowledge of these factors would allow for better risk stratification and help guide more aggressive therapy potentially avoiding permanent LV dysfunction.

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PREDICTING READMISSION AFTER IMPLANTABLE CARDIOVERTER DEFIBRILLATOR USING A RISK MODEL

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Objectives: The goal of this study was to implement the ICD risk stratification model developed through NCDR data to determine if patients could be identified for 30-day readmission.
Background: Previous analysis of the National Cardiovascular Data Registry (NCDR) ICD database identified clinical risk factors for procedure-related complications.
Methods: Patients scheduled to undergo ICD implantation were prospectively identified. Preoperative NCDR ICD risk score was calculated by assigning points for age > 70 years; female sex; prior valve surgery; chronic lung disease; dual or biventricular device; history of atrial fibrillation/flutter; NYHA class II-IV heart failure; non-elective hospitalization; and BUN >30; and re-implantation other than elective generator change. A logistic regression model determined the association of variables and pre-procedure risk to all-cause 30-day readmission rate.
Results: 182 consecutive patients undergoing ICD implantation were assessed. Mean age was 69 years (SD=11.00), with 72% (n=131) of the group consisting of men. The 30-day readmission rate was 17.6%. Four variables from the ICD Adverse Outcome Risk Model, (BUN >30, history of lung disease, NYHA Class IV and device implant during an inpatient hospital stay) were identified as predicative of 30-day readmission. Patients with a combination of 2 or more out of the 4 risks were more likely to be readmitted (Hosmer-Lemeshow test (χ^2 (8) = 5.20, P = .74), c-statistic = .71, and Nagelkerke R square = 0.15).
Conclusion: In a typical group of patients receiving ICD implant, the four variables were predictive of all-cause 30-day readmission rate. The risk factors identified were similar to previous studies.

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LONG-TERM EVALUATION OF BIOTRONIK LINOX AND LINOXSMART ICD LEADS

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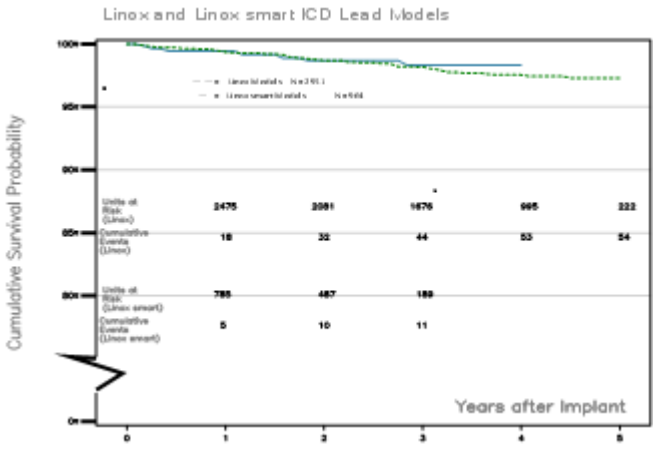
Introduction: Spurred by a rash of recent ICD lead failures and advisories, systematic assessment of post-implant lead performance has risen to the level of imperative in the collective conscience of both physicians and industry, alike. GALAXY (NCT00836589) and CELESTIAL (NCT00810264) are ongoing multi-center, prospective, non-randomized observational studies being used to effect such evaluation by analysis of long-term safety and performance data of BIOTRONIK leads.
Methods: ICD and CRT-D pts are being followed for lead performance and safety of the Linox and Linoxsmart ICD leads for 5 yrs post-implant. All procedural and system-related adverse events (AEs) are assessed at each follow-up along with lead electrical parameters. An independent CEC of 5 EPs adjudicates all AEs to determine AE category and lead relatedness. Adjudicated AEs are then categorized per ISO 5841-2 (3rd edition). Figure 1 displays a Kaplan-Meier actuarial graph by Linoxsmart and Linox ICD model groups.
Results: A total of 3915 leads were implanted in 3833 pts (73.0% male, mean age 67.0 ± 12.2 yrs) at 146 US centers. The estimated cumulative survival probability is 97.3% at 5 yrs after implant for Linox leads and 98.3% at 4 yrs after implant for Linoxsmart leads. The most common AEs were oversensing (19, 0.49%), failure to capture (10, 0.26%), and conductor fracture (9, 0.23%), abnormal pacing impedance (7, 0.18%), lead dislodgement (7, 0.18%), insulation breach (5, 0.13%).
Conclusion: Linox and Linoxsmart ICD lead-related AEs are rare; and, lead electrical performance and cumulative survival probability are excellent.



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POTENTIAL OF AMINOGLYCOSIDE ANTIBIOTIC GENTAMICIN TO CORRECT FUNCTIONAL EXPRESSION OF TRUNCATED HERG CHANNELS LINKED TO LONG QT SYNDROME, SYNCOPE AND UNEXPECTED SUDDEN DEATH

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Background: Long QT syndrome (LQTS) refers to a group of genetically cardiac rhythm disorders Mutations in the human ether-a-go-go-related gene (hERG) are linked to LQTS type 2 (LQT2), the most common form in China. A compound mutation (L539fs/47-hERG) responsible for truncated hERG channels was identified in a Chinese family experiencing LQTS, syncope and unexpected sudden death.
Objective: The present study aimed to evaluate the potential of gentamicin on the compound mutation L539fs/47-hERG bearing premature termination codon.
Methods: The L539fs/47-hERG and WT plasmids were transfected into the HEK293 cells to simulate heterozygous mutant. Whole cell patch-clamp technique were used to measure hERG currents in control conditions and exposed to gentamicin. Additionally, laser confocal scanning microscopy was used to evaluate the membrane distribution of hERG channel protein using a green fluorescent protein tagged to the N-terminus of hERG.
Results: After cells were cultured in the presence of 400 g/ml gentamicin for 24 h and then cultured in drug-free drug-free MEM at 37℃ for 1 hour to washout the drugs, the maximal density of tail currents in cells expressing WT in control conditions and exposed to gentamicin were 54.86±2.098 and 64.86±3.328, respectively, corresponding an increasing effect of 18.2%. The counterparts of heterozygous mutant (WT+L539fs/47-hERG) were and 22.93±0.6733 pA/pF and 37.34±2.401 pA/pF, respectively, the increasing effect is 62.8%. Additionally, gentamicin results in an obvious increase of hERG channel protein expression on the cell membrane and improves the retention of hERG channel proteins in the endoplasmic reticulum in cells expressing heterozygous mutant.
Conclusion: The function and expression of the truncated HERG channels due to a heterozygous mutation (WT+L539fs/47-hERG) can be partially corrected by gentamicin. This suggests the possibility to explore relevantly therapeutic strategies to benefit LQTS individuals.

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SURVEY OF DISPATCHER-ASSISTED CARDIOPULMONARY RESUSCITATION AFTER IMPLEMENTATION OF CONTINUOUS QUALITY IMPROVEMENT PROJECT IN ISHIKAWA PREFECTURE

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Background: In 2007, the Ishikawa Medical Control Council initiated the continuous quality improvement (CQI) project for telephone-assisted cardiopulmonary resuscitation (telephone-CPR), which included instruction on chest-compression-only CPR, education on how to recognise out-of-hospital cardiac arrests (OHCAs) with agonal breathing, emesis and convulsion, recommendations for on-line or redialling instructions and feedback from emergency physicians. We investigated the sensitivity and specificity of our new DA-CPR protocol after CQI project for achieving implementation of bystander CPR in out-of-hospital cardiac arrest victims not already receiving bystander CPR.
Methods and Results: Fire departments prospectively collected the data. The incidence of telephone-CPR and bystander CPR significantly increased after the project (from 42% to 62% and from 41% to 56%, respectively). After the project (2009-2011), DA-CPR was attempted in 2747 patients; of these, 417 (15.2%) did not experience cardiac arrest. The sensitivity and specificity of the 2007 protocol versus estimated values of the previous standard protocol were 72.9% versus 50.3% and 99.6% versus 99.8%, respectively. We identified key words that may be useful for detecting out-of-hospital cardiac arrest. Multiple logistic regression analysis revealed that the occurrence of cardiac arrest after an emergency call (odds ratio, 16.85) and placing an emergency call away from the scene of the arrest (odds ratio, 11.04) were potentially associated with failure to provide DA-CPR. Furthermore, at-home cardiac arrest (odds ratio, 1.61) and family members as bystanders (odds ratio, 1.55) were associated with bystander noncompliance with DA-CPR. No complications were reported in the 417 patients who received DA-CPR but did not have cardiac arrest.
Conclusions: Our 2007 protocol is safe and highly specific and may be more sensitive than the standard protocol. Understanding the factors associated with failure of bystanders to provide DA-CPR and implementing public education are necessary to increase the benefit of DA-CPR.

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IDEAL TARGET TEMPERATURE DURING THERAPEUTIC HYPOTHERMIA AFTER OUT-HOSPITAL CARDIAC ARREST

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Background: Out-hospital cardiac arrest (OHCA) carries a high mortality (~60%). Therapeutic hypothermia is the first intervention to improve outcomes after OHCA. Nevertheless, there is no conclusive ideal temperature to cool patients. Formal recommendation still proposes 32-34C as target temperatures. This study aims to determine the effect modification of different temperatures during therapeutic hypothermia on outcomes using pooled data from existing literature.
Methods: We identified studies by searching electronic databases (Medline, Embase, and Cochrane Library). We included randomized controlled trials (RCTs) and cohort studies describing hospital mortality and neurological outcomes of comatose survivors of OHCA after therapeutic hypothermia. Additional eligibility criteria included: age >15 years old, any initial rhythm, reported achieved temperature during cooling. Eligible studies underwent data extraction and quality assessed for risk of bias. Data from hypothermia receiving groups, with acceptable risk of bias, were pooled and grouped by achieved target temperature. Outcomes were contrasted across temperatures (32°C, 33°C, 34°C, 35°C, and 36°C).
Results: The search strategy identified 32,275 studies. Yet, 24 studies met eligibility criteria, accounting for 33 hypothermia groups. Pooled data accounted for 4420 patients with mean age of 60 years, and 77% male proportion. Total of 20 cooling arms enrolled patients regardless of initial rhythm, while 9 and 4 included either shockable or non-shockable rhythm respectively. Shockable rhythms accounted for 70% of all cardiac arrests, while a cardiac cause triggered 80% of arrests. Average downtime was 25.6 minutes. Overall, mortality around discharge was 43.4% with rate of good outcome of 43%. There was no difference in hospital mortality or good neurological outcomes across cooling temperatures after OHCA (p=0.99 and (p=0.89 respectively).
Conclusion: After pooling data from existing literature, therapeutic hypothermia after out-hospital cardiac arrests seems to provide same benefit on mortality or good neurological outcomes at discharge across different target temperatures (32°C-36°C).

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IMPACT OF CONDUCTION VELOCITY ON LOCAL CAPTURE OF ATRIAL FIBRILLATION INDUCED BY RAPID PACING

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Objectives: Rapid pacing of atrial fibrillation (AF) can induce local atrial capture. The present model-based study investigated the impact of atrial tissue conduction velocity on AF capture ability during rapid septal pacing.
Methods: The AF model combined a membrane kinetics model with geometry based on computed tomography of AF patients. Conduction velocity was varied ±20% over a baseline AF model based on multiple reentrant wavelets. Rapid pacing of AF was applied from the septum for 50s with pacing cycle length (PCL) computed as percent of mean AFCL. Analysis of 24 electrode pairs evenly distributed on the atrial surface yielded percentage of captured tissue (CL within ±5% of PCL). Capture window was the range of PCL with capture > 50%. Reentrant wavelets quantity (#W) was computed before and during pacing. Optimal PCL was leading to the highest capture. Results were averaged on 10 AF simulations.
Results: AFCL did not change significantly with conduction velocity, and optimal PCL was comparable for the 3 velocity values. An increase/decrease in velocity reduced/extended the capture window. The maximum capture was obtained with a decreased conduction velocity even if #W was higher prior to pacing.
Conclusions: Changes in atrial tissue conduction properties produced significant differences in rapid pacing outcomes, suggesting that different types of AF may respond differently to therapeutic pacing. Optimal capture parameters depended on AF dynamics but not AFCL.

Atrial Tissue	**AF**		**Capture**	**Capture at Optimal PCL**		
Conduction Velocity	AFCL (ms)	#W AF	Capture Window	Optimal PCL	Captured Tissue	#W Capture
Baseline-20%	81±23	12.9±3.3	75-95%	79% AFCL	98%	3.5±2.5
Baseline	76±21	10.6±3.1	83-99%	87% AFCL	80%	5.8±2.2
Baseline+20%	75±20	8.1±2.7	83-93%	87% AFCL	65%	6.8±2.1

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LATE RE-CONDUCTION SITES IN THE SECOND SESSION AFTER PULMONARY VEIN ISOLATION USING ADENOSINE-PROVOCATION FOR ATRIAL FIBRILLATION

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Aims: Intravenous adenosine triphosphate (ATP) administration could reveal dormant conduction (DC) gaps on the ablation line of a pulmonary vein isolation (PVI). We compared the ATP-provoked DC sites in the initial PVI with the PV re-conduction sites in the second session in patients with paroxysmal atrial fibrillation (AF).
Methods: We conducted a multicenter, observational study from a prospective registry undergoing AF ablation. A total of 110 consecutive drug-refractory paroxysmal AF patients were enrolled in this study. DC was detected by an ATP provocation of up to 40 mg during a continuous isoproterenol infusion (0.5-2*f*Êg/ min). The DC sites at each of the right and left PVs were precisely determined by using double spiral catheters under the guidance of a 3-dimensional constructed anatomical mapping system.
Results: In the initial session, DC was observed in 35 patients (31.8%, 1.3 gaps /patient), and the sites of the DC were commonly observed in the carina region (43.5%). AF recurrence was confirmed in 33 patients (30.0%) during follow up (27.1 months), and a second session was performed in 24 of 33 patients (70.6%). In the second session, the re-conduction sites were also commonly observed in the carina region (59.5%).
Conclusions: The carina region was still a dominant re-conduction site even after the elimination of any ATP-provoked DC in the index procedure.

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DOES THE DEVELOPMENT OF DEPENDENCY ON PACING IN PATIENTS WITH IMPLANTED PACEMAKERS IMPACT ON SURVIVAL

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Introduction: Pacemaker (PM) dependency is defined as an absence of a stable, life sustaining native rhythm without artificial pacing. The impact of PM dependency on survival is not well described.
Methods: We reviewed 60 PM dependent patients (cases), and 60 age-and-sex matched patients who were not PM dependent (controls). Device indications, comorbidities, time of PM dependency, and last follow up or death were recorded.
Results: Mean age at implant was 70 (±12) years for cases and controls. There was no statistically significant difference in the baseline prevalence of coronary artery disease, diabetes, or hypertension at PM implant amongst cases and controls (all P=NS). Left ventricular ejection fraction at implant was 57% in cases and 59% in controls (P=0.320). For cases, PM dependency occurred a median 2.3 (mean=3.6) years after implant. Atrioventricular block was more common in cases (48% vs. 17%, P=0.002) and sick sinus syndrome was more common in controls (37% vs. 10%, P=0.005). For cases, total follow up was a median 7.4 (mean=9.9) years and for controls, total follow up was a median 4.4 (mean=5.3) years. There were 4 deaths in each group, none of which were attributable to pacemaker malfunction. Patients who became PM dependent derived an additional median 4.0 (mean=6.3) years of survival. There was no statistically significant difference in overall survival of cases and controls (p=0.572).
Conclusions: The overall survival of PM dependent patients was comparable to age and sex matched controls who were not PM dependent. The development of PM dependency does not impart a worse prognosis. Given the aging world population and increasing rates of PM implantation, this is clinically relevant information for patients and physicians.

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COMPARISON OF LEFT VENTRICULAR EJECTION FRACTION VALUES OBTAINED USING INVASIVE CONTRAST LEFT VENTRICULOGRAPHY, GSPECT AND TWO-DIMENSIONAL ECHOCARDIOGRAPHY

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Background: Measurement of left ventricular ejection fraction (LVEF) provides valuable diagnostic and prognostic information in patients with ischemic heart disease. LVEF is measured using a variety of techniques including invasive contrast left ventriculography, gated single proton emission computed tomography (gSPECT) and two-dimensional echocardiography (2DE). LVEF measurement may be duplicated if the patient receives more than one of these tests. This may increase risk and add cost to the evaluation. This study assesses the relation of these three modalities to one another in the measurement of LVEF.
Methods: Retrospective chart review was conducted on patients with chest pain who underwent LVEF evaluation using each of the aforementioned modalities using standard protocols within a three month period not interrupted by acute coronary syndrome by percutaneous or surgical coronary revascularization. Comparison of LVEF values between techniques was accomplished using Pearson correlation coefficients. A p value <0.05 was required for statistical significance.
Results: LVEF was evaluated using all three modalities in 58 patients (all males) whose mean age was 65 ± 10 years. Correlations and associated p values were as follows: invasive contrast left ventricularography vs. gSPECT ($r=0.80$, $p<0.001$); invasive contrast left ventriculography vs. 2DE ($r=0.69$, $p<0.001$); and gSPECT vs. 2DE ($r=0.69$, $p<0.001$).
Conclusion: LVEF measured using either gSPECT or 2DE significantly and strongly correlates with LVEF measured using invasive contrast left ventriculography. Thus, if LVEF has been obtained using either gSPECT or 2DE before cardiac catheterization, invasive contrast left ventriculography need not be performed, thus reducing the cost of the procedure and the risk associated with exposure to iodinated contrast media and fluoroscopy

NOVEL DIAGNOSTIC METHODS AND IMAGING TECHNIQUES

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INFLUENCE OF ESTROGEN AND PROGESTIN THERAPY ON PROGRESSION OF PERICARDIAL ADIPOSE TISSUE IN POSTMENOPAUSAL WOMEN

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Background: Prophylactic effect of postmenopausal hormone replacement therapy (HRT) on coronary atherosclerosis remains controversial. We therefore examined the influence of a combined estrogen/progestin therapy on progression of pericardial adipose tissue (PAT), which reflects atherosclerotic burden of coronary arteries and is very sensible to changes in lipid metabolism. Additionally extent of coronary calcifications (CAC) was determined.
Methods: We determined the extent of PAT and CAC in 244 women (age 58.0 ± 6.1 years, time after menopause 4.8 ± 2.5 years, group I) at the beginning of HRT using multislice computed tomography. For quantification volume of PAT in [ml] and volume score of CAC was calculated. After an observation period of 3 years progression of PAT and CAC in a second scan was evaluated. Results were compared to an age and risk factor adjusted group of postmenopausal women without HRT (group II).
Results: No significant difference in PAT volume (121 ± 48 ml vs. 143 ± 43 ml, n.s.), CAC volume score (59 ± 95 vs. 52 ± 88, n.s.), or risk factor distribution between both groups at study entry was found. In 51 women of group I and 47 women of group II CAC were excluded on initial scan, n.s.. After a mean observation period of 35.7 ± 5.7 months increase of PAT volume (46 ± 22 ml vs. 79 ± 36 ml, $p < 0.01$) between both groups was significantly different, whereas no significant difference of CAC increase was determined (20 ± 24 vs. 23 ± 27, n.s.).
Conclusion: We observed a reduced progression of PAT in postmenopausal women under a combined estrogen/progestin therapy compared to a matched group of women without HRT. Still we could not find a reduced progression of CAC, indicating that PAT might be more sensitive to short term changes of atherosclerotic burden.

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IMPACT OF HYPERLIPIDEMIA ON SUBCLINICAL ATHEROSCLEROSIS IN ASYMPTOMATIC INDIVIDUALS

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Objectives: The purpose of this study was to investigate the impact of hyperlipidemia on the risk of subclinical atherosclerosis in asymptomatic individuals.
Background: Little is known about subclinical atherosclerosis on coronary computed tomographic angiography (CCTA) in asymptomatic individuals with hyperlipidemia.
Methods and Results: We analyzed 6,311 consecutive asymptomatic individuals aged 40 and older with no prior history of coronary artery disease (CAD) who voluntarily underwent CCTA evaluation as part of a general health examination between January 2007 and December 2011. The mean age of the study population was 54.7±7.4 years, and 4,594 (72.8%) were male. Of the study population, 1,970 (31.2%) had hyperlipidemia. After adjustment using age and gender distributions from the 2010 South Korean population census, individuals with hyperlipidemia had a significantly higher prevalence of plaque (standardized rate ratio [SRR], 1.30; 95% confidence interval [CI]: 1.15–1.46; p<0.001), non-calcified plaque (SRR, 1.26; 95% CI: 1.05–1.52; p=0.013), calcified plaque (SRR, 1.37; 95% CI: 1.18–1.58; p<0.001), mixed plaque (SRR, 1.17; 95% CI: 0.90–1.51; p=0.244), significant CAD (SRR, 1.65; 95% CI: 1.25–2.17; p<0.001), and significant CAD in the in the left main or proximal left anterior descending artery (SRR, 2.13; 95% CI: 1.39–3.28; p=0.001) compared with those without.
Conclusions: Hyperlipidemia was associated with subclinical atherosclerosis on CCTA. These findings suggest the importance for control of lipid in asymptomatic individuals.

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ASSOCIATION OF GENDER AND BODY MASS INDEX WITH SUBCLAVIAN INNOMINATE ARTERY TORTUOSITY IN PATIENTS UNDERGOING RIGHT TRANS RADIAL CARDIAC CATHETERIZATION

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Background: Subclavian-innominate artery (SIA) tortuosity has been shown to be an independent predictor of failure of Trans Radial (TR) cardiac catheterization. We sought to investigate the factors related to the presence of SIA tortuosity in patients who underwent right TR cardiac catheterization.
Methods: We did a retrospective study of who underwent right TR cardiac catheterization between March 2011 and August 2014. The group consisted of 127 consecutive patients with SIA tortuosity and 272 patients who did not have SIA tortuosity. Demographics and clinical characteristics were compared between the two groups.
Results: Mean age of the patients (N=399) was 58.3±12.5 and 73% were males. When patients were divided into two categories based on body mass index (BMI) patients with BMI more than 35 were more likely to have SIA tortuosity compared to patients with BMI less than 35 (62.7% vs 24.4% respectively, $p<0.01$). SIA tortuosity was more prevalent in males compared to females (35.7% vs 21.2%, $p<0.01$). Age and height did not correlate significantly with the presence of SIA tortuosity.
Conclusion: In patients who underwent right TR catheterization, SIA tortuosity was more likely to be present in patients with BMI more than 35 and in males. Age and height did not correlate significantly with the presence of SIA tortuosity

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THE USEFULNESS OF THE TDI TEI INDEX IN LEFT VENTRICULAR FUNCTIONAL ASSESSMENT OF CHRONIC HEMODIALYSIS PATIENTS. COMPARATIVE STUDY BEFORE AND AFTER DIALYSIS

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Objectives: The purpose of this study is to evaluate the effect of a dialysis session diastolic function of the left ventricle using conventional sonographic markers (pulsed and tissue Doppler) and in particular the use of TDI TEI index in adults with end-stage renal disease.
Background: 16 adults with chronic end-stage renal failure (9 men, 7 women, mean age 65 years) underwent a standard dialysis session. The echocardiographic parameters studied were the velocity of transmitral flow (MVpeak E), the ratio E / A, ratio E/E', speeds at the tissue Doppler, the integral of the flow velocity of the aortic valve (MeanPG) and TDI TEI index. The ultrasound data were collected 20 minutes before and after dialysis and then compared.
Methods and Results: The dialysis resulted in reducing the speed of transmitral flow (MVpeak E, $p=0.005$), a small decrease in the integral of the flow velocity of the aortic valve (MeanPG, $p<0.0001$), reducing end diastole left ventricular filling pressures ($p=0.05$) and a reduction of end diastole volume ($p=0.001$).No significant change was observed in the tissue velocities and in tissue TEI index (TDI TEI INDEX) after dialysis.
Conclusions: Velocities TDI and TDI TEI index minimally affected by the reduction of preload while the other indicators showed ultrasound change as inherent to the diastolic function, which is directly dependent on the preload.

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IMPACT OF FACTORS ASSOCIATED WITH ARTERIAL AND/OR VENOUS THROMBOSIS ON ACETYLSALICYLIC ACID AND CLOPIDOGREL RESPONSE VARIABILITY IN PATIENTS PRESENTING WITH ACUTE CORONARY SYNDROME

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Objectives: We sought to investigate whether the factors associated with arterial and/or venous thrombosis influence response variability of acetylsalicylic acid and clopidogrel loading doses in patients presenting with acute coronary syndrome (ACS) and those undergoing percutaneous coronary intervention (PCI).
Methods: We analyzed the data of 166 patients presenting with ACS and those undergoing PCI. Clinical data included assessments of genetic polymorphisms (angiotensin converting enzyme-ACE I/D, Prothrombin G20210A, Factor V R506Q and methylenetetrahydrofolate reductase-MTHFR C677T) and haematological factors (thrombin activatable fibrinolysis inhibitor-TAFI activity, von Willebrand Factor antigen-vWF:Ag, Factor VIII, protein S, protein C activity and antithrombin 3-AT 3 activity). *Results:* In multivariate regression analysis, ACE D/D polymorphism (OR 2.369, p=0.043), TAFI levels (OR 1.017, p<0.001) and vWF:Ag levels (OR 1.014, p=0.003) were found as independent variables, which had statistically significant effects on clopidogrel resistance, and these effects were marked in STEMI patients. In ROC curve analysis of STEMI patients, TAFI level ≥136 iu/dL measured had a 78% sensitivity and 95% specificity, vWF:Ag level ≥122.5 iu/dL measured had a 65% sensitivity and 95% specificity in predicting clopidogrel resistance.
Conclusions: ACE D/D polymorphism and higher plasma levels of vWF:Ag and TAFI were associated with clopidogrel resistance in ACS patients undergoing PCI, thereby adding evidences for possible relationships. Therefore ACE D/D polymorphism, TAFI and vWF:Ag levels may be useful markers in predicting loading dose of clopidogrel resistance after PCI in ACS, particularly in STEMI patients. These findings could draw attentions to aspects of explaining antiplatelet resistance other than drug metabolism, especially in era of newer antiplatelet agents.
Acknowledgements: The study (AR-2011/56) was supported by research grant from Gulhane Military Medical Faculty Research Center.

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PLASMA PHENYLALANINE / TYROSINE RATIO AS PREDICTOR OF QUERCETIN EFFECT ON LEFT VENTRICULAR REMODELING AFTER STEMI

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Background: The endothelial NO-synthase (eNOS) is one of the most important cardioprotective signaling pathways. Cardioprotector quercetin (Qn) modulates eNOS activity, which also depends on the bioavailability of tetrahydrobiopterin (4HB). In recent studies the increase in plasma phenylalanine/tyrosine ratio (plPhe/Tyr) was considered as a marker of 4HB deficiency.
Objective: to evaluate the baseline plPhe/Tyr for prognosis of Qn effectiveness on the left ventricular remodeling (LVR) in patients (pts) with ST-elevation myocardial infarction (STEMI).
Methods: We examined 36 pts with STEMI, who received treatment according to clinical guidelines and additionally soluble Qn intravenously for five days. In all the pts the echocardiography (EchoCG) on the first and tenth days and analysis of baseline plasma Phe and Tyr levels by cation-exchanged liquid-column chromatography were performed. The outcome effect was measured as minimal difference between baseline wall motion score index (WMSI) and WMSI on the tenth day by amount 1/16 or 0.0625 (where 16 is a total number of LV segments). Thus, the decrease of WMSI by ≥ 0.0625 was a criterion of positive LVR.
Results: The plPhe/Tyr in pts without positive LVR (2.41±0.74, n=14) was increased by 67.4% vs healthy control (1.44±0.59, n=15, $p<0.01$) and by 41.8% vs pts with positive LVR (1.70±0.77, n=22, $p<0.05$). The plPhe/Tyr was an independent predictor (by multiple logistic regression after adjustment for all demographic, anamnestic, clinical and EchoCG data) of positive LVR (OR 0.30, 95%CI 0.10-0.88, $p<0.05$) with an area under ROC curve 0.75 (95%CI 0.57-0.88, p=0.006). The sensitivity and specificity of plPhe/Tyr $\leq$ 2.06 (95%CI 1.29-2.06) were 81.8% and 71.4% respectively.
Conclusion: An absence of increase in baseline plPhe/Tyr is an independent predictor of positive LVR in early period after STEMI treated with Qn.

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OUTCOMES OF BIVALIRUDIN VERSUS HEPARIN ALONE IN PERCUTEANEOUS CORONARY INTERVENTION

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Objective: To compare the real-world efficacy and safety of bivalirudin versus heparin in patients undergoing percutaneous coronary intervention.
Background: Clinical trials have suggested that bivalirudin is as effective as heparin with lower rates of bleeding. However, more recent studies have questioned these outcomes, especially when heparin is used without adjuvant IIb/IIIa inhibitors.
Methods: We analyzed 8442 consecutive coronary interventions during a 10 year period ending December 2012. Patients who received IIb/IIIa inhibitors were excluded. Multivariable logistic regression was performed to correct for baseline differences.
Results: Bivalirudin was used in 5319 cases and heparin in 3123. When adjusted for all covariates, there were no differences in the rates of procedural success or acute closure. However, bivalirudin was associated with a lower incidence of severe post procedural complications including death (OR 0.45 [0.30-0.68]), vascular complications (OR 0.68 [0.48-0.95]), retroperitoneal bleeding (OR 0.11 [0.03-0.38]) and transfusions (OR 0.44 [0.34-0.56]).
Conclusion: For patients undergoing PCI, bivalirudin provides similar efficacy and reduced risk compared with heparin alone.

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TREATMENT DETERMINANTS OF NON CULPRIT VESSELS IN NOT COMPLICATED ACUTE MYOCARDIAL INFARCTION: SINGLE SESSION VS DEFERRED

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Introduction: Among 20 - 60% of patients treated with primary coronary angioplasty (PTCA) have multiple vessels disease (MVD), this being a predictor of mortality. The strategy of complete revascularization (CR) in the same session is questioned.
Objective: To analyze clinical and angiographic variables of treatment decision and clinical outcomes of early deferred CR (during the same hospitalization or within 30 days) vs. the index procedure.
Method: Population: From May 2000 to December 2014, 374 patients with AMI were consecutively treated, 189 of whom had MVD. In this period, 58 pts (group A) had CR in the same session, while 35 pts (group B) completed deferred revascularization. Baseline characteristics: mean age 58±11 vs 57±9 years, diabetes 15(29%) vs 7(20%); previous infarction 6(10) vs 6(17); Killip Kimball C - D 9(15) v 1(3) p=0.08; IIbIIIa using 3(5) vs 9(26) p=0.008; time door to balloon 110±60 vs 107±59 minutes; anterior descending artery not related to infarction 21(36) vs 1(3) p=0.0001; initial TIMI 0 32(55) vs 21(60); DES 10(17) vs 6(17); fluoroscopy time 19.2±15 vs. 16.9±13 minutes; dye 267.3±91 vs 236 milliliters.
Results: In-hospital: final TIMI III flow 58(100) vs 31(88) p=0.03, blush TIMI 3 final 52(90) vs 30(85) p=0.8; cardiac death 2(3) vs 0 p=0.5; reinfarction 1(2) vs 0 p=0.7. At follow-up 18±21.8 vs 23.9±18 months cardiovascular death 0 vs 1 (3) p=0.3; reinfarction 2 (4) vs 2(6) p=0.6, rePCI “de novo” lesions 3(7) vs 2(6) p=1 and restenosis rePCI 2(4) vs. 3(8) p=0.3.
Conclusion: CR in AMI in the same session showed not higher risk or higher reintervention rate against deferred modality in patients with MVD. The class > B in Killip Kimball; anterior descending artery unrelated to the infarction support the decision for CR in the same session. The chronic total occlusion and use of IIbIIIa made differ the CR.

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MAGNITUDE AND DECADE LONG TRENDS (2001-2011) IN PRE-HOSPITAL DELAY IN ELDERLY PATIENTS HOSPITALIZED WITH ACUTE MYOCARDIAL INFARCTION (AMI): INSIGHTS FROM THE WORCESTER HEART ATTACK STUDY

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Background: Early and aggressive intervention with medical and/or revascularization interventions remains the cornerstone of AMI management. However, several high risk groups, especially the elderly, are known to delay seeking medical care after the onset of AMI symptoms. Current trends and factors associated with prolonged pre-hospital delay among older patients presenting with AMI, particularly in different age strata within the elderly, are presently unknown.
Methods: Data from the Worcester Heart Attack Study, an ongoing population- based study of residents of central MA hospitalized at all 11 medical centers in central MA with AMI on a biennial basis between 2001 and 2011 were used.
Results: The mean duration of pre-hospital delay was 3.7 hours in patients 65 years and older. The average delays were 3.9 hours, 3.9 hours, and 3.0 hours among those 65-74, 75-84, and 85 years and older, respectively. While there was some suggestion of a slight decline in the average duration of pre-hospital delay in the total study population (mean =4.0 hours 2001/2003; 3.2 hours 2009/2011), these encouraging declines were not consistently observed in each of the elderly age strata examined. A variety of socio-demographic, medical history and clinical factors are being evaluated in relation to prolonged pre-hospital delay in this patient population.
Conclusions: Prolonged care seeking behavior remains a continuing problem in elderly patients hospitalized with AMI, though some recent improvements in care seeking behavior may be taking place. Data will be presented on the characteristics of patients who exhibit prolonged, as compared to those with shorter delay in the setting of AMI.

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IMPACT OF DIABETES MELLITUS ON ACUTE HEART FAILURE

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Background and aim: The prevalence of heart failure among diabetic patients is reported as 20%. Conversely, several heart failure registry data reported high prevalence of diabetes mellitus reaching 40%. Although, the outcomes in heart failure patients combined with diabetes mellitus (DM-HF) have been suggested worse than those without diabetes (non-DM-HF), the effect of glycemic control has not been reported yet.
Methods: We analyzed data from the Korean Acute Heart Failure (KorAHF) which is a registry of patients hospitalized for acute heart failure syndrome in ten regionally-representative tertiary university hospitals in Korea.
Results: 1) Among KorAHF registry patients, 40.0% had diabetes mellitus. DM-HF patients were older (70.1¡¾11.6 vs 67.4¡¾16.0, p < 0.001), more men (55% vs 52%, p = 0.017), had more hypertension (72% vs 50%, p < 0.001), chronic renal disease (21.6% vs 9.5%, p < 0.001), whereas had less atial fibrillation (25.2% vs 29.1%, p =0.001) than non-DM-HF.
2) Ischemia was both the leading cause (52.7%) and the most frequent aggravating factor (36.1%) in DM-HF patients, which were far more than in non-DM-HF patients (27.5% and 19.8% respectively).
3) In-hospital mortality among DM-HF patients was 60% higher than non-DM-HF patients (6.1% vs 3.9%, p < 0.001). The difference remained significant after adjusting gender, age, history of hypertension, ischemic heart disease, functional status and serum creatinine.
Conclusions: DM-HF patients had worse prognosis than non-DM-HF patients. Hyperglycemic control status might have little impact either on in-hospital mortality or short-term follow up. Although DM-HF-OHA patients did not have worse outcome than non-DM-HF patients, DM-HF-Insulin patients have three folds higher in-hospital mortality, which warrants long-term study.

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OBESITY AND LIPID INDEXES IN PATIENTS SUFFERING A FIRST ACUTE CORONARY SYNDROME

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Background and objectives: Obesity has reached epidemic proportions both in adults and children in recent years and has been suggested to have adverse cardiovascular effects. The plasma concentration ratio of triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C) can identify cardiometabolic risk and cardiovascular disease. Low-density lipoprotein cholesterol (LDL-C) and non-HDL cholesterol have also been related to adverse CV prognosis and the ratio of total cholesterol (TC) and HDL-C has been associated with carotid intima-media thickness. However, to the best of our knowledge the capability of the different Obesity indexes to predict these lipid indexes has not been systematically and specifically assessed in patients suffering a first acute coronary syndrome (ACS).
Methods: We conducted a study including 98 consecutive patients suffering a first ACS. Patients´ height, waist, hip and weight were specifically measured in hospital, fasting, at 7 a.m. and three days after the coronary event, using calibrated devices. Standardized questionnaires were used to determine participants' past medical history, medication, and cardiovascular risk factors. Fasting venous samples were collected in all patients for the assessment of total cholesterol, HDL-C cholesterol, low-density lipoprotein (LDL), cholesterol, and TG levels, which were all assessed using standard enzymatic methods.
Result: Correlation analyses showed a significant association between patients weight, Body mass index and waist-hip ratio, and both TG/HDL (r=0.21,p=0.04;r=0.25, =0.01; r=0.21,p=0.04, respectively) and TC/HDL(r=0.22,p=0,03; r=0.31,p=0.003; r=0.21,p=0.04). No significant association was found between the obesity indexes and LDL cholesterol and Non cholesterol.
Conclusions: Our results suggest that in patients suffering a first acute coronary event weight, BMI and waist hip-ratio are good predictors of TG/HDL-C and TC/TG indexes. However, none of these obesity indexes were associated with LDL-C and non-HDL-C. Probably, the main influence of obesity in the lipid profile relies on TG and HDL-C but not in other cholesterol fractions.

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TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION REDUCES METABOLIC DISTURBANCES INDUCED BY HIGH-FRUCTOSE DIET IN RATS

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Background: Metabolic syndrome (MS) precedes the development of insulin-independent diabetes. The sensory nerves (SN) are involved into the regulation of carbohydrate and lipid metabolism. Moreover, the obesity and diabetes often resulted in sensory neuropathy.
Objective: The purpose of present study is to investigate the effects of SN low-frequency transcutaneous electrical stimulation (TES) on the development of MS induced by high-fructose diet in rats.
Methods: Male Wistar rats received 12,5 % fructose solution in their drinking water for 10 weeks. Control rats were given tap water to drink. 8 weeks after drinking fructose or tàp water rats were subjected to TES (1mA, 2 Hz, pulse duration 0,5 msec, 10 min, daily for 2 weeks) applied to the paws. The blood contents of triglyceride (TG), products of lipid peroxidation (PLP) and glucose in intraperitoneal glucose tolerance test were quantified spectrophometrically.
Results: The consumption of fructose resulted hypertriglyceridemia, oxidative stress, impaired glucose tolerance. TES applied to rats with fructose diet induced the decrease in content of TG and products of PLP versus control values and improved glucose tolerance test ($P< 0,05$). TES had no effect on these parameters in control rats. There was no difference in the fasting glucose concentration between all groups.
Conclusion: We can conclude that TES reduces the MS-induced disturbances and decreased the risk of insulin-independent diabetes development.

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INDIVIDUAL FACTORS, LIFE EVENTS AND GENETIC VARIABILITY ASSOCIATED WITH OBESITY, MEDELLIN, COLOMBIA

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Objective: Relate to individual factors, life events and genetic variability associated with obesity.
Background: Obesity is a complex and multifactorial, chronic disease which is the result of the interaction between genetic factors, behavioral and environmental.
Methods: Study of quantitative, analytical, type descriptive-correlational study scope. We included people between 18 and 30 years with a diagnosis of obesity in which the following instruments were used: YSQ-L2 (early wrong adaptive schema), NEO PI-R (personality), USQ (vital events); in addition the genotyping for polymorphisms rs1501259 of the ADIPOQ gene, rs6265 of the BDNF gene and rs9939609 the gene FTO.
Results: We included 74 patients, with an average age of 40.3 years; the 88.1 per cent were women, and the average body mass index was 38 Kg/m2. With respect to the genotyping, the found frequencies were as follows: 0.25 and 0.74 for the alleles A and C of the ADIPOQ gene rs1501299 polymorphism, respectively; 0.20 and 0.79 for the T and C polymorphism of BDNF gene rs6265 alleles, respectively; and 0.35 and 0.64 for alleles A and T of the gene FTO rs9939609 polymorphism, respectively.
Conclusions: The minimum allelic frequency identified for the T allele of the rs6265 is expected for a not synonymous polymorphism with involvement on the function of the protein. The frequencies of allele found in this study are similar to those reported for the European population.

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RELATIONSHIP BETWEEN ADMISSION FREE TESTOSTERONE LEVEL AND INSULIN-RESISTANCE IN ACUTE MYOCARDIAL INFARCTION

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Background: Previous studies in elderly men have shown an association between low levels of testosterone and higher risk for Cardio Vascular Disease; however, prospective studies in younger men lacking. Sweden researchers reported a strong and independent association between concentrations of testosterone and AMI was observed in men with type 2 diabetes. (2013 ESAD: European Association for the Study of Diabetes).
Objective: The aim of this study is to examine the association between free testosterone (fT) and insulin-resistance in AMI. Testosterone impact of insulin-resistance remains unclear.
Methods and Results: This study included of 126 subjects who underwent primary percutaneous coronary intervention. Patients were divided 3 groups according to 75g OGTT. Diabetes mellitus group were 45 and IGT group were 34 and normal glucose tolerance were 47.And patients divided into two groups according to median fT level(7.8pg/ml).We investigated a low plasma free testosterone level is related to atherosclerosis in men with coronary risk factor. Patients we underwent measurement of CAVI, AI, RHI (endothelial function) and insulin-resistance were enrolled. The relation between low fT and CAVI, AI, RHI and insulin-resistance were analyzed. Low fT patients were significantly 45 and correlated with Admission insulin (R=-0.41,p=0.01),HOMA-IR(R=-0.30,p=0.04), while HOMA-I β (R=-0.02,p=0.88)was not. FT is a trend of an inverse association between serum testosterone and fasting insulin (R=-0.28,p=0.06).Low fT patients with DM showed high CAVI compared to high fT patients (P=0.04), not high AI nor low RHI. Low fT patients with IGT and normal glucose tolerance did not high CAVI.
Conclusion: We think low testosterone with diabetes patients where early vascular aging is observed and suggest that low testosterone is associated insulin-resistance.

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BEST PREDICTOR OF METABOLIC SYNDROME: COMPARISON OF VARIOUS ANTHROPOMETRIC AND ATHEROGENIC PARAMETERS IN THE KAZAKH POPULATION IN XINJIANG PROVINCE

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Aims: Few studies have investigated the metabolic syndrome (MetS) in the Kazakh population in China. This study aimed to evaluate the best single predictor of the MetS by comparing various anthropometric and atherogenic parameters in adult Kazakhs.

Methods: 4094 Kazakhs were recruited from the Cardiovascular Risk Survey which was carried out from 2007 to 2010. Anthropometric data, blood pressure, serum total cholesterol, triglyceride, low density lipoprotein cholesterol, high density lipoprotein cholesterol and fasting plasma glucose were documented. MetS and its components were confirmed according to IDF criteria. Areas under the curve (AUCs) of each variable for the presence of MetS were compared. The sensitivity (Sen), specificity (Spe), shortest distance in the receiver's operating characteristic curve (ROC) and cutoffs of each variable to diagnose MetS were calculated.

Results: 28.6% of men and 31.0% of women had MetS in the Kazakh population. In men, WHtR had the highest AUC value 0.821, followed by BMI (0.801), TG/HDL-C (0.792), WHR (0.776) and BAI (0.666). In women, WHtR also had the highest AUC value (0.835), following by BMI (0.789), WHR (0.778), TG/HDL-C (0.778) and BAI (0.751). Similarly, among all 5 anthropometric and atherogenic parameters, WHtR had the shortest ROC distance of 0.37 (Sen=81.09%, Spe=68.50%); the optimal cutoff for WHtR was 0.55 in men. In women, WHtR also had the shortest ROC distance of 0.35 (Sen=84.59%, Spe=68.97%); the optimal cutoff of WHtR was 0.54.

Conclusion: WHtR was the best predictor of MetS in both Kazakh men and women.

LEFT VENTRICULAR HYPERTROPHY / HYPERTROPHIC CARDIOMYOPATHY / DIASTOLIC DYSFUNCTION

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YAMAGUCHI SYNDROME: A POTENTIALLY UNDER-RECOGNIZED ENTITY?

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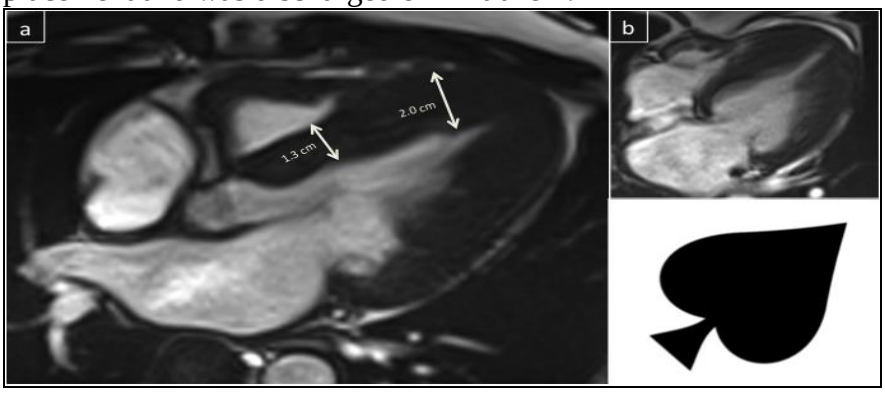
Background: Yamaguchi syndrome, also known as apical variant hypertrophic cardiomyopathy (HCM), as per most studies, accounts for only 1-2% of all HCM cases in non-Japanese population. We report a cases series of this rare HCM variant in African-American patients suggesting the possible under-recognition in this population.
Cases: **(1)** A 57 year old Afro-American male who was hospitalized for distal radius fracture, reported transient dizziness. Electrocardiogram (EKG) showed left ventricular hypertrophy (LVH) with giant T wave inversions in antero-septal leads. Trans-thoracic echocardiogram (TTE) showed abnormal apical hypertrophy without mid-cavitary gradient. Cardiac MRI (CMR) was obtained confirming apical-variant HCM. He was later discharged on Metoprolol. **(2)** A 53 year old Afro-American female presented following a syncopal episode. She reported intermittent dizziness for last 2 months. EKG showed LVH and deep T wave inversion in pre-cordial leads. TTE showed severe apical hypertrophy. CMR confirmed the Yamaguchi syndrome. Pt had recurrent non-sustained ventricular tachycardia during hospitalization. She underwent implantable defibrillator placement and was discharged on Diltiazem.



Discussion: Apical HCM is characterized by hypertrophy of the myocardium predominantly in the apical region of the left ventricle (LV). Most patients have a relatively benign course, but occasionally significant arrhythmias, sudden cardiac death and apical infarctions with apical aneurysms can occur. Typical features include "giant" T wave negativity on the EKG, particularly in the precordial leads and a “spade-like configuration” of the LV cavity at end-diastole on left ventriculography.
Echocardiography has its limitations in evaluating the apex. CMR is the preferred modality for diagnosis, as it not only helps identify functional and morphological abnormalities of the apex but can aid in detection of apical myocardial injury.
Given these cases of apical HCM presented in a short time-span, it raises the question whether it is potentially under-recognized in the Afro-American population!

LEFT VENTRICULAR HYPERTROPHY / HYPERTROPHIC CARDIOMYOPATHY / DIASTOLIC DYSFUNCTION

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TRANSTHYRETIN AMYLOID CARDIOMYOPATHY TREATMENT WITH AN ANTISENSE OLIGONUCLEOTIDE INHIBITOR OF TTR (ISIS-TTR RX)

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Introduction: Transthyretin (TTR)-mediated amyloidosis (ATTR) is a systemic protein deposition disease characterized by peripheral neuropathy and restrictive cardiomyopathy. In prior studies we have shown that progression of cardiac amyloidosis can be documented over a 12 month period by measuring left ventricular mass (LVM) by both echocardiography and magnetic resonance imaging (MRI). We have now initiated a single center, investigator sponsored, open-label clinical study to assess the safety and tolerability and as a secondary objective to determine if disease progression can be attenuated by suppressing the hepatic synthesis of TTR by treatment with ISIS-TTR Rx, a 2nd-generation 2'-MOE chimeric ASO specific for the TTR mRNA. Previous studies have demonstrated ISIS-TTR Rx produced 95% reductions in serum TTR levels in a transgenic mouse model.
Methods: Subjects are admitted to study with biopsy-proven ATTR and LV wall thickness of ≥1.3 cm. Baseline studies include echocardiography and cardiac MRI. Echocardiography is conducted at 12 and 24 months. MRI is conducted at 24 months. Serum TTR levels and safety measures are monitored at regular intervals throughout the 24 month treatment period. ISIS-TTR Rx 300 mg is administered weekly by subcutaneous injection.
Results: Five patients have been admitted to the study. To date, three of the patients have been treated >4 months and two patients >1 month. ISIS-TTR Rx appears to be well tolerated.
Conclusion: ISIS-TTR Rx appears to be well tolerated in patients with ATTR cardiomyopathy. Efficacy evaluation awaits longitudinal studies aimed at determining stability of left ventricular mass.

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GENETICS AND GENOTYPE-PHENOTYPE CORRELATIONS IN FINNISH PATIENTS WITH DILATED CARDIOMYOPATHY

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Background: Despite our increased understanding of the genetic basis of dilated cardiomyopathy (DCM), the clinical utility and yield of clinically meaningful findings of comprehensive next-generation sequencing (NGS) based genetic diagnostics in DCM has been poorly described. We utilized a high quality oligonucleotide-selective sequencing (OS-Seq) based targeted sequencing panel to investigate the genetic landscape of DCM in Finnish population and evaluate the utility of OS-Seq technology as a novel comprehensive diagnostic tool.

Methods and results: Using OS-Seq, we targeted and sequenced the coding regions and splice junctions of 101 genes associated with cardiomyopathies in 145 unrelated Finnish patients with DCM. We developed effective bioinformatic variant filtering strategy and implemented strict variant classification scheme to reveal diagnostic yield and genotype-phenotype correlations. Implemented OS-Seq technology provided high coverage of the target region (median coverage 410x and 99.42% of the nucleotides were sequenced at least 15x read depth). Diagnostic yield was 34.5% (familial 47.6% and sporadic 24.4%, p=0.004) when both pathogenic and likely pathogenic variants are considered as disease causing. Of these, 20 (53%) were TTN truncations (nonsense and frameshift) affecting all TTN transcripts in 20 cases. TTN truncations accounted for 20.6% and 14.6% of the familial and sporadic DCM cases, respectively.

Conclusion: Panel-based high-quality NGS enables high diagnostic yield especially in familial form of DCM and bioinformatic variant filtering is a reliable step in the process of interpretation of genomic data in a clinical setting.

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THE CARDIOPROTECTIVE EFFECTS OF GRANULOCYTE-COLONY STIMULATING FACTOR (GCSF) IN PATIENTS RECEIVING ANTHRACYCLINE CHEMOTHERAPY

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Background: Anthracycline cardiotoxicity is an adverse effect in patients treated for malignancies. In clinical practice, GCSF is used in adjunct to myelosuppressive chemotherapy. There has been benefit with GCSF in post myocardial infarction patients by modulating the regeneration of myocardial tissue. However, the cardioprotective role of GCSF in patients with anthracycline cardiotoxicity has not been well studied. In this study we evaluated GCSF and its effect on systolic function in patients receiving anthracycline chemotherapy.
Methods: From January 2006 to December 2010, a retrospective cohort study was done to identify all patients who received anthracycline chemotherapy treated either with or without GCSF and had at least 2 transthoracic echocardiograms. The primary measure was the change in left ventricular ejection fraction measured before and after anthracycline chemotherapy in patients who received GCSF compared to patients who did not receive GCSF. Simpson's technique was used to evaluate the change in LVEF while t-test and regression analysis were used to compare differences between both groups.
Results: Seventy-nine patients were identified. Overall there was a decrease in mean LVEF between patient who did not received GCSF (baseline LVEF M=61.9% vs. post treatment LVEF M=59.0%, CI95%, p=0.026) compared to those who received GCSF (baseline LVEF M=61.7% vs. post treatment LVEF M=59.2%, CI95%, p=0.033). There was a greater decrease in mean LVEF in the non GCSF group (2.9%) compared to the GCSF group (2.5%). When adjusted for age, gender, use of beta-adrenergic antagonists, ACE inhibitors, and adjunctive cardiotoxic drugs, there was no significant difference between both groups (beta: 0.26; p=0.890).
Conclusion: The present study suggests that GCSF preserves systolic function in patients receiving anthracycline chemotherapy. Further prospective studies are needed to better discern the relationship between GCSF and its cardioprotective role and other echocardiogram parameter in patients who receive anthracycline chemotherapy.

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HOSPITAL ADMISSIONS IN A HIGH RISK HEART FAILURE POPULATION MANAGED WITH A TEAM BASED APPROACH IN A LARGE URBAN HEALTHCARE DELIVERY MODEL

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Background: Hospital admissions drive heart failure (HF) costs. Team based management improves outcomes.
Purpose: Demonstrate the impact of a team based program at Cedars Sinai Healthcare Foundation on hospital admissions and readmissions.
Methods: High risk patients were identified from an outpatient panel of 3,500 patients. The HF program includes cardiologists, a clinical pharmacist, nutritionist, home nurse practitioners, and palliative care. Services offered included education, medication reconciliation and optimization based on clinical parameters, serum brain natriuretic peptide, and point of care ultrasound IVC measurements. Retrospective review of over 28 months (11/2012-2/2015) was conducted. Cedars Sinai Hospital and Olympia Medical Center hospital admissions were included.
Results: 6 months Of 213 patients, 34 were excluded (HF resolved/discharged 4; Declined follow-up 11; Transfer of care 8; Lost to follow-up 2; Hospice 4; Deceased 5). 179 patients (84%) participated for 6 months. There were 148 hospital admissions (0.8/patient) and 32 30-day readmissions (0.18/patient) 6 months pre-enrollment. There were 81 hospital admissions (0.46/patient) and 23 30-day readmissions (0.13/patient) 6 months post-enrollment. These findings resulted in a 45.3% reduction in hospital admissions (p 0.00004) and a 28.1% reduction in 30-day readmissions (p 0.4).12 months Of 163 patients, 50 were excluded (HF resolved/discharged 8; Declined follow-up 11; Transfer of care 9; Lost to follow-up 4; Hospice 10; Deceased 8). 113 patients (69.3%) participated for 12 months. There were 114 admissions (0.1/patient) and 23 30-day readmissions (0.2/patient) 12 months pre-enrollment. There were 65 admissions (0.6/patient) and 12 30-day readmissions (0.1/patient) 12 months post-enrollment. These findings resulted in a 43.0% reduction in hospital admissions (p 0.0002) and a 47.8% reduction in 30-day readmissions (p 0.05).
Conclusions: The HF program demonstrated reduced hospital admissions at 6 and 12 months. 30-day readmissions decreased at 12 months.

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ECHOCARDIOGRAPHIC PROFILE AND IMMUNOLOGIC FUNCTION IN HIV-INFECTED PATIENTS

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Echocardiographic abnormalities are commonly identified in HIV-infected individuals even while on treatment with highly active antiretroviral therapy. The present case series was meant to provide a descriptive profile of the putative correlation between the type and severity of echocardiographic cardiac abnormalities and the immunologic status in terms of CD4 count and HIV viral load. The study was designed as a retrospective cross-sectional cohort of adult patients infected with HIV on treatment with antiretroviral agents, seen in the outpatient Cardiology clinic between January 2007 and January 2013. Electronic medical records were reviewed for eligible patients whose cardiomyopathy was from no other source other than HIV infection which was serologically confirmed. Of the twenty patients screened consecutively, nine patients with relatively preserved immunologic status and low viral load were found to have varying degrees of echocardiographic abnormalities including pulmonary hypertension, systolic dysfunction, severe valvular regurgitation, pericardial effusion, and diastolic dysfunction. There was no discernible trend between the degree of echocardiographic abnormalities and the extent of immunologic dysfunction. The relatively preserved CD4 count of more than 200/mL and substantially low viral load of less than 100,000 copies/mL did not appear to predict the degree of systolic dysfunction and pulmonary hypertension while on HAART regimen. The echocardiographic abnormalities could not be attributed solely to HIV infection, level of viral load and CD4 count. Other factors might potentially contribute to the development of cardiac abnormalities among HIV-infected individuals while on treatment.

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PHARMACIST INVOLVEMENT TO IMPROVE CARE OF HEART FAILURE PATIENTS AS THEY TRANSITION FROM HOSPITAL TO HOME

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Background: Better Outcomes by optimizing Safe Transition (also known as BOOST) is a project/program aimed at improving care of patients as they transition from hospital to home. It provides evidence-based clinical interventions that can be easily adapted and integrated into each unique hospital environment. The goal for pharmacy was to identify/intervene on heart failure medication related issues in moderate to high risk patients, which included: side effects, drug interactions, polypharmacy, education, cost, family involvement, and efficient collaboration with other providers and disciplines. The primary purpose of this study is to increase pharmacist patient encounter at discharge and thereby increase hospital consumer assessment of healthcare providers and systems (HCAPS) score for patient understanding of heart failure medications.
Method: High risk heart failure patients were simply identified as patients with >5 medications and/or with diagnosis for heart failure. Pharmacist was consulted upon admission to reconcile home medications and other medication related issues, such as cost, side effects, polypharmacy, compliance etc. Upon discharge pharmacist was consulted to give a comprehensive verbal and written (calendar) medication education. HCAPS scores were reported monthly through patient survey.
Results: In 2012 pharmacist discharge counselling/support for one heart failure floor was approximately 200 encounters, 2013 it was approximately 700 encounters, by 2014 it increased to approximately 900 encounters. There was a 77% increase in pharmacist involvement for safe medication discharge. This translated to 73% HCAPS score for patient's positive "understanding of what medicine is for" from 55 % prior to BOOST project.
Conclusion: Pharmacist involvement in heart failure patients at discharge and during hospitalization was associated with increase in patient understanding of heart failure medications, which translates to patient safety and better compliance.

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ANDROGENIC ANABOLIC STEROIDS INDUCED DILATED CARDIOMYOPATHY PRESENTED WITH ISCHEMIC STROKE

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Backgrounds: Androgenic anabolic steroids (AAS) are often used by many athletes or bodybuilders to increase muscle mass and to enhance performance. This comes with multiple side effects, some of which can be life-threatening or irreversible. There have been a few case reports that previously suggested an association between AAS use and dilated cardiomyopathies. We report a case of a patient with chronic AAS use, who presented with an acute ischemic stroke and severe dilated cardiomyopathy with systolic dysfunction.
Case: This is a 37 year old bodybuilder male with a past medical history of hyperlipidemia and tobacco abuse who presented with an acute ischemic stroke. He had been self-administering anabolic androgens for the past three years. He presented with left-sided weakness, slurred speech and left facial droop. He had shortness of breath with activity and occasional palpatations for a few weeks prior to the admission. An initial CT scan of the brain did not show any acute process. He was given tPA upon arrival to the hospital. An echocardiogram showed global dilatation of the heart with global hypokinesia of the left ventricle. An estimated ejection fraction was 20%. A follow-up MRI of the brain showed hemorrhagic conversion of the infarction. A CT angiogram of the coronary arteries was normal. The patient was treated and discharged with lisinopril, metoprolol and spironolactone. A cardiac MRI two months later also showed severe left ventricular enlargement and severe global hypokinesia without any areas of delayed contrast enhancement.
Conclusions: This patient developed an ischemic stroke as a complication of dilated cardiomyopathy which was possibly associated with the use of AAS. It is important for physicians to be mindful of potential side effects associated with chronic AAS use. We have presented an unusual and near lethal presentation of a potential condition induced by anabolic steroid use.

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STRUCTURED EATING PLAN IN PATIENTS WITH HEART FAILURE

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Objective: To test the feasibility of 3-month structured eating plan (STEP), assess the effectiveness of the intervention, and assess potential barriers to dietary behavior in veterans with heart failure (HF).
Background: HF outcomes are related to patient compliance, adherence to lifestyle and diet, and medication management. Adherence to dietary guidelines has been shown to be lower than adherence to medications and is associated with increased admissions for HF. While proper nutrition is recognized as an important part of HF management, the official dietary guidelines for patients with HF are limited and somewhat vague and inconsistent. *Methods*: This is prospective observational pilot study. Twenty-three veterans with HF were recruited in the intervention. Patients' dietary barriers were assessed using semi-structured questionnaires. Patient-centered, individualized, and structured meal plan was formulated in collaboration with HF nurse practitioner (NP) and dietitian talking into patients' food preference, assess, availability, and affordability.
Results: The percentage of patients who agreed to participate was 72%; the percentage of patients who were recruited and completed the intervention was 52%; and the percentage of patients who completed the food records and kept their intervention was 80%. Blood tests were measured pre and post intervention. Serum creatinine level was significantly improved after intervention ($P < 0.05$).
Conclusions: The findings of this pilot study showed that a structured, patient-specific eating plan for veterans with HF was feasible in the VA healthcare system.

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THE ROLE OF EPIDEMIOLOGICAL CORONARY ARTERY DISEASE RISK FACTORS IN TAKO-TSUBO CARDIOMYOPATHY

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Background: Tako-tsubo cardiomyopathy (TTC) is a syndrome that present with ST elevation/ depression on electrocardiogram, elevated cardiac enzymes and signature echocardiogram findings. Severe physical and emotional stressors have been shown to precipitate this syndrome.
Objectives: We aim to study the incidence of both the modifiable and non-modifiable CAD risk factors in patients presenting with TTC and STEMI at our tertiary care center.
Methods: Retrospective analysis of 429 patients who presented with ST elevation, raised cardiac enzymes and wall motion defect between July 2012 to May 2014, was performed. They were classified into TTC group without significant CAD and STEMI group with obstructive CAD on coronary angiography. Different traditional modifiable and non-modifiable CAD risk factors were compared between the two populations.
Statistical analysis was performed using SPSS 22 version (Armonk, NY: IBM Corp).
Results: Among all 429 patients, TTC group had 182 patients with mean age of 69±12.4 years versus the STEMI group who had 247 patients with mean age of 61.2±13.1 years (<0.001).
The distribution of different CAD risk factors in TTC group versus STEMI group included female gender with 90.2% versus 26% (p<0.001); family history of premature CAD in 27% versus 5.3% (p<0.001); hypertension in 50% versus 66.8%(p<0.001); diabetes in 16.5% versus 24.7% (p=0.05); dyslipidemia in 61 % versus 73.6% (<0.5); history of tobacco use in 32.4% versus 46.2%(p<0.05) respectively.
Anxiety and depression was the precipitating cause in 12.6 % (23) patients in the TTC group.
Conclusions: CAD risk factors have a good association with TTC as with STEMI. Female gender and family h/o premature CAD had significant correlation with the TTC whereas hypertension, diabetes and tobacco history had higher probability with STEMI. Our study suggests that there may be a missing link with the risk factors promoting atherosclerosis in patients with Tako-tsubo cardiomyopathy despite established neurogenic pathogenesis.

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IMPACT OF THE BETA-1 ADRENERGIC RECEPTOR POLYMORPHISM ON TOLERABILITY AND EFFICACY OF BISOPROLOL THERAPY IN HEART FAILURE PATIENTS

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Background: The association between the coding region variations of adrenergic receptor genes and the therapeutic effect were investigated in congestive heart failure (CHF) patients.
Methods and Results: 100 symptomatic CHF patients with LVEF < 45% were enrolled. Enrolled patients started bisoprolol 1.25mg once daily, up-titrated to the maximally tolerable dose, and were treated for 1 year. Genotypic analysis was carried out, but the results were double-blinded throughout the study period. 1) At position 389 of the beta-1 adrenergic receptor, the observed minor Gly allele frequency was 21% and no deviation from Hardy-Weinberg equilibrium was seen in the genotypic distribution of Arg389Gly (p=0.75). 2) Heart rate was reduced from 80.8±14.3 to 70.0±15.0 BPM (p<0.0001). There was no significant difference in the final heart rate across the genotypes. However, Arg389Arg genotype group required significantly larger amount of bisoprolol compared with Gly389X (Gly389Arg+Gly389Gly) group (5.26±2.62 mg vs 3.96±2.05mg, p=0.022). 3) There were no significant differences in the changes of LVEF or remodeling between two groups. There was no significant difference in exercise capacity or BNP level change, either. 4) However, interestingly, there was two-fold higher rate of readmission (21.2% vs 10.0%, p=0.162) and one HF-related death in Arg389Arg group. *Conclusion*: ABRB1 Gly389X genotype showed greater response to bisoprolol than Arg389Arg genotype, suggesting the potential of individually tailoring of beta-blocker therapy according to genotypes.

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A RARE CASE OF CARDIAC TAMPONADE INDUCED BY CHRONIC RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disease primarily involving the joint synovium. The severity of the disease and symptom manifestations are variable from patient to patient. RA is a systemic disease, which has many known extra-articular manifestations.
Case: We present a unique case of a patient with long standing RA on adalimumab and hydroxychloroquine who presented with a primary complaint of chest and back pain. Echocardiography revealed borderline normal left ventricular function and a large pericardial effusion with the finding of elevated intrapericardial pressure suspicious for cardiac tamponade. Infectious workup including Human Immunodeficiency Virus, Ebstein Barr Virus, Cytomegalovirus, Tuberculosis and Mycoplasma were all found to be negative. The presence and elevation of anti-cyclic citrullinated peptide antibody, rheumatoid factor and C-reactive protein confirmed that the patient was having an active flare up of his longstanding rheumatoid arthritis. It was determined that this flare up was the cause of the cardiac tamponade. A pericardiocentesis was performed and 850 cc of bloody fluid was drained. Additionally, colchicine was prescribed to help reduce the pericardial thickening and prevent relapse. The patient remained stable and asymptomatic following the pericardiocentesis and was discharged with instructions to follow up with cardiology and rheumatology. At his follow up visit, repeat echocardiogram showed no signs for pericardial effusion or thickening.
Conclusion: Although there has been extensive study of rheumatoid arthritis, there are only a few documented cases noting the occurrence of cardiac tamponade in these patients. Therefore, it is important for the clinician to be aware of and recognize this potentially serious cardiac outcome associated with a common rheumatologic condition.

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STATIN INTOLERANCE - MECHANISMS, RISK FACTORS, DEFINITION AND MANAGEMENT

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Statins are one of the most commonly prescribed drugs in clinical practice. They are usually well tolerated and effectively prevent cardiovascular disease (CVD) events. Most statin therapy-related adverse effects are muscle-related, such as statin-induced myalgia or myopathy (SIM), as well as muscle weakness and myosis. The recent consensus paper of the European Atherosclerosis Society (EAS) has focused on statin-associated muscle symptoms (SAMS), and avoided the use of the term 'statin intolerance'. Although muscle syndromes are the most common adverse effects observed after statin therapy (even up to 29% according to the EAS statement), excluding other side effects might underestimate the number of patients with statin intolerance, which might be observed in 10 - 15% of patients. In case of these patients one should also always remember to exclude other causes of statin intolerance, including so-called nocebo effect. In clinical practice, statin intolerance limits effective treatment of patients at risk of, or with, CVD. Knowledge of the most common adverse effects of statin therapy that might cause statin intolerance and the clear definition of this phenomenon is crucial to effectively treat patients with lipid disorders. Therefore, the recent position paper of International Expert Lipid Panel was prepared to suggest a unified definition of statin intolerance, and to complement the recent EAS statement on SAMS, where the pathophysiology, diagnosis and the management were comprehensively presented. Besides the discussion around statin intolerance definition, the lecture will also discuss in details the most important issues on the suitable statin intolerance management, especially in patients at high CV risk.

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GENETICS OF TRIGLYCERIDE-RICH LIPOPROTEINS AND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

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Triglyceride-rich lipoproteins (TGRLs) comprise a vast array of intestinally-derived and hepatically-secreted particles with distinct compositions and associations with risk for atherosclerotic cardiovascular disease (ASCVD) or pancreatitis. Although the contribution of plasma/serum triglycerides (triacylglycerols [TG]) to increased risk of ASCVD was established in multivariate models that adjust for major risk markers, including LDL cholesterol and HDL cholesterol. Despite the association of circulating TGRL levels with atherosclerosis, it has been uncertain whether abnormal TGRL metabolism and/or TGRL lipolytic products are involved in the causal pathway for ASCVD. Human genetic studies identified new proteins involved in TGRL metabolism, revealed insights into the genetic architecture of plasma TG, and clarified the contribution of TGRL to human CVD. The genetic architecture for TG in the population appears to be a mosaic comprised of rare large-effect variants, common small-effect variants, and environmental influences. Variants associated with common, complex traits like plasma TG range from common (>1:20 frequency), to low frequency (1:200 to 1:20), to rare (<1:200). About 50% of interindividual plasma TG variability is estimated to come from DNA sequence variants. A comprehensive logistic regression model from GWAS that included clinical variables and both common and rare genetic variants explained 42% of total variation in hypertriglyceridemia diagnosis. Genetics can be used to distinguish causal from reactive processes in humans and such studies suggested that plasma TG causally relates to CHD. Common, low frequency, and/or rare DNA sequence variants in 4 TGRL metabolism genes that are functionally related to LPL have been convincingly associated with CHD risk. Human genetic data suggest that therapeutic strategies that enhance LPL function, decrease APOC3 function, decrease ANGPTL4 function, or enhance APOA5 function are important targets for prevention of ASCVD.

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USE OF PCSK9 INHIBITORS IN STATIN INTOLERANT PATIENTS: ROLE FOR THE FUTURE?

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While the HMG-CoA reductase inhibitors have been lifesaving drugs for many millions of patients, intolerance to these agents has estimated to be 5-10% of patients, and may approach 20% in certain populations. The new PCSK9 inhibitors (Proprotein Convertase Subtilisin/Kexin Type 9) will soon be reviewed for approval in United States and Europe and may play a significant role in patients with previously demonstrated SAMS (Statin-Associated Muscle Symptoms) in that they lower LDL cholesterol via a different pathway. PCSK9 affects the ability of the LDL Receptor to separate from the LDL after delivering LDL to the hepatocyte; PCSK9 inhibitors allow the LDL Receptor to recycle thus be more effective in lowering the total LDL level. The first drugs (manufacturers) to apply for approval are anticipated to be alirocumab (Sanofi/Regeneron), evolocumab (Amgen) and bococizumab (Pfizer). All are expected to apply to the FDA for the indication of "statin intolerance". Effectiveness studies have shown a differential response likely based on the underlying level of PCSK9 in individual patients, along with a variable response in tolerance, including myalgias, when compared to standard therapy. These will be discussed along with anticipated role for the PCSK9s in statin intolerant patients. Conclusion: PCSK9 inhibitors offer a different mechanism than the HMG-CoA reductase inhibitors to lower LDL cholesterol and may provide an opportunity to achieve LDL goals even in patients intolerant to HMG-CoA reductase inhibitors due to SAMS.

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A LARGE PRAGMATIC TRIAL OF STATINS IN PRIMARY PREVENTION: THE NEXT FRONTIER

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Atherothrombotic disease is the most common cause of death in the world. Pharmacologic LDL lowering has been shown to reduce coronary heart disease (CHD) events according to the LDL level achieved with no demonstrated level below which events do not decrease with additional LDL lowering. Further, available data suggest that the earlier the LDL lowering occurs, the greater the therapeutic effect of a given decrease.
Objective: The purpose of the proposed study (Elimination of Coronary Artery Disease [ECAD]) is to determine whether pharmacologic lowering of serum low density lipoprotein cholesterol (LDL), initiated in healthy young to middle-aged adults, can eliminate, or markedly reduce CAD.
Study design: ECAD is a randomized, multicenter, primary prevention clinical trial designed to compare a strategy of usual guideline based lipid management to a strategy of LDL lowering medication (atorvastatin 20 mg daily) for the primary prevention of atherothrombotic events (all cause death, excluding those due to cancer and trauma, myocardial infarction, stroke, or coronary revascularization) in healthy middle aged men and women.
Study subjects are men 35 to 50 years of age and women of non-child bearing potential 45 to 59 years of age without any prior history of CHD, stroke, or peripheral vascular disease who have one additional risk factor (hypertension and waist circumference >100 cm in men or >90 cm in women, family history of premature coronary atherosclerosis, or smoking) and LDL from 1.8 mmol/l (70 mg/dL) to the minimum LDL for which the current ACC/AHA Guidelines recommend pharmacologic treatment in the presence of a single additional risk factor.
Intervention or Treatment: Usual guideline-based therapy versus usual guideline-based therapy with the addition of atorvastatin 20 mg daily.
Sample Size: A total of 15,000 patients will be recruited to participate in this trial from 300 primary care practices.

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NOVEL BIOMARKERS OF LIPID AND LIPOPROTEIN METABOLISM

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Objectives: Cardiovascular disease (CVD) can occur in individuals with low LDL-cholesterol (LDL-c). We investigated whether detailed measures of LDL subfractions and other lipoproteins can be used to assess CVD risk in a population with both low LDL-c and high C-reactive protein that was randomized to high-intensity statin or placebo.
Methods and Results: In 11,186 JUPITER participants, we tested whether lipids, apolipoproteins, and ion mobility (IM)-measured particle concentrations at baseline and after random allocation to rosuvastatin 20 mg/d or placebo were associated with first CVD events (n=307) or CVD/all-cause death (n=522). In placebo-allocated participants, baseline LDL-c was not associated with CVD (adjusted HR per SD, 1.03, 95% CI 0.89-1.20). In contrast, associations with CVD events were observed for baseline non-HDL-cholesterol (non-HDL-c: 1.18, 1.02-1.37), apolipoprotein B (apoB: 1.28, 1.11-1.49), and IM-measured non-HDL particles (non-HDL-p: 1.19, 1.05-1.36) and LDL particles (LDL-p: 1.21, 1.06-1.38). Association with CVD events was also observed for several LDL and VLDL subfractions, but not for IM-measured HDL subfractions. In statin-allocated participants, CVD events were associated with on-treatment LDL-c, non-HDL-c, and apoB; these were also associated with CVD/all-cause death, as were several LDL and VLDL subfractions albeit with a pattern of association that differed from the baseline risk.
Conclusions: In JUPITER, baseline LDL-c was not associated with CVD events, in contrast with significant associations for non-HDL-c and atherogenic particles: apoB and IM-measured non-HDL-p, LDL-p, and select subfractions of VLDL-p and LDL-p. During high-intensity statin therapy, on-treatment levels of LDL-c and atherogenic particles were associated with residual risk of CVD/all-cause death.

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THE ROLE OF STATINS IN PREVENTION OF CONTRAST-INDUCED ACUTE KIDNEY INJURY

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Contrast induced acute kidney injury (CIAKI) is a common cause of acute renal failure in patients undergoing coronary angiography and/or percutaneous coronary interventions (PCI). Patients at risk for CIAKI include those with diabetes mellitus, renal insufficiency, heart failure, hypotension and shock and those receiving nephrotoxic medications. Other risk factors include high volumes of high-osmolality radiographic contrast media, anemia and use of an intra-aortic balloon pump. Multiple pharmacologic and non-pharmacologic interventions have been studied in an attempt to prevent this complication in at-risk patients. The most successful interventions to date are pre-procedure, intravenous hydration using normal saline or sodium bicarbonate and use of non-ionic, iso-osmolar radiographic contrast media. In recent years, there has been increasing interest in the role of HMG-CoA reductase inhibitors (statins) in the prevention of CIAKI in patients undergoing coronary angiography and/or PCI. Prior studies have involved patients on chronic statin therapy and those receiving short-term (often high-dose) statin therapy prior to and following contrast exposure. Patients studied include those with acute coronary syndromes and those undergoing elective coronary angiography with or without PCI. A wide variety of hydrophilic and lipophilic statins have been used. Non-randomized studies have, for the part, shown a reduction in the incidence of CIAKI with statin use. Randomized clinical trials investigating this issue have reported mixed results. Most, but not all have reported a decrease in the risk of CIAKI. Studies showing a reduction in CIAKI risk include those employing short-term and long-term statin therapy, high and low-dose statins as well as hydrophilic and lipophilic statins. The preponderance of evidence suggests that statins are capable of reducing the risk of CIAKI in patients undergoing coronary angiography and PCI.

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STATIN USE AND LIPID CONTROL BY ACC/AHA STATIN ELIGIBILITY GROUP IN UNITED STATES ADULTS 2011-2012

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Background: The 2013 ACC/AHA Cholesterol Management Guidelines identify four statin eligible groups, those with: 1) known atherosclerotic cardiovascular disease (ASCVD), 2) LDL-C ≥190 mg/dl, 3) diabetes aged 40-75, and 4) primary prevention ≥7.5% 10-year ASCVD risk aged 40-75. We examined the number of potentially statin eligible US adults in these groups and the current extent of statin therapy and lipid control based on prior guidelines.
Methods: We identified US adults aged ≥21 years from the US National Health and Nutrition Examination Survey (NHANES) 2011-2012 in the above statin eligible groups and determined the proportion of each on a statin prescription. Among those with LDL-C levels available, we also determined the proportion at recommended LDL-C levels. NHANES 2-year sample weights were applied to all estimates.
Results: Among a total of 5,206 adults representing 219 million persons, we identified 1,696 adults representing 63 million adults which fit into one of the four statin eligible groups. The table below notes the estimated number of US adults within each statin eligible group and proportion receiving statin therapy, and who were at recommended LDL-C levels.
Conclusion: Significant proportions of US adults eligible to receive statins based on the ACC/AHA guidelines are not taking statins and goal attainment is suboptimal.

Statin Eligible Group	Sample n	Weighted N (millions)	% on Statin	% at LDL-C goal *
ASCVD	549	19.3	59.9	15.2
**LDL-C≥190 mg/dl	53	2.6	19.3	n/a
Diabetes, all	444	14.3	45.5	47.1
ASCVD 10-year risk				
<7.5%	187	6.1	32.3	39.9
≥7.5%	257	8.2	55.4	52.1
Primary Prevention ASCVD 10-year risk≥7.5%	650	27.2	28.8	62.0

* Among all subjects with LDL-C levels regardless of statin use: LDL-C goals for ASCVD: <70 mg/dl, Diabetes: <100 mg/dl, >=7.5% group: <130 mg/dl; n/a for LDL-C≥190 mg/dl group since defined on the basis of elevated LDL-C only. **Does not include persons on treatment but controlled to LDL-C<190 mg/dl.

*This study was funded by a contract from Regeneron to the University of California, Irvine.
Dr Khan is an employee of Sanofi-Aventis Pharmaceuticals, Bridgewater, NJ and Dr. Sanchez is an employee of Regeneron Pharmaceuticals, Tarrytown, NY.

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SUCCESSFUL ROLE OF CASCADE SCREENING IN FAMILIAL HYPERCHOLESTEROLEMIA IN INDIAN POPULATION

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Background: Familial Hypercholesterolemia (FH) is an inherited disorder of lipid metabolism characterized by high low density lipoprotein (LDL) cholesterol since birth resulting in atherosclerosis and premature coronary artery disease (CAD) and family history of early CAD. FH is caused by mutations in LDL receptor, ApoB100 and PCSK9 gene. Frequency is estimated to be 1 in 350.
Objectives: To identify carriers of FH mutations by Cascade screening of family members of subjects positive for the mutation and provide appropriate interventions.
Results: Mutation screening was done in index cases with suspicion of FH. Modified Dutch Lipid Network Criteria (DLNC) criteria was used to identify subjects which led to identification of 36 disease causing mutations (9 novel) in LDLR gene in 42 FH index cases. Ten cases out of 42 were homozygous while 32 were heterozygous for a LDLR mutation. Of 42 index cases, 126 family members were screened. 86 (68%) were found to harbor the mutation and had significantly higher LDL cholesterol levels than the non mutation carrier family members. Of 86 affected family members, 71 were adults (Mean age 37.8 years) and 15 were children (Mean age 12.3years). Out of 86, 15 (17%) had CAD and 42 (48%) were already on lipid lowering therapy.
Conclusions: Cascade screening led to identification of 71 new cases who were at a very high risk of developing premature CAD. Affected family members were referred to cardiology and hyperlipidemia clinic for lifestyle modification and drug therapy, if required. It proved to be a successful initiative towards primary prevention of CAD.

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PSYCHOMETRIC EVALUATION OF A TREATMENT ACCEPTANCE MEASURE IN PATIENTS RECEIVING SUBCUTANEOUS INJECTION TREATMENT

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Objectives: Alirocumab, a PCSK9 inhibitor, significantly reduces low density lipoprotein – cholesterol, but requires subcutaneous injections rather than oral pills. To quantify patients' acceptance of this treatment modality, a new patient reported outcome, the injection–treatment acceptance questionnaire (I-TAQ), was developed and psychometrically evaluated with high cardiovascular risk patients receiving alirocumab.

Methods: The 22-item, five domain, I-TAQ was developed through literature review and qualitative patient interviews to confirm content validity. The measure was administered once to 151 patients enrolled in alirocumab clinical trials. Analyses conducted included evaluation of item response distributions, factor and multi-trait analyses, inter-item correlations, correlations with an existing measure of acceptance (convergent validity) and comparison of known groups.

Results: Completion rates were high with no patients missing >2 items and 91.4% with no missing data. All items displayed high ceiling effects (>30% at ceiling) due to high treatment acceptance. Factor analysis supported the a priori hypothesized item-domain structure with strong fit indices (RMSEA= 0.070; CFI= 0.988). All items demonstrated strong item convergent validity (item-scale correlation = >0.4), except for the side effects domain due to small response numbers (n=46). All but two items correlated most highly with the domain they were included in (item discriminant validity). Internal consistency reliability was strong for all domains (Cronbach's alpha range: 0.72-0.88). Convergent validity was supported by a logical pattern of correlations.

Conclusions: The newly developed I-TAQ has strong psychometric properties in patients treated with subcutaneous alirocumab and should prove to be a valuable patient-reported outcome for therapies requiring subcutaneous injection.

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EFFICACY OF SPECT/CT MPI VERSUS ADDITIONAL PRONE SPECT MPI FOR ATTENUATION CORRECTION OF INFERIOR WALL DEFECTS

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Objective: To avoid extra radiation to the patient from SPECT/CT if there is no significant difference between SPECT/CT and additional prone SPECT.
Background: When the patient has an enlarged heart, the heart may rest lower on the diaphragm rather on the inner chest wall, so it can be difficult to determine whether the patient has a real inferior wall infarct. To resolve this problem, attenuation correction (AC) by SPECT/CT or additional prone SPECT can be performed.
Methods: Patients in the period from 1/1/2012 to 12/31/2014 who underwent MPI and additional prone SPECT or SPECT/CT to evaluate inferior wall defects were recorded. Cases were excluded if they had no inferior wall defects on MPI or there was no attempt at AC. We collected and compared the results to determine efficacy between SPECT/CT and additional prone SPECT. We also compared the results in patients with enlarged hearts; a cut-off value of 150 for left ventricular end-diastolic volume was used.
Results: Out of a total of 1,086 cases, 681 received SPECT/CT and 405 received additional prone imaging. 542 cases out of 681 had AC in SPECT/CT and 274 cases out of 405 had AC in additional prone imaging ($p<0.0001$). In patients with enlarged hearts, 103 cases out of 157 from SPECT/CT had AC and 34 cases out of 67 from additional prone imaging had AC ($p=0.037$). In patients with normal heart sizes, 439 cases out of 524 from SPECT/CT had AC and 240 cases out of 338 from additional prone imaging had AC ($p<0.0001$).
Conclusions: We conclude that SPECT/CT is significantly better than additional prone imaging when AC is performed to detect inferior wall defects both in patients with enlarged hearts and those with normal-sized hearts. Unless there are any contraindications, we recommend SPECT/CT with AC when inferior wall defects are suspected.

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COMPARATIVE STUDY OF FFR, IFR AND PD/PA - IS THERE STILL A PLACE FOR ADENOSINE USE IN THE CATH LAB?

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Introduction: Fractional flow reserve (FFR) is an hemodynamic index measured at maximum adenosine induced hyperemia, validated for the functional assessment of coronary stenosis. Given the potential complications and procedure delay, alternative methods without adenosine administration have been investigated, including the instantaneous wave-free ratio (iFR) and the resting distal coronary pressure to aortic pressure ratio (Pd/Pa).Objective: To evaluate the diagnostic accuracy of iFR and Pd/Pa in the functional assessment of coronary stenosis when compared to FFR.
Methods: observational study of patients undergoing coronary angiography with borderline coronary lesions. iFR and Pd/Pa were measured. FFR was subsequently assessed during intravenous administration of adenosine. Diagnostic accuracy was assessed by the area under the receiver operating characteristic curve (AUC), considering < 0,80 as the FFR cut-off value for hemodynamic significance.
Results: 72 borderline coronary stenosis were evaluated in 52 patients (71±10 years; 79% male). FFR was highly correlated with iFR (Pearson R=0.77; p <0.001) and Pd/Pa (Pearson R=0.67; p <0.001). iFR was found to have the best diagnostic accuracy (AUC=0.89; 95% CI 0.82-0.97 versus Pd/Pa=0.81, 95% CI 0.69 to 0.93) for hemodynamic significance. Diagnostic thresholds were 0.90 and 0.93 for iFR and Pd/Pa, respectively. iFR validity stemmed from its high negative predictive value in excluding angiographic hemodynamic significance for a >0.90 value (negative predictive value: 91.8%; positive predictive value: 70.8%).
Conclusion: iFR assessment could be an intermediate step for interventional decision. An iFR value >0.90 excludes an hemodynamically significant lesion. Notwithstanding FFR should be used when in the presence of an iFR value below 0,90 as it does not assure functional significance.

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RELATIONSHIP OF DIASTOLIC FUNCTION AND MAXIMAL EXERCISE CAPACITY AMONG PATIENTS WITH LOW RISK FOR CORONARY ARTERY DISEASE: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Background: There is a significant correlation between exercise capacity and diastolic function parameters in patients at high cardiovascular risk and with proven cardiovascular diseases. This study aims to determine the relationship of diastolic function and maximal exercise capacity among patients with low risk for CAD.
Methods: 189 patients were retrospectively studied who underwent stress echocardiography from September 2013 until February 2014 at The Medical City. They were divided into two groups according to their exercise capacity (METS). Group 1 with MET <7 and Group 2 with >7 MET. Diastolic variables were mitral inflow velocities, early diastolic velocity (E), late diastolic velocity (A), E/A ratio, E' wave velocity, E/E' ratio, isovolumetric relaxation time and left atrial volume index.
Results: Among 189 patients, mean age was 45.7 ± 8.68 and mostly were male. Normal diastolic function was observed in 67%; 30% showed grade 1 diastolic dysfunction and 3% showed grade 2 diastolic dysfunction. 16% had increased filling pressures. Clinical parameters that correlated with a low functional capacity were female gender (p-value: 0.003), age (p-value: 0.006), dyslipidemia (p-value: 0.026), family history of heart disease (p-value: 0.002) and a positive treadmill exercise stress echocardiography (p-value: 0.022). In relation to the echocardiographic parameters, A wave velocity (p-value: 0.000), E/A ratio of the mitral flow (p-value: 0.002), E' wave velocity of the mitral annulus (p-value: 0.001) and the E/E' ratio (p-value: 0.007) were associated with MET < 7. The comparative analysis of the MET < 7 and MET > 7 groups in relation to the presence of increased filling pressures (E/E' > 10), 25.4% of patients with normal functional capacity and 50% with low functional capacity had impaired left ventricular filling pressure.
Conclusion: Diastolic dysfunction by echocardiography is associated with a low exercise capacity even among patients with low risk for coronary artery disease.

CARDIOVASCULAR IMAGING MODALITIES FOR EVALUATION OF CORONARY CIRCULATION, CARDIAC STRUCTURE AND FUNCTION

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CORRELATION BETWEEN USCOM-DERIVED HAEMODYNAMIC VARIABLES AND SEVERITY OF CHRONIC HEART FAILURE

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Background: Ultrasonic Cardiac Output Monitor (USCOM)-derived inotropy has been shown to discriminate patients with New York Heart Association (NYHA) stage IV from healthy controls. This study aims to investigate whether inotropy and other haemodynamic variables correlate with NYHA class and ejection fraction (EF).
Methods: Ethical approval was obtained to conduct a prospective, single-centre, observational study of patients presenting with heart failure symptoms to the echocardiography clinic at Prince of Wales hospital. The echocardiography and USCOM assessments were conducted by separate trained technicians who were blind to results from each other. The primary outcome was difference in mean inotropy between NYHA classes I, II, III, and IV. Secondary outcome was correlation between USCOM hemodynamic parameters and left ventricular ejection fraction (LVEF). (Clinical trial no. NCT02289508)
Results: Between June 2014 and January 2015, a convenience sample of 117 subjects were enrolled (NYHA Class I, n=28 (24%); Class II, n=58 (50%); Class III, n=22 (19%); Class IV n=7 (6%)). Differences between stroke volume index (SVI) and DO2 were found to be significant across NYHA classes ($p<0.05$). Differences in inotropy, cardiac index (CI) and systemic vascular resistance index (SVRI) were not significant. USCOM-SVI showed moderate correlation with Echo-LVEF ($r=0.41$; $p<0.01$). USCOM-SVRI ($r=0.30$, $p<0.01$), USCOM-CI ($r=.29$, $p<0.01$), and USCOM-inotropy ($r=0.27$, $p<0.01$) also showed weak to moderate correlation with LVEF.
Conclusion: The preliminary finding of this study shows that the USCOM-SVI and USCOM-DO2 correlated with NYHA stages of heart failure, and USCOM-SVI correlated with LVEF. The preliminary finding of this study suggests a possible role of USCOM to augment bedside assessment of patients with nonspecific heart failure presentation.

CARDIOVASCULAR IMAGING MODALITIES FOR EVALUATION OF CORONARY CIRCULATION, CARDIAC STRUCTURE AND FUNCTION

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THE ASSESSMENT OF CORONARY ARTERY CALCIFICATION IN HIGH-RISK CORONARY ARTERY DISEASE POPULATIONS

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Introduction: The detection of coronary artery calcification using multidetector computed tomography is diagnostic of coronary artery disease (CAD) and arterial plaque burden. In addition, the degree of coronary calcification is a powerful prognostic tool used to guide therapy and management of patients at risk for coronary artery disease. We sought to assess patterns of coronary artery calcification in a real-world patient population referred for CAC score quantification to determine relative risk contribution for a variety of cardiovascular risk factors.
Methods: 138 Patients underwent unenhanced CT (120 KV, 100 mA, 3 mm slices) of the four major coronary vessels, utilizing a standard CAC score protocol. coronary arterial calcification and plaque burden.
Results: In total, 552 coronary arteries were evaluated in 138 patients. The mean age for females was 64.4 years and for the males, 60.0. The calcium scores were measured at each of the four main epicardial vessels. The odds of diabetic subjects having a total calcium score over 100 relative to non-diabetic subjects was 5.64 times higher even after controlling for other cardiovascular risk factors (95% CI: 1.49 to 21.31, $p < 0.011$). The odds ratios for a calcium score > 100 matched to age, gender and smoking was also computed and yielded 1.12, 3.62 and 4.59, respectively, with adjustment for other risk factors. Thus, diabetes mellitus and smoking, two potentially modifiable risk factors, were by far the most contributory risk factors for the development of coronary calcification.
Conclusion: Diabetes mellitus and smoking are acknowledged CAD risk factors resulting in both micro- and macro-vascular complications. This may lead to alterations in the therapeutic approach towards cardiovascular disease in diabetics and smokers, and reemphasizes the need to manage these risk factors in particular before the occurrence of adverse cardiovascular events.

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OPTICAL COHERENCE TOMOGRAPHY IN ACUTE CORONARY SYNDROME

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This in-vivo study determined the novel imaging technique of optical coherence tomography can be applied to the clinical setting to provide a more accurately defined morphology of coronary plaque in acute coronary syndrome as compared to current imagining modalities, which will aid in identifying the pathways in the etiopathogenesis of acute coronary syndrome; thus, the targeted therapy can be established. This understanding may further help to prevent the occurrence of coronary heart disease in the first place.

Of the 26 patients in this prospective study, plaque rupture was associated with acute coronary syndrome in 61 percent of patients, while plaque erosion was seen in 39 percent of patients, which is statistically significant ($p < 0.05$). Additionally, fibrocalcific nodule was not seen in this early stage of observational data. Plaque erosion was seen more commonly in women (60%) as compared to men who have higher plaque rupture (69%) with statistical significance ($p < 0.05$). Smokers have higher incidence of plaque erosion (80%) as compared to plaque rupture (44%), which is statistically significant ($p < 0.05$). Patients with hypertension had higher incidence of plaque rupture (81%) than plaque erosion (70%).

This study found: 1. Plaque rupture is more commonly associated with acute coronary syndrome as compared to plaque erosion, 2. Women tend to have more plaque erosion as compared to men, who tend to have plaque rupture, 3. Smokers have higher incidence of plaque erosion as compared to plaque rupture, 4. Incidence of plaque rupture and plaque erosion did not differ based on the involvement of the culprit artery, and 5. The presentation of ST segment elevation myocardial infarction is more common in patients with plaque rupture, whereas non-ST segment elevation myocardial infarction is more frequent in those with plaque erosion.

CELLULAR AND MOLECULAR MECHANISMS OF CARDIOVASCULAR DISEASE, BASIC RESEARCH

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DUAL HCM AND LQT1 PHENOTYPES ASSOCIATED WITH TETRAD HETEROZYGOUS MUTATIONS IN MYH7, MYLK2, KCNQ1 AND TMEM70 GENES IN A THREE-GENERATION CHINESE FAMILY

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Objective: Hypertrophic cardiomyopathy (HCM) mainly results from autosomal-dominant inherited single heterozygous mutations in cardiac sarcomere genes. Contributions of multiple gene mutations to disease heterogeneity in a three generation family was investigated.
Background: As a heterogeneous disease, HCM demonstrates phenotypic variation in the degree of hypertrophy, arrhythmias, left ventricular outflow tract obstruction, even sudden death susceptibility. Single mutation in cardiac sarcomere gene could not easily to explain.
Methods: Clinical, electrocardiographic (ECG) and echocardiographic examination in members of a three-generation Chinese family was followed by exon and boarding intron analysis of 96 genes in the proband using second-generation sequencing. The identified mutations were confirmed by bi-directional Sanger sequencing in all family members and 300 healthy controls.
Results and conclusions: Four missense mutations were detected in the family. These were two novel MYH7-H1717Q and MYLK2-K324E mutations accompanied by the KCNQ1-R190W and TMEM70-I147T mutations. The proband carried all four mutations and showed overlapping HCM and LQT1 phenotypes. Five family members each carried two mutations. Subject II-2 only carried TMEM70-I147T. MYH7-H1717Q and TMEM70-I147T came from the paternal side, whereas KCNQ1-R190W and MYLK2-K324E came from the maternal side. Left ventricle mass indexes in MYH7-H1717Q carriers were significantly higher than in non-H1717Q carriers (90.05 ± 7.33g/m^2, 63.20 ± 4.53 g/m^2 respectively, $P<0.01$). Four KCNQ1-R190W carriers showed QTc intervals that were significantly more prolonged than those in non-R190W carriers (472.25 ± 16.18 ms and 408.50 ± 7.66 ms ms respectively, $P<0.05$). All MYLK2-K324E carriers showed inverted ECG T waves. The subject with only a TMEM70-I147T mutation showed normal ECG and echocardiographs suggesting that this had less pathological effects at least in this family. For the first time, we demonstrate dual HCM and LQT1 phenotypes in this multiple HCM and LQT1 related gene mutation carrier family and suggest that LQT-related gene mutations associate with QT interval prolongation and/or arrhythmia in HCM patients.

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GENETIC VARIABILITY IN PAR-1 DOES NOT AFFECT RISK OF BLEEDING OR ISCHEMIA AFTER PERCUTANEOUS CORONARY INTERVENTION

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Objectives/Background: Platelet reactivity is associated with recurrent ischemia and bleeding following percutaneous coronary intervention (PCI). Protease-activated receptor-1 (PAR-1), encoded by F2R, is a high affinity thrombin receptor on platelets and the target of the antiplatelet drug vorapaxar. The intronic single nucleotide polymorphism F2R IVS-14 A/T affects PAR-1 receptor density and function. We hypothesized that carriers of the T allele, who have decreased platelet reactivity, would be at lower risk for ischemic events, but higher risk for bleeding following PCI.
Methods: Using BioVU, the Vanderbilt DNA repository linked to the electronic medical record, we studied 572 patients who underwent PCI for unstable or stable coronary artery disease. Primary outcome measures were major adverse cardiovascular events (MACE, composite of revascularization, MI, stroke, death) and bleeding (assessed by Bleeding Academic Research Consortium scale) over 24 months.
Results: The minor allele (T) frequency was 15.0%. There were no genotypic differences in the frequency of MACE or bleeding (Table 1). In a Cox regression model, fully adjusted for age, race, sex, body mass index, and smoking status, carrying a T allele was not associated with MACE (HR 1.19, 95% CI 0.89-1.59, P=0.23) or bleeding (HR 0.73, 95% CI 0.37-1.4, P=0.34).
Conclusion: In our population, F2R IVS-14 PAR-1 variability does not affect risk of MACE or bleeding following PCI.

Table 1: Frequency of Major Adverse Cardiac Events or Bleeding Stratified by *F2R* IVS-14 Genotype

	GENOTYPE			
	A/A (n=416)	A/T (n=140)	T/T (n=16)	P value
MACE, n (%)	161 (38.7%)	49 (35.0%)	6 (37.5%)	0.62
BLEEDING, n (%)	66 (15.8%)	19 (13.6%)	3 (18.8%)	0.76

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GENETICS AND HYPERTENSIVE HEART DISEASE. STUDY ON THE RELATIONSHIP BETWEEN 5HT2A AND HYPERTENSIVE HEART DISEASE

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Background: Many different types of heart diseases run in families and can be inherited. Though the role of lifestyle in heart disease is clearly understood, little is known on the role played by genetics. Since heart disease remains the number one killer in the U.S, the need to better understand the role of genetics in risk of heart disease has become very important.
Objective: The study objective is to determine if any association exists between genetics and hypertensive heart disease.
Subjects: 85 subjects across 8 clinical research sites in the US. 42 diagnosed with hypertensive heart disease (ICD9 codes 401(Essential hypertension), and 401.9 (Hypertension Unspecified). Mean Age 49, Males 27, Females 16, and 43 controls matched for age, race and gender.
Methods: Subjects were genotyped using Taqman® SNP Genotyping Assays (Life Technologies, Carlsbad, CA). It consists of a panel of 12 single nucleotide polymorphisms (SNPs) in genes encoding for proteins expressed in the mesolimbic reward pathway. These genes include: 5HT2a, 5-HTTL, COMT, ANKK1/DRD2, DRD1, DRD4, DAT, DBH, MTHFR, OPRK1, GABA-A receptor gamma2, and OPRM1.
Results: A chi-square test using IBM SPSS V21 found significant association between 5-HT2a -1438G/A (rs7997012) and hypertensive heart disease: Over dominant Model (G/A vs. G/G-A/A) p= 0.036, Two sided fisher's exact 0.047). Logistic regression (p= 0.035) showed that G/A variation is more likely to be associated with subjects with hypertensive heart disease compared to the controls. (p= 0.038, OR, 2.583). Significant association was found between male subjects and hypertensive heart disease subjects (p= 0.002 OR 4.219).
Conclusion: This study suggests that 5-HT2a (rs7997012) may play a role in genetic predisposition to hypertensive heart disease. Findings in this study will hopefully help improve understanding on the role of genetics in heart disease.

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EFFECT OF GENE DELIVERY PLASMID ENCODING INTERLEUKIN-19 ON RAT EXPERIMENTAL AUTOIMMUNE MYOCARDITIS

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Objectives: To evaluate the effect of gene delivery plasmid encoding Interleukin-19 on rat Experimental Autoimmune Myocarditis (EAM) and possible mechanism.
Background: IL-19 is a novel, recently identified member of the IL-10 family, however, little is known about the exact biological role in immunological regulation.
Methods: The rat was immunized on day 0 and were injected with plasmid encoding IL-19 on day 6, all the rats were sacrificed on day 17. The effect of IL-19 gene delivery was evaluated by measuring of heart weight/body weight and myocarditis area, The relative gene expression levels of heart failure markers atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) were detected by real-time RT-PCR. Cardiac Function were performed by Echocardiography. Furthermore, we examined the effect of serum containing IL-19 on the expression of immune-relevant genes in IL-1-stimulated Spleen cells cultured from EAM rats.
Results: IL-19 gene therapy was effective in controlling EAM as monitored by decreased ratio of heart weight / body weight and the myocarditis area, The level of ANP and BNP were significantly lower and cardiac function parameters improved in IL-19 treatment group than those in control group. The serum containing IL-19 significantly decreased the expression of IL-18, IL-1beta, IL-12p35, IFN-gamma and upregulated IL-4 and IL-10 expression in IL-1-stimulated spleen cells cultured from EAM rats.
Conclusion: IL-19 effectively prevented progression of EAM by blocking related inflammatory immune genes expression. This might be a possible mechanism of the amelioration of EAM by IL-19 gene therapy.

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VAGAL ACTIVATION BENEFITS FOR CELLULAR CALCIUM HOMEOSTASIS IN CARDIOVASCULAR DISEASE

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Background: A hallmark of cardiovascular disease (CVD) is impaired cytoplasmic calcium handling of cell. Previous studies showed that increasing vagal tone ameliorated cardiovascular damages. Nevertheless, the effects of vagal activation to the calcium regulation are unclear.
Objectives: The present studies investigated whether vagal activation benefited for cellular calcium homeostasis in CVD.
Methods: The in vivo ischemia/reperfusion (I/R) and in vitro hypoxia/reoxygenation (H/R) models were adopted. Vascular function, calcium concentration and protein expression were detected by a myograph system, confocal microscopy and western blot, respectively. Specific protein knockdown was performed with siRNA.
Results: Our studies demonstrated that acetylcholine (ACh) significantly ameliorated dysfunctional vasoconstriction and reduced calcium-sensing receptor expression and activity in H/R arteries. Choline, a muscarinic ACh receptor agonist, markedly improved abnormal expression of calcium-cycling proteins though inhibiting calcium-calmodulin-dependent kinases in I/R arteries. These effects of vagal activation may be contributed to depress cytoplasmic calcium overload. In addition, we observed that ACh inhibited the formation of endoplasmic reticulum-mitochondria junctions to attenuate mitochondria calcium overload in H/R endothelial cells, indicating that ACh is involved in inter-organellar calcium transport. Furthermore, we paid attention to the calcium downstream signaling. Results showed that ACh could suppress apoptosis of myocardial cells via inhibition of calpain and calpastatin.
Conclusion: ACh not only depress cytoplasmic calcium overload, but also reduced calcium downstream proteic activity and endoplasmic reticulum-mitochondria communication. Our findings firstly clarified the potential roles of vagal activation in calcium regulation, and further help to develop novel therapeutic strategies targeting enhancing vagal activity for the treatment of CVD.
Supported by: grant from National Natural Science Foundation of China (Major International Joint Research Project, No. 81120108002; General Project, No. 81473203), Specialized Research Fund for the Doctoral Program of Higher Education (No. 20130201130008).

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GLUCOSE TOLERANCE AND NON-FASTING GLUCOSE ARE BETTER PREDICTORS OF ATHEROSCLEROSIS THAN INSULIN RESISTANCE OR FASTING GLUCOSE IN APOE-/- STAINS

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A major reason behind poor understanding on diabetes-accelerated atherosclerosis is the lack of appropriate animal models. We recently found that apolipoprotein E-deficient (Apoe-/-) with the C57BL/6 background develop type 2 diabetes and accelerated atherosclerosis on a Western diet. Multiple Apoe-/- mouse strains were made to discover diabetes-related phenotyptic variations that might predict atherosclerosis development. Evaluation of both early and advanced lesion formation in aortic root revealed that C57BL/6, SWR, and SM Apoe-/- mice were susceptible to atherosclerosis and C3H/HeJ and BALB/cJ Apoe-/- mice were relatively resistant. On a chow diet, fasting plasma glucose varied among strains with C3H/HeJ having the highest and BALB/cJ the lowest level. On a Western diet, fasting plasma glucose rose significantly in all strains, with C57BL/6, C3H/HeJ and SWR exceeding 300 mg/dl. BALB/cJ and C3H/HeJ were more tolerant to glucose loading than other 3 strains. C57BL/6 was sensitive to insulin while other strains were resistant. Non-fasting blood glucose was significantly lower in C3H/HeJ and BALB/cJ than C57BL/6, SM, and SWR. Glucose loading induced the 1st and the 2nd phase of insulin secretion in BALB/cJ, but the 2nd phase was not observed in other strains. Morphological analysis showed that BALB/cJ had the largest islet area and C57BL/6 had the smallest one. These findings indicate that glucose tolerance and non-fasting glucose are better predictors of atherosclerosis than insulin resistance or fasting glucose in Apoe-/- stains.

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THE INFILTRATING MACROPHAGE-SECRETED GALECTIN-3 PLAYS ESSENTIAL ROLE IN PRESSURE OVERLOAD-INDUCED CARDIAC FIBROSIS VIA CTGF EXPRESSION

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Background: Cardiac fibrosis is the major pathophysiological process, contributing to the development of diastolic heart failure. We examine the role of macrophage-derived galectin-3 (gal-3) in cardiac fibrosis in response to transverse aortic constriction (TAC) and elucidate the underlying molecular mechanism.
Method : Wild-type (WT) and gal-3 knock-out (KO) mice subjected to TAC, immunohistochemistry for assessment of myocardial macrophage infiltration,gal-3,and CTGF (connective tissue growth factor) expression, picrosirius and Masson stains for myocardial fibrosis, MTT and Brdu incorporation assays for cell proliferation, flow-cytometry analysis for cell differentiation, co-immunoprecipitation and confocal microscopy for lectin-carbohydrate interaction and co-localization respectively.
Result: WT mice after TAC showed significant increase of myocardial macrophage infiltration, gal-3 and CTGF expression, fibroblast proliferation/differentiation, and interstitial fibrosis, compared with sham-operated animals ($n=10$, $p<0.01$). Macrophage depletion or gal-3 Knock-out markedly suppressed myocardial fibrosis and vice versa. In in-vitro, co-immunoprecipitation and confocal microscopy confirmed gal-3-EGFR interaction and co-localization on cell membrane. Treatment with recombinant gal-3 increased EGFR and downstream ERK phosphorylation, and CTGF expression in cultured cardiac fibroblasts or their gal-3 knock-down cells. Moreover, using MTT and Brdu incorporation assays either direct addition of recombinant gal-3 or co-culture with macrophages significantly promoted cardiac fibroblast proliferation via CTGF expression.
Conclusion: Pressure-overload promotes myocardial macrophage infiltration and the infiltrating macrophage -secreted gal-3 cross-links with its cell surface glycoconjugate, EGFR, resulting in its autophosphorylation, activation of subsequent mitogenic ERK signaling, myocardial CTGF expression, fibroblast proliferation/differentiation and myocardial fibrosis. Our findings provide molecular basis for gal-3 as a potential therapeutic target in heart failure.

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IDENTIFICATION OF ASPIRIN RESPONSE RELATED GENE PROFILES IN CAD PATIENTS OLDER THAN 50 YEARS

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Aims: The phenomenon that responses to aspirin response vary from one patient to another has aroused lots of concern. Recent studies observed that aspirin exposure lead to changes in expression of various genes. The aim of our study was to identify aspirin response related gene profiles, and to investigate the roles of multiple factors in promoting cardiovascular events.
Methods: An observational and prospective study of CAD patients older than 50 years on 100mg/d aspirin were enrolled since January 2014. Hospitalization and follow-up records were collected. Cardiovascular events were defined as the occurrence of myocardial infarction, stroke, cardiovascular death and/or revascularization during regular aspirin therapy. Besides, whole blood samples were collected for further total RNA extraction. Expression of fourteen genes (CLU CMTM5 CTTN MPL TMEM64 SELP HLA-DQA1 HLA-DRB4 ITGA2B ITGB3 THBS1 CXCL5 PPBP SPARC) were measured using real-time quantitative PCR method.
Results: A total of 190 CAD patients older than 50 years were enrolled, with an average age of 77.01± 7.75. HAPR(high on aspirin platelet response) was defined as 0.5 mmol/L AA-induced platelet aggregation ≥15.17%—upper quartile of the enrolled population. Eight genes (MPL HLA-DQA1 HLA-DRB4 ITGA2B CLU CMTM5 SELP SPARC) were differentially expressed in HAPR group. Besides, COX regression analysis showed that previous PCI history, co-morbidities including diabetes and hypertension contributed to the occurrence of cardiovascular events, while statins administration significantly reduce its risk. Expression of ten genes (CTTN ITGB3 CLU THBS1 PPBP SPARC SELP TMEM64 CMTM5 HLA-DQA1) were potential risk factors in predicting future cardiovascular events.
Conclusion: The eight differentially expressed genes in HAPR group might help distinguish patients with poor aspirin responses. Besides, previous PCI history, co-morbidities including diabetes and hypertension contributed to the occurrence of cardiovascular events, while statins administration was proved to be protective. Expression of ten genes might help distinguish high risk CAD patients.

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DUAL AT1 RECEPTOR/NEPRILYSIN INHIBITION (ARNI) VS. AT1 RECEPTOR BLOCKADE IN DIABETIC TGR(MREN2)27 RATS

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The combination of an Angiotensin Receptor blocker (ARB) and a Neprilysin Inhibitor (NEPi) has beneficial effects on clinical progression and mortality of heart failure patients as compared to enalapril. However, since NEP also degrades endothelin-1 (ET-1), ARNI may cause side-effects by increasing ET-1. Indeed, we recently observed in hypertensive TGR(mREN2)27 rats that a low but not a high dose of the NEPi thiorphan reduced blood pressure and cardiac hypertrophy on top of the ARB irbesartan (IRB). This was due to the fact that the high dose increased ET-1, upregulated constrictor vascular ET-1 type B receptors and induced an increase in renal sodium–hydrogen exchanger 3 protein abundance. In the present study, we evaluated the effects of the low thiorphan dose on top of IRB in TGR(mREN2)27 rats, made diabetic with streptozotocin for 5 or 12 weeks. Rats were treated in the final 3 weeks with vehicle, IRB or IRB +thiorphan (ARNI). Haemodynamics were measured by telemetry in the 5-week diabetic animals. In the 12-week diabetic animals vascular reactivity was determined in mesenteric arteries, renal Na+-transporters were analysed by immunoblotting, and plasma and urine were collected for biochemical analysis. Baseline mean arterial blood pressure (MAP) was 157±5 mmHg. IRB and ARNI lowered MAP identically over the 3-week period, a maximum reduction of approximately 50 mmHg being reached around day 7. Heart weight/tibia length ratio was reduced after treatment with ARNI only. Proteinuria and albuminuria were observed from 8 weeks of diabetes onwards and proteinuria was significantly reduced by ARNI treatment only. Urinary volume and plasma and urinary creatinine did not change. No ET-1 rises were observed, vascular reactivity was not influenced, and the pattern of kidney sodium transporters was not affected by ARNI or IRB treatment. Conclusion: ARNI reduces cardiac hypertrophy and proteinuria in diabetic TGR(mREN2)27 rats independently of blood pressure.

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GI PROTEIN AS POTENTIAL TARGET FOR THE TREATMENT OF HYPERTENSION

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Guanine nucleotide regulatory proteins (G proteins) play an important role in the regulation of a variety of physiological functions including blood pressure through the activation of different effectors. We have previously shown an overexpression of inhibitory G proteins (Gialpha proteins) in spontaneously hypertensive rats (SHR) and other models of hypertensive rats. The enhanced expression of Gialpha proteins precedes the development of hypertension in SHR and DOCA-salt hypertensive rats. Treatment of prehypertensive SHR with pertussis toxin that inactivates both Gialpha-2 and Gialpha-3 proteins prevented the development of hypertension in SHR suggesting the implication of enhanced expression of Gialpha proteins in the pathogenesis of hypertension. In the present study, we investigated if both the Gialpha-2 and Gialpha-3 proteins are implicated in the development of hypertension and used the antisense (AS) approach. The knockdown of Gialpha-2 protein by Gialpha-2 AS prevented the development of hypertension up to 6 weeks of age, thereafter it started increasing and reached the same level at 9 weeks as that of untreated SHR. On the other hand, the treatment of SHR with Gialpha-3 AS did not significantly attenuate the increased BP. Furthermore, the levels of Gialpha-2 and Gialpha-3 proteins in heart, kidney and aorta from 6 week-old SHR treated with Gialpha-2-AS and Gialpha-3-AS were significantly decreased compared to control SHR. However, these treatments did not attenuate the increased BP and overexpression of Gialpha-2 and Gialpha-3 proteins in 9 week-old SHR. Furthermore, treatment of prehypertensive SHR with C-ANP4-23; an agonist of natriuretic peptide receptor-C (NPR-C) and resveratrol, attenuated the development of hypertension and overexpression of Gialpha proteins in heart and aorta. These results suggest that Gialpha-2 protein plays an important role in the development of hypertension in SHR and that the new therapies targeting Gialpha proteins may be developed for the treatment of hypertension (Supported by grant from CIHR).

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NEW OUTCOME-BASED RECOMMENDATIONS FOR IMPROVING HYPERTENSION DIAGNOSIS AND TREATMENT TO REDUCE RISK OF VASCULAR EVENTS

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Diagnosis of hypertension and clinical decisions regarding its treatment are typically based upon clinic blood pressure (BP) measurements, occasionally supplemented by wake-time patient self-assessment. Yet, correlation between BP level and target organ damage, cardiovascular disease (CVD) risk, and long-term prognosis is greater for ambulatory BP monitoring (ABPM) than daytime in-clinic measurements. Additionally, consistent evidence of numerous studies substantiates the ABPM-determined asleep BP mean is an independent and stronger predictor of CVD risk than the awake or 24h means. Most importantly, when the asleep BP mean is adjusted by the awake mean, only the former is a significant independent predictor of CVD outcome. The MAPEC Study, first prospective randomized treatment-time investigation testing the worthiness of bedtime hypertension treatment to specifically target attenuation of asleep BP, not only documents the asleep BP mean is the most significant prognostic marker of CVD and stroke morbidity and mortality, but it also substantiates attenuation of the asleep BP mean significantly reduces CVD risk, both in the general hypertension population and in patients of greater vulnerability and enhanced CVD risk, i.e., those diagnosed with chronic kidney disease, diabetes, and resistant hypertension. Preliminary findings from the Hygia Project, a multicenter, prospective, controlled study designed to evaluate the prognostic value of ABPM and that has recruited so far >16,000 subjects who undergo periodic, at least annual, 48h ABPM evaluation, corroborates sleep-time systolic BP mean, but not daytime clinic BP measurement or ABPM-derived awake BP mean, is the only significant and independent prognostic marker of CVD morbidity and mortality. These collective findings indicate: (i) CVD risk assessment should be based on ABPM, mainly of asleep systolic BP, as a new gold standard; and (ii) pharmacologic intervention in hypertension should take into account the variable of treatment-time to properly reduce asleep BP as a novel therapeutic target.

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RESISTANT HYPERTENSION: DIAGNOSTIC AND TREATMENT ISSUES

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By current definition, hypertension is considered resistant to treatment when lifestyle measures plus ingestion of at least 3 hypertension medications, one preferably a diuretic unless contraindicated, in therapeutic doses fail to reduce systolic and diastolic blood pressure (BP) to recommended clinic thresholds. However, published reports document the correlation between BP level and target organ damage, cardiovascular (CVD) risk, and long-term prognosis is far greater for ambulatory BP monitoring (ABPM) than clinical BP measurements. An increasing number of studies document sleep-time BP is abnormally elevated in most patients with resistant hypertension thereby indicating diagnosis of true resistant hypertension cannot be decided solely by comparison of office BP with either wake-time patient BP self-measurements or awake BP mean from ABPM, as so far customary in the published literature. Moreover, the ABPM-determined asleep BP mean is an independent and stronger predictor of CVD risk than either daytime office and ABPM-derived awake or 24h means. Results of the recently completed prospective outcome MAPEC Study that included a large cohort of patients with resistant hypertension, establish treatment time, relative to the rest-activity cycle of each individual patient, constitutes a critically important, yet often neglected, variable regarding BP control; bedtime compared to morning ingestion of the full dose of at least one BP-lowering medications results both in better therapeutic normalization of sleep-time BP and reduced CVD morbidity and mortality, including in patients with resistant hypertension. Collectively, recent findings of the above cited and other prospective studies indicate a bedtime hypertension medication regimen, in conjunction with proper patient evaluation by ABPM to corroborate the diagnosis of true resistant hypertension, should be the therapeutic scheme of choice for patients who, by conventional cuff methods (and in the absence of the application of ABPM) and an inappropriate morning-treatment regimen, may have been mistakenly judged to be resistant to therapy.

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MYOCARDIAL INTERSTITIAL DISARRAY AND CARDIOVASCULAR APOPTOSIS AND REMODELING IN PULMONARY HYPERTENSION DYSPNEA, COMPLICATED WITH LATE INFECTION

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Purpose: The study aims to investigate unknown pathophysiology of myocardial interstitial disarray, arising from Metalloproteinase-2 (MMP-2) activity in Pulmonary Hypertension (PH) dyspnea patients (Pts), correlated with serum Procalcitonin (PCT) levels and other Biomarkers.
Methods: 55 PH dyspnea Pts, 34 males and 21 females (mean age 68±14 years) and 33, matched control, normal individuals, were submitted to 1) Serum evaluation of PCT, MMP-2, Troponin-I (Tr-I), Erythropoietin (EPO) and NT-ProBNP. 2) Clinical, ECG, Chest X-ray and Computed Tomography (CT) examination, 3) Pulmonary Function Tests (PFTs), Arterial Blood Gasses (ABGs) and Blood tests, 4) Echocardiography.
Results: The results Showed: 1)Abnormal serum values of PCT=0.39 ng/ml, MMP-2=376 ng/ml, Tr-I=2 ng/ml, EPO=26 m/U/ml, NT-ProBNP=4.242 pg/ml, 2) Restrictive impairment of pulmonary function tests and hypoxemia with extremely increased alveolo-arterial oxygen difference [P(A-a)0_2]= 49mmHg, 3) Normal ejection fraction (EF), left atrial and right ventricular enlargement (LAD,RVID), RVSP=52 mmHg, 4) Primary significant correlation of MMP-2 with a) PCT (r=0.630), b) Tr-I (r=0.390), c) EPO (r=-0.340), d) PCO_2(r=0.340), and e) NT-ProBNP (r=0.310), 5) Statistical correlations of any significance were not confirmed with ABGs, excluding PCO_2.
Conclusions: We conclude that: 1) Serum MMP-2 activity on the grounds of PH dyspnea is obviously leading to myocardial interstitial disarray, arising mainly from the related serum PCT presence, expressing original contribution of an infective reaction pathophysiology. 2) The related serum Tr-I, EPO and NT-ProBNP values indicate existence of myocardial cell apoptosis and congestive remodeling, due to PH of cardiac origin, possibly co-induced from PCT infective reaction, 3) However, the infection related PCO_2 levels looks contributing to myocardial interstitial fibrosis, further possibly connecting with inflammation and Thrombogenesis, 4) PFTs and the rest of ABGs do not seem correlated with infection induced pathophysiology of MMP-2 activity in PH dyspnea.

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ADVANCES IN THE THERAPY OF PULMONARY ARTERIAL HYPERTENSION

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Pulmonary arterial hypertension is a group of diseases, probably with a genetic predisposition and possibly an environmental trigger, leading to elevated pulmonary arterial tree resistance, right heart failure, and a generally poor prognosis. Since the development of intravenous epoprostenol as the first approved therapy for pulmonary arterial hypertension, multiple agents have been and are being investigated. Based on the pathophysiology of the disease(s), therapies have been developed that affect the three main pathways believed responsible for arterial vasodilation: the endothelin pathway, the nitric acid pathway, and the prostaglandin pathway. These drugs act largely by stimulating receptors leading to vasodilation, blocking receptors that lead to vasoconstriction, and/or lessen vessel wall cell wall proliferation. Work is also done on compounds that may reduce vessel wall inflammation in these diseases. These medical therapies include oral, transdermal, inhaled, and intravenous delivery options. For some, the combination of these therapies may have the capability to transform the lives of our patients from that with a poor prognosis and the need for the continuous or frequently administered therapy, to a life with an almost "forgettable" disease, at least in terms of day to day activities.

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PROGNOSTIC STRATIFICATION IN PULMONARY HYPERTENSION: A MULTI-BIOMARKER APPROACH

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Introduction: Pulmonary hypertension (PH) is associated with an increase in pulmonary vascular resistance leading to right ventricular failure. Risk stratification is crucial for adequate prognostic and therapeutic assessment. However, the accuracy of the conventional parameters is limited, specially regarding to biomarkers.
Objectives: Determine the prognostic value of new biomarkers and their combination in a multibiomarker approach to predict outcome in patients with PH.
Methods: Prospective cohort study of patients with PH. Patients underwent clinical, echocardiographic and laboratory evaluation, including quantification of serum NT-proBNP and the following new biomarkers: MR-proADM, copeptin, endothelin-1, MR-proANP and soluble interleukin-33 receptor (ST2). The accuracy of different parameters in the prediction of death from any cause and death or hospitalization for cardiac causes was determined. The prognostic value of a multibiomarker score based on the tertile distribution of serum NT-proBNP, MR-proANP, renin and ST2 was tested.
Results: Forty-three patients (72.1% female; 59±15 years) were included. Most patients (65.1%) had group 1 PH. During a median follow-up of 34 months, 26% of patients died and 35% were hospitalized for cardiac causes. NT-proBNP (log) [HR: 31.14; 95% CI: 3.12 to 310.7; P=0.003)] and renin (HR: 1.02; 95% CI: 1.005 to 1.038; P=0.009) were independent predictors of mortality. MR-proANP (HR: 1.008; 95% CI 1.004 to 1.011; P <0.001) and ST2 (HR: 1.005; 95% CI 1.001 to 1.009; P = 0.04) were predictors of death or hospitalization. The prognostic value of the multibiomarker score was higher than any of the conventional parameters, allowing the identification of risk groups (high risk group with a mortality at 3 years of 77.8%).
Conclusion: a multibiomarker strategy provided superior risk stratification beyond any single-marker approach. The score that incorporates NT-proBNP, MR-proANP, renin and ST2 accurately identifies patients with low, intermediate and high risk.

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MORTALITY IS HIGHER BUT NOT DIFFERENT AMONG RESISTANT HYPERTENSION PATIENT COHORTS DEFINED BY DIFFERENT CRITERIA

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Background: The implications of the use of different definitions for resistant hypertension on survival outcomes have not been fully determined.
Purpose: To compare survival among cohorts of resistant hypertension patients defined by current working definitions.
Methods: Using hypertension medications from outpatient visits notes in 2009, 2 cohorts of resistant hypertension patients were built using current definitions. Patients with BP 140 over 90 mmHg and above despite a 3 drug regimen including a diuretic were classified as uHTN and those on 4 or more hypertension drugs to maintain BP control were labelled as cHTN. The two groups were compared with known patients with hypertension (kHTN).
Results: Survival at 4 years was 79.1% with 317 deaths and 1169 censored patients, (unadjusted hazard ratio HR 3.29, p<0.0001) in the uHTN cohort and 78.8 % with 356 deaths, 1274 censored patients (HR 3.33, p<0.0001) in the cHTN group compared to 93.3% in the kHTN cohort with 665 deaths and 8341 censored patients. After adjusting for age, sex, atrial fibrillation/flutter, heart failure, CKD, CAD, acute myocardial infarction, stroke, obesity, diabetes, sleep apnea and pulmonary hypertension, HR was 1.83, p<0.0001 for uHTN and 1.66, p<0.0001 for cHTN compared to the kHTN group. There was no difference in survival between the uHTN and cHTN cohorts (unadjusted HR 0.99, p<0.89) although cardiovascular comorbidities were more prevalent in the cHTN group.
Conclusion: Although survival was worse resistant hypertension patients compared to known hypertension patients, there was no apparent difference among the 2 cohorts of resistant hypertension as defined by contemporary criteria.

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LEFT ATRIAL ENLARGEMENT AS A PREDICTOR OF PULMONARY HYPERTENSION IN PATIENTS WITH DIASTOLIC DYSFUNCTION

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Background: Pulmonary Hypertension (PH) is a frequent complication of left heart disease. The development of PH in patients with left heart disease is associated with poor prognosis. Objective: To investigate predictive factors for PH in patients with diastolic dysfunction (DD).
Methods: We retrospectively analyzed echocardiograms of 1,584 patients performed at a University hospital. Patients were classified into normal (n=529, 33.4%) & those with DD (n=1055, 66.7%), including Impaired Relaxation (IR, n=869, 54.9%), Pseudonormal (PN, n=161, 10.2%), & Restrictive pattern (Res, n=25, 1.6%). To investigate predictive factors for PH (RVSP>40) in patients with diastolic dysfunction (DD).
Results: In patients with DD, we found 17.4% with PH vs 82.7% with no PH p<0.0001. The presence of PH is more frequent in IR (55.8%) vs control (24.9%), but not for the two higher levels of DD (15.4% & 4.0%, respectively). There is a significant difference in presence of PH among the levels of DDX severity, with the highest being 40% for DDX=3, and decreasing for each lower level (29.2% for DDX=2, 14.5% for DDX=1 and 9.8% for DDX=0). In the multivariate (logistic regression) analysis, we examined LA volume (or LA index), Pro BNP and DD as predictors for Pulm HTN(RVSP>40). LA volume is a predictor for Pulm HTN (RVSP) with an OR=1.020, 95% CI=1.012-1.028, p<0.0001. Also LA volume is associated with Pulm HTN in patients with Pseudonormal DD (stage 2) vs control (OR=1.016, 95%CI=1.008-1.025, p<0.0001).
Conclusions: In patients with PH adjusting for Pro BNP and DD, LA enlargement can be a predictor factor for development of PH.

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PREVALENCE OF HYPERTENSION AND DIFFERENCE OF BLOOD PRESSURE CONTROL BETWEEN METABOLICALLY OBESE NORMAL BODY WEIGHT (MONW) AND METABOLICALLY HEALTHY OBESE BODY WEIGHT (MHO) IN HIV POPULATION

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Objective: The aim of this study is to identify the prevalence of hypertension in these two groups of HIV-infected patients as well as to investigate the relative success of blood pressure control, in a community hospital in East Harlem, New York.
Background: Research has shown that HIV patients can become metabolically unhealthy and/or obese just as other non-HIV infected patients, but also secondary to their illness or and/or its treatment. However, the prevalence of hypertension and its control in MONW and MHO HIV-infected patients has until now not been systematically studied.
Methods: 472 HIV patients were identified in the registry of Metropolitan Hospital Center from January, 2012 to December 2014. Retained cases were assigned to either the metabolically-obese-normal-weight (MONW) group or the metabolically-healthy-obese (MHO) group as defined by the National Cholesterol Education Program–Adult Treatment Panel (NCEP–ATP) III definition of metabolic syndrome. We applied the JNC 8 Hypertension blood pressure guidelines. All data were analyzed using SAS Ver. 9.4.
Results: 466 patients were included in the study. Normal weight group was 36.1%, overweight group was 34.2% and obese group was 29.7%. Prevalence of hypertension was 33.3% among MONW and 5.7% among MHO. Mean systolic blood pressure was 129.1±18 mmHg and diastolic blood pressure was 76.9±10 mmHg in MONW, 118.1±13 mmHg and 70.1±9.8 mmHg in MHO. MONW cases showed statistically non-random associations with uncontrolled blood pressure as compared to MHO cases [Odds ratio (OR): 0.018, 95% Confidence Interval (CI): 0.003-0.119]. Female sex [OR: 6.5, 95% CI: 1.447-29.208] and high LDL [OR: 6.08, 95% CI 1.148-32.245] was found to be the risk factors for uncontrolled blood pressure for both groups.
Conclusions: MONW HIV patients are more prone to uncontrolled blood pressure and require more intensive blood pressure management and strategies to diminish cardiovascular complications than MHO HIV patients.

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LONG-TERM EFFECTS OF ISCHEMIC POSTCONDITIONING ON CLINICAL OUTCOMES

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Background: In the Effects of Postconditioning on Myocardial Reperfusion in Patients with ST-segment Elevation Myocardial Infarction (POST) trial, ischemic postconditioning failed to improve myocardial reperfusion. However, long-term effects of ischemic postconditioning on clinical outcomes are not known in patients with ST-segment elevation myocardial infarction (STEMI).
Methods: A total of 700 patients undergoing primary percutaneous coronary intervention (PCI) were randomly assigned to the postconditioning group or the conventional primary PCI group in a 1:1 ratio. Postconditioning was performed immediately after restoration of coronary flow by balloon occlusion 4 times for 1 minute. Complete follow-up data for major clinical events at 1 year were available in 695 patients (99.3%) and analyses were done by the intention-to-treat principle. The primary outcome was a composite of death, myocardial infarction, severe heart failure, or stent thrombosis at 1 year.
Results: At 1 year, a composite of death, myocardial infarction, severe heart failure, or stent thrombosis occurred in 21 patients (6.1%) in the postconditioning group and 16 patients (4.6%) in the conventional PCI group (hazard ratio [HR] 1.32; 95% confidence interval [CI] 0.69–2.53; P=.40). The risk of death (4.9% versus 3.7%; HR 1.32; 95% CI 0.64–2.71; P=.46), heart failure (2.6% versus 2.3%; HR 1.13; 95% CI 0.44–2.94; P=.80), and stent thrombosis (2.3% versus 1.7%; HR 1.34; 95% CI 0.46–3.85; P=0.59) did not differ significantly between the 2 groups.
Conclusions: Ischemic postconditioning does not seem to improve the 1-year clinical outcomes in patients with STEMI undergoing primary PCI.

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ELECTROCARDIOGRAPHIC LEFT ATRIAL ENLARGEMENT AS AN INDEPENDENT PREDICTOR FOR IN-HOSPITAL HEART FAILURE IN PATIENTS WITH NON-ST ELEVATION MYOCARDIAL INFARCTION

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Background: Electrocardiographic left atrial enlargement is frequently observed in various cardiovascular diseases. Enlarged left atrial determined by echocardiography has been shown to predict adverse cardiovascular events. However little is known about the prevalence and prognostic value of electrocardiographic left atrial enlargement among patient with Non-ST Elevation Myocardial Infarction.
Methods: We performed a retrospective analysis of 481 consecutive patients with NSTEMI who underwent coronary angiography. Patients with atrial fibrillation and atrial-paced rhythm were excluded. Enlarged left atrial on the electrocardiogram was defined as either P-wave duration>120ms in 2 lead or P-terminal force in lead V1>40ms•mm. Baseline and angiographic characteristics, in-hospital heart failure as well as in-hospital major adverse cardiac event (MACE) including death, recurrent myocardial infarction, and target vessel revascularization were compared between the two groups.
Results: Among 452 patients, 142 patients (31.4%) had electrocardiographic left atrial enlargement. There was no significant difference in age, or in the rate of history of previous myocardial infarction or previous revascularization procedures between patients with and without electrocardiographic left atrial enlargement. Patients with electrocardiographic left enlargement had a higher left ventricular end-diastolic pressure (LVEDP) (20 [14-27] mmHg vs. 18 [14-23] mmHg, p=0.037) and a lower left ventricular ejection fraction (LVEF) (55% [37-60] vs. 60% [45-65], p=0.013). Patients with electrocardiographic left atrial enlargement had a higher incidence of in-hospital heart failure (28.9% vs. 9.0%, p<0.001). There was no significant difference in the rate of in-hospital MACE between the two groups. By multivariable analysis, electrocardiographic left atrial enlargement was an independent predictor of in-hospital heart failure after adjusting for age, LVEDP and LVEF (odds ration 4.1; 95% confidence interval 1.88 to 9.02; p<0.001).
Conclusion: Electrocardiographic enlarged left atrial was associated with lower LVEF and higher LVEDP in patients with NSTEMI. By multivariate analysis, electrocardiographic enlarged left atrial was an independent predictor of in-hospital heart failure.

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COMPLETE REVASCULARIZATION IN ACUTE MYOCARDIAL INFARCTION IS SAFE AND WITHOUT MORE REINTERVENTIONS: STRATEGY DEFERRED VS. INDEX PROCEDURE

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Introduction: Forty percent of patients treated with primary angioplasty (PCI) have multi vessel disease (MVD) an independent mortality predictor. It is reported that during an acute coronary syndrome (ACS), a diffuse inflammatory process in which multiple plaques with complicated atheroma takes place.
Objective: To analyze clinical outcomes of complete deferred revascularization (during the same hospitalization or within 30 days) vs. the index procedure in PCI.
Method: Population: From May 2000 to December 2014, 374 consecutive pts with AMI were treated, 189 of whom had MVD. Same session CR was done in 58 pts (group A), while deferred CR in 35 pts (group B). Baseline characteristics: mean age 58 ± 11 vs 57 ± 9 years, diabetes 15 (29%) vs 7 (20%); previous infarction 6 (10) vs 6 (17); Killip Kimball C - D 9(15) vs 1(3) p=0.08; IIbIIIa using 3(5) vs 9(26) p= 0.008; door to balloon time 110±60 vs 107±59 minutes; anterior descending artery unrelated to infarction 21(36) vs 1(3) p=0.0001; initial TIMI 0 32(55) vs 21(60); DES 10(17) vs 6(17); thromboaspiration 4(7) vs 6(17), radial access 21(36) vs 16(46), fluoroscopy time 19.2±15 vs. 16.9±13 minutes; dye material 267.3±91 vs 236±98 milliliters.
Results: In-hospital: final TIMI III 58(100) vs 31(88) p=0.03, blush TIMI 3 final 52(90) vs 30(85) p=0.8; cardiac death 2(3) vs 0 p=0.5; reinfarction 1(2) vs 0 p=0.7. At follow-up 18 ± 21.8 vs 23.9 ± 18 months cardiovascular death 0 vs 1(3) p=0.3; reinfarction 2(4) vs 2(6) p=0.6, rePCI novo lesions 3 (7) vs 2(6) p=1 and restenosis rePCI 2(4) vs. 3(8) p=0.3.
Conclusion: In our practice, we try to implement early CR in AMI. This "aggressive" strategy showed no increased clinical risk for patients without penalizing with more re-interventions at follow up.

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FIXED DOSING OF UNFRACTIONATED HEPARIN IN ST-ELEVATION MYOCARDIAL INFARCTION TO IMPROVE DOOR-TO-PCI TIME

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Background: Weight based unfractionated heparin (UFH) dosing is used as initial therapy for ST-elevation myocardial infarction (STEMI).
Objectives: We evaluated the effects of using a fixed dose UFH dose in patients undergoing primary percutaneous coronary intervention (PCI) for STEMI.
Methods: We analyzed 270 consecutive patients that underwent primary PCI for STEMI. Patients were given 4000 IU of UFH on presentation. The use of bivalirudin, additional UFH and glycoprotein IIb/IIIa inhibitor (GPI) was at operator discretion. Patients were reclassified based on weight based dose: Group 1 (< 50 U/kg), Group 2 (50-70 U/kg), and Group 3 (> 70 U/kg). Primary outcomes were the 30-day rate of death, myocardial infarction, stent thrombosis, TIMI major bleeding and a composite end point of major adverse composite events (MACE).
Results: There was no significant difference in MACE after adjusting for confounding variables using logistic regression analysis by age, gender, diabetes, hyperlipidemia or bivalirudin use (Table 1).
Conclusions: Standardized heparin dosing resulted in an door-to-PCI time of 52 minutes. There was no difference in adverse outcomes when analyzed for weight. Utilizing a simplified fixed heparin dose allows for significantly shorter reperfusion times without compromising clinical outcomes.

Table 1. Patient Demographics & Clinical Outcomes

	Group 1 (N=164)	Group 2 (N=88)	Group 3 (N=16)	P value
Age (years)	58 ± 12	64 ± 13	70 ± 13	<0.0001
Male	134 (81.7%)	56 (63.6%)	3 (18.8%)	<0.0001
Diabetes	48 (29.3%)	13 (14.8%)	4 (25%)	0.03
HTN	116 (70.7%)	56 (63.6%)	12 (75%)	0.43
Smoking	83 (50.6%)	36 (40.9%)	8 (50%)	0.33
Hyperlipidemia	105 (64%)	51 (58%)	15 (93.8%)	0.02
Bivalirudin	81 (49.4%)	26 (29.5%)	2 (12.5%)	<0.001
GPI use	63 (38.4%)	42 (47.7%)	8 (50%)	0.29
Outcomes				
Myocardial Infarction	3 (1.8%)	0	0	0.38
Stent thrombosis	5 (3%)	0	0	0.19
Death	7 (4.3%)	2 (2.3%)	2 (12.5%)	0.16
TIMI Major Bleeding	2 (1.2%)	0	0	0.52
Cardiovascular Death	6 (3.7%)	2 (2.3%)	1 (6.2%)	0.67
MACE	13 (7.9%)	2 (2.3%)	2 (12.5%)	0.12
Door to PCI time (min)	52.1 ± 17.6	52.5 ± 15.6	50.6 ± 19.3	0.92

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EARLY VERSUS DELAYED INVASIVE STRATEGY FOR NON-ST SEGMENT ELEVATION ACUTE CORONARY SYNDROME: A META-ANALYSIS OF RANDOMIZED CONTROLLED CLINICAL TRIALS

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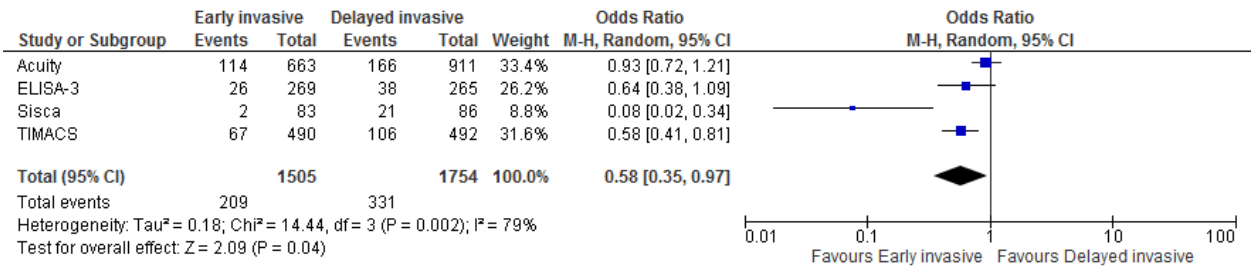
Objective: To compare early versus delayed invasive strategy in high risk patients with Non-ST segment elevation acute coronary syndrome (NSTE-ACS).
Background: Some early trials showed a benefit of early PCI in patients with non ST segment elevation acute coronary syndrome(NSTE-ACS) but later on bigger randomized controlled trials did not indicate clear benefit of early percutaneous coronary intervention (PCI) (<24 hours) in patients with (NSTE-ACS) as compared to delayed PCI(>24 hours). Nonetheless recent data suggests benefit of early PCI in high risk NSTE-ACS patients. We put together existing data and performed meta-analysis.
Methods: Medline, PubMed and abstracts from major cardiology conferences were searched. Randomized control trials (RCTs) comparing the composite of death and/or myocardial infarctions (MI) and/or repeat revascularization within 6 months of early or delayed PCI for high risk patients with NSTE-ACS were included. High risk was defined as TIMI score >5 or GRACE score >140. The effects of both methods were analyzed by calculating pooled estimates for death, MI and repeat revascularization. Analyses were performed for the outcome by using odds ratio (OR) by random effects model. Heterogeneity among studies was assessed by calculating I″ measure of inconsistency.
Results: We merged the data from four studies (ACUITY, ELISA-3, TIMACS and SISCA). Total of 3259 patients who met our inclusion criteria were included. The incidence of the composite of death and/or MI and/or repeat revascularization was lower in early PCI group [209/1505(13.8%)] delayed PCI [331/1754(18.8%)] (OR 0.58 CI-0.35-0.97, P=0.002)
Conclusion: Contrary to the previous meta-analysis, our results indicate that early invasive strategy (<24 hours) in high risk patients with TIMI>5 or Grace >140 does reduce the incidence of the composite of death and and/or MI and/or repeat revascularization within 6 months.



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IMPROVING SURVIVAL AFTER TREATMENT FOR ST-ELEVATION MYOCARDIAL INFARCTION - A 16 YEAR JOURNEY FROM 1997 TO 2013

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Objectives and Background: There have been major changes in the evidence based treatment of ST-elevation myocardial infarction (STEMI) over the last 20 years including direct percutaneous intervention (DPCI). But do the improved outcomes demonstrated in clinical trials also occur in all-comer clinical populations?

Methods: Retrospective audit of STEMI patients admitted to our Department from Oct 1 through Dec 31 in 1997-2002, 2006, 2010 and 2013. Baseline characteristics, in-hospital investigations, discharge medications and one year outcomes were compared between years.

Results: In 2013, there were 59 STEMI patients, median age was 67 years, 76% men, 25% current smokers, 22% had diabetes and 19% had previous MI. DPCI was performed in 51(86%): of the other 8 patients, 3 presented >24 hours after onset of symptoms and 2 received PCI before discharge, 1 refused DPCI, 2 had extensive co-morbidities, and the diagnosis was missed in 2 but both received PCI before discharge. DPCI rates were 78% in 2010, 67% in 2006, 22% in 2001/02 and 7% in 1997/98. One year after discharge, Death or Death/Myocardial infarction occurred in 7.4% and 9.3% in the 2013 cohort compared with 8.8% and 10.3% in 2010, 10% and 12% in 2006, 13% and 18% in 2001/02 and 18% and 24% in 1997/98, $p<0.01$, chi-square.

Conclusion: Between 1997 and 2013, increased use of DPCI and evidence based medications have resulted in an 11% absolute increase in survival and a 25% absolute increase in survival free from repeat myocardial infarction one year after STEMI.

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CONTEMPORARY TROPONIN USE IN A LARGE US HOSPITAL SYSTEM

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Background: Troponin measurement is integral to the diagnosis of acute coronary syndromes (ACS). Current guidelines recommend assessing troponin in patients with possible ACS followed by serial measurement if the initial value is normal. We sought to assess current clinical utilization of Troponin in a large Hospital system.
Methods: All encounters for which troponin was assayed were recorded from 13 Hospitals in a large US healthcare system from June 2013 to June 2014. When available, each Troponin value was associated with a primary encounter diagnosis.
Results: Troponin was assayed in a total of 98,811 patient encounters. Primary diagnoses were available for 93,436 encounters. There were 179,239 Troponin measurements, an average of 1.81 per encounter. 147,051 (82.1%) measurements were considered normal. However, 59,897 (33.4%) of normal Troponins were not followed by serial measurements. 21% of encounters had a possible ACS diagnosis. Positive troponins were found in 8% of these encounters. There was significant heterogeneity in Troponin values in the remaining 79% of patient encounters. No positive troponins were found in encounters associated with primary diagnoses of Hypertension, Dizziness, Abdominal Pain, Anxiety, Dehydration and Headache (6127 total encounters). Several primary encounter diagnoses, however, where associated with higher rates of positive troponins than were associated with a primary diagnosis of ACS, including CVA (10% of 865), septicemia (26% of 1976) and acute respiratory failure (28% of 626).
Conclusion: We find evidence that troponin measurement in practice deviates significantly from current guidelines and is often positive in clinical scenarios unlikely to represent ACS.

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DOES THROMBUS ASPIRATION IMPROVE CLINICAL OUTCOMES IN ST ELEVATION MYOCARDIAL INFARCTION?

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Introduction: Multiple studies including TAPAS trial suggested improved 1-year cardiac outcomes, resulting in a guideline recommendation and substantial increase in routine thrombectomy utilization. On the contrary, TASTE and TOTAL trials have been negative. We sought to investigate this controversy by evaluating STEMI clinical outcomes with thrombectomy utilization in real world patient population at our community hospital.
Aim: To compare 90 day rehospitalization and repeat revascularization rates with routine thrombus aspiration before angioplasty compared to angioplasty alone in patients presenting with ST elevation myocardial infarction.
Methods: Retrospective chart review of 100 consecutive patients above age of 18 years with diagnosis of STEMI between 1/2013-1/2014 at our center was performed. We compared 90 day rehospitalization and revascularization rates in patients who underwent thrombectomy followed by angioplasty to angioplasty alone.
Results: No significant demographic differences were seen between the two groups. Of the 100 patients included in this study, 60 patients had angioplasty alone and 40 patients had thrombectomy followed by angioplasty. There was no significant difference observed in the 90 day rehospitalization rate in the two groups. 90 day repeat revascularization rates were also similar in the two groups. These differences persisted at different levels of thrombus grades seen during the index coronary angiography.
Conclusion: Our study revealed no difference in rehospitalization and repeat revascularization rates with utilization of thrombus aspiration in STEMI patient population at our hospital. Our study is a single center study and results are hypothesis generating.

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IN VIVO PROTEASE-ACTIVATED RECEPTOR -1 MEDIATED CORONARY VASOREACTIVITY CORRELATES WITH PAR-1 EXPRESSION DISTRIBUTION IN THE CORONARY VASCULAR WALL

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In humans, in vivo Protease Activated Receptor -1 (PAR-1) activation increases forearm blood flow, however, the in vivo effects of PAR-1 activation on coronary vascular tone in any species is unknown. Therefore we conducted a study evaluating the in vivo effects of PAR-1 activation in the canine and porcine coronary vasculature. To study the in vivo effects of canine PAR-1 agonist peptides on the canine coronary vasculature, we first established the effects on canine platelets and in isolated canine coronary microvascular endothelial cells (CCAMECs). PAR-1 agonist peptide failed to activate canine platelets, but dose-dependently increased intracellular calcium levels in CCAMECs. To examine the in vivo PAR-1 response, PAR-1 agonist peptide was infused into canine and porcine coronaries and coronary diameters were measured and coronary blood flow (CBF) and coronary vascular resistance (CVR) were calculated from doppler-derived velocities. Intracoronary infusion of PAR-1 agonist peptide caused a dose-dependent statistically significant decrease in coronary diameter in the canine accompanied by a statistically significant decrease in CBF and an increase in CVR. In contrast, in vivo administration of PAR-1 agonist peptide in the porcine coronary vasculature increased CBF and decreased CVR. Immunostaining of coronary arteries demonstrated that PAR-1 expression is more highly expressed in the media of the vascular wall in the canine, while largely limited to the coronary endothelium in the porcine. In conclusion, in vivo PAR-1 agonist peptide resulted in platelet-independent vasoconstriction of both canine epicardial coronary arteries and the canine coronary microvasculature. In contrast, PAR-1- agonist peptide vasodilated the porcine coronary microvasculature. The difference in vasoreactivity between the species correlates with the expression pattern of PAR-1 in the coronary vascular wall. These results describing the off-target platelet effects of PAR-1 activation on the coronary vasculature may partly explain the discrepant results observed with PAR-1 antagonism observed in clinical trials.

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EXTRACELLULAR HSP27 AND TLR4 ATTENUATE FUNCTIONAL RECOVERY IN AGING MOUSE HEARTS FOLLOWING ISCHEMIA

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Objectives: The aim of this study was to determine the role of extracellular heat shock protein (HSP) 27 and Toll-like receptors (TLRs) in cytokine production and functional injury caused by ex vivo global ischemia/reperfusion (I/R) in aging hearts.
Background: While cardiac functional recovery is poor in the elderly following cardiac surgery with obligatory global myocardial I/R, the underlying mechanism remains incompletely understood. We found recently that human and mouse myocardium releases HSP27 during global I/R, and extracellular HSP27 plays a role in post-ischemic inflammatory response in adult mouse hearts.
Methods and Results: Isolated hearts from aging (18-24 months) and adult (4-6 months) mice were perfused by the Langendorff system and subjected to global normothermic I/R (20 min/120 min). Augmented release of HSP27 in aging hearts preceded greater production of cytokines (MCP-1, KC, IL-6 and TNF-alpha) and worse functional recovery. Anti-HSP27 suppressed the inflammatory response and markedly improved functional recovery in aging hearts. Perfusion of recombinant HSP27 to aging hearts resulted in greater cytokine production and contractile depression. TLR2 KO and TLR4 deficiency, particularly the latter, markedly reduced cytokine production and contractile dysfunction in aging hearts exposed to recombinant HSP27. Interestingly, aging hearts had higher TLR4 protein levels and displayed enhanced TLR4-mediated NF-kappaB activation.
Conclusion: The enhanced myocardial inflammatory response to global I/R in aging mouse hearts is due, at least in part, to augmented myocardial release of HSP27. Extracellular HSP27 up-regulates myocardial cytokine production and depresses cardiac contractility through TLR2 and TLR4. Augmented HSP27 release and elevated myocardial TLR4 levels jointly play an important role in the enhanced inflammatory response and worse post-ischemic functional recovery in aging hearts.

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VASONATRINPEPTIDE ATTENUATES MYOCARDIAL ISCHEMIA/REPERFUSION INJURY IN DIABETIC RATS AND UNDERLYING MECHANISMS

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Objectives: This study was designed to investigate the effects of the artificial synthetic natriuretic peptide − vasonatrin peptide (VNP) on myocardial ischemia/reperfusion (MI/R) injury in diabetic rats and its mechanisms.
Background: Diabetes mellitus (DM) increases morbidity/mortality of ischemic heart disease. Although the ability of the natriuretic peptides to modulate cardiac function and cell proliferation has already been recognized, their effects on MI/R injury, especially in diabetic state, is still unclear.
Methods: The high-fat diet-fed streptozotocin induced diabetic rats were subjected to MI/R (30 min/4 h) and VNP treatment (100 μg/kg, i.v., 10 min before R).
Results: The diabetic state aggravated MI/R injury and showed more severe myocardial functional impairment than normal state. VNP treatment significantly improved ± LV dP/dt_{max} and LVSP, and decreased infarct size, apoptosis index, caspase-3 activity, serum CK and LDH levels. Moreover, VNP inhibited endoplasmic reticulum (ER) stress by suppressing GRP78 and CHOP, and consequently increased the antiapoptotic protein Akt and ERK1/2 expression and phosphorylation levels. These effects were mimicked by 8-Br-cGMP, a cGMP analogue, whereas inhibited by KT-5823, the selective inhibitor of PKG. Pretreated DM rats with TUDCA, a specific inhibitor of ER stress, couldn't promote the VNP's cardioprotection. In additional experiments H9c2 cardiomyocytes were subjected to hypoxia/reoxygenation and incubated with or without VNP. Gene knockdown of PKG1α with siRNA blunted VNP's inhibition of ER stress and apoptosis, while overexpression of PKG1α resulted in significant decreased ER stress and apoptosis.
Conclusions: VNP protects diabetic heart against MI/R injury by inhibiting ER stress via cGMP-PKG signaling pathway.

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CTRP1 OVEREXPRESSION INDUCES HYPERTENSION THROUGH SMOOTH MUSCLE CONTRACTION

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We previously reported that CTRP1 stimulates aldosterone production by upregulating the transcription of cytochrome P-450 11beta-hydroxylase 2 (Cyp11b2), which is a rate-limiting enzyme for aldosterone production. Because the previous study was performed in vitro, here, the physiological role of CTRP1 in blood pressure (BP) regulation was investigated in vivo.CTRP1 transgenic (TG) mice showed a hypertensive phenotype without changes to cardiac, vascular, and renal structures and hypertensive patients showed a significant increase in circulating CTRP1 levels. CTRP1 treatment significantly increased the contracting force in the aortic ring. In MOVAS cells, CTRP1 activated the Rho/Rho kinase (ROCK) pathway, thereby leading to increased myosin light chain (MLC) phosphorylation and intracellular Ca2+ levels. On the other hand, hypertension was rescued in CTRP1 TG mice by the administration of inhibitors of renin (ramipril), angiotensin-converting enzyme (nifedipine), angiotensin II receptor 1 (AT1R; losartan), and aldosterone receptor (spironolactone). CTRP1 did not bind to AT1R; instead, CTRP1 induced AT1R membrane localization. To identify factors that induce CTRP1 production, WT mice were treated with various stressors; mice treated with acute electric foot shock showed elevated circulating CTRP1 levels and increased BP. CTRP1 induces vasoconstriction by increasing intracellular Ca2+ levels and inducing AT1R trafficking to the plasma membrane. Acute psychological stress also increases circulating CTRP1 levels, indicating the potential role of CTRP1 as a novel stress-mediated vasoconstrictor. Thus, CTRP1 could be a novel therapeutic target for the development of anti-hypertensive drugs.

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ACETYLCHOLINE REDUCES INFLAMMATORY AND ISCHEMIC INJURY BY INHIBITING ENDOPLASMIC RETICULUM STRESS

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Background: Endoplasmic reticulum (ER) stress plays an important role in regulation of protein homeostasis and cell death. Acetylcholine (ACh), the neurotransmitter of vagal nerve, exerts beneficial effect in cardiovascular diseases. However, little information is available on the influence of ACh on ER stress.
Objectives: This study was designed to evaluate the effect of ACh on ER stress in response to inflammatory and ischemic injury.
Methods: Using models of tumor necrosis factor alpha (TNF-alpha)-stimulated H9c2 cells and hypoxia/reoxygenation (H/R)-injured endothelial cells, we examined the protein changes of ER stress sensors by western blot. Cell apoptosis was shown by TUNEL. The structure of ER was analyzed with transmission electron microscopy.
Results: Our results showed that (1) TNF-alpha stimulation increased index of ER stress (GRP78, CHOP) and TUNEL positive cells in H9c2 cardiomyocytes, which was prevented by ACh. The salutary effects of ACh were blocked by epidermal growth factor receptor (EGFR)/muscarinic ACh receptor-2 (M2AChR) siRNA, indicating that EGFR/M2AChR pathway may be involved in the benefits of ACh in cardiomyocytes. (2) In endothelial cells, ACh reduced H/R-induced ER stress, cell apoptosis as well as ER ultrastructural changes. M3AChR/AMP-activated protein kinase (AMPK) siRNA diminished the attenuation of GRP78, CHOP and cleaved-caspase-12 expression elicited by ACh. ACh-induced endothelial protection may be attributed to the up-regulation of M3AChR activated AMPK signaling.
Conclusion: ACh inhibited ER stress and protected cardiomyocytes and endothelial cells through muscarinic receptor-mediated signaling cascades in inflammatory and ischemic injury, suggesting that inhibition of ER stress may be a novel mechanism underlying ACh-induced cardiovascular protection.
ischemic injury.
Supported by: grant from National Natural Science Foundation of China (Major International Joint Research Project, No. 81120108002; General Project, No. 81473203), Specialized Research Fund for the Doctoral Program of Higher Education (No. 20130201130008).

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ROLE OF AMP-ACTIVATED PROTEIN KINASE (AMPK) IN VASCULAR ENDOTHELIAL PROTECTION

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Background: Adenosine monophosphate-activated protein kinase (AMPK), although known for its role in regulating cellular metabolism, has recently emerged as an important kinase involved in vascular endothelial protection. We noted it to have similar actions as those of MnSOD, HO-1 and DAF, genes that protect the endothelium from inflammatory and oxidative stress, and so we investigated whether AMPK's cytoprotective activity includes the induction of these genes and explored the signalling pathways that may be involved.
Methods: Human umbilical vein endothelial cells first underwent a flow perfusion assay. They were then treated with AICAR (an AMPK activator), for 24 hours, AMPK adenovirus (Ad CA-AMPK) for 18 hours or the combination of atorvastatin and rapamycin for 2 hours and either immunoblotted for various proteins or analysed via flow cytometry. Transcription factor CREB was silenced using siRNA.
Results: In this study we showed that oscillatory shear stress may be responsible for down-regulating levels of phospho-AMPK and HO-1. Cells treated with AICAR had a significant increase in MnSOD, HO-1 and DAF protein expression. Ad CA-AMPK was shown to deliver active forms of AMPK into the cells and infection of this adenovirus also up-regulated the levels of MnSOD, HO-1 and DAF. We also showed that AMPK activates CREB. Our results suggest that depletion of CREB with siRNA reduces MnSOD protein induction by Ad CA-AMPK.
Conclusion: We showed that AMPK activation induces the cytoprotective genes MnSOD, HO-1 and for the first time, DAF. We have also suggested that CREB may be involved in the pathway for AMPK-dependent induction of MnSOD and that AMPK activation may be a future therapy target.

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THE PROTECTIVE EFFECTS OF CATECHIN ON PALMITIC ACID -INDUCED CYTOTOXICITY IN MOUSE BRAIN ENDOTHELIAL CELL

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Aims: The approximate prevalence of the metabolic syndrome (MS) in patients with coronary heart disease (CAD) is 50%, with a prevalence of 37% in patients with premature CAD. Effective prevention or treatment of MS significantly reduces the risk for developing serious complications. Palmitic acid (PA) is a saturated fatty acid, when being excessive, is a significant risk factor for development of MS or cardiovascular accident. Lipotoxicity in endothelial cells (EC) has been well documented but how PA affects EC Ca2+-signaling and other functions remain largely unexplored. Catechin has been implicated in benefiting almost every organ system such as cardioprotective and anti-obesity; and also beneficial for blood vessel health. This study aims to investigate the lipotoxic alteration of mouse brain endothelial cell line (bEND.3 cells) function mediated by PA; and how PA modulates EC ion channels, and also to assess the potential protective effects of catechin.
Methods: Cell apoptosis assessed by TUNEL-Assay. Cytosolic Ca2+ in bEND was measured with Fura-2 method. Mitochondria membrane potential (MMP) measured by MMP-Assay Kit. Cell viability was measured By MTT-Assay. The $p < 0.05$ were considered significant (ANOVA).
Results: Exposure of bEND to PA (300 micromolar) for 48 h resulted in apoptosis. PA (100, 300 micromolar) increased expression of CHOP but not phosphorylated eIF2-alpha. PA (300 micromolar) pretreatment diminished (Ca2+agonist) ATP-triggered Ca2+ release and Ca2+ influx. 300 micromolar PA pretreatment diminished (SR Ca2+-pump blocker) CPA-triggered Ca2+ release and Ca2+ influx. Thus PA at this high concentration reduced the size of Ca2+ pool. PA at 100 micromolar, however, did not reduce CPA-induced Ca2+ release but suppressed Ca2+ influx. Thus PA at this concentration inhibits store-operated Ca2+ entry. PA-induced cell death was significantly alleviated by co-treatment of bEND with catechin (300 micromolar).
Conclusion: Cell death was apoptotic and related to endoplasmic reticulum(ER) stress and cytosolic Ca2+ elevation. Co-treatment of bEND with catechin (300 µM) significantly prevented PA-induced cell death.

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INTERFERON GAMMA SIGNALLING IN ATHEROSCLEROSIS: PRO-ATHEROGENIC ACTIONS AND THERAPEUTIC APPROACHES

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Objectives: To investigate the mechanisms underlying the effects of interferon-gamma on macrophages in atherosclerosis and how therapeutic agents attenuate the actions of this pro-inflammatory cytokine.
Background: Atherosclerosis is an inflammatory disease of medium and large arteries regulated by cytokines. The pro-atherogenic cytokine interferon-gamma (IFN-gamma) plays a pivotal role in all stages of the disease and hence represents a promising therapeutic target. The purpose of this study was to investigate how IFN-gamma modulates macrophage function and properties in this disease along with the mechanisms underlying the inhibition of its actions by therapeutic agents.
Methods: The studies used a combination of macrophage cell lines and primary cultures together with analysis of gene expression and signal transduction pathways, RNA interference assays and biochemical approaches.
Results: IFN-gamma induced macrophage foam cell formation and the expression of several pro-inflammatory genes, such as monocyte chemotactic protein-1 and intercellular adhesion molecule-1, and microRNAs. The extracellular signal-regulated kinase (ERK) pathway played a pivotal role in the action of the cytokine on the promotion of modified lipoprotein uptake by macrophages and the regulation of expression of pro-atherogenic genes. ERK modulated the phosphorylation-mediated activation of signal transducer and activator of transcription-1 (STAT1), a key transcription factor in IFN-gamma signalling. The pro-atherogenic actions of IFN-gamma were attenuated by statins, activators of anti-atherogenic nuclear receptors, and nutraceuticals such as dihomo-gamma-linolenic acid. The mechanisms underlying the inhibitory actions of such agents along with the role of the ERK:STAT1 axis in the promotion of atherosclerotic in vivo are currently being investigated.
Conclusions: The studies provide key mechanistic insights into the pro-atherogenic actions of IFN-gamma and the effects of therapeutic agents on signalling by this cytokine.
Funding: British Heart Foundation

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MICRORNA-15/16 PROMOTES SMOOTH MUSCLE CONTRACTILE PHENOTYPE AND ATTENUATES VASCULAR NEOINTIMA FORMATION BY TARGETING YES-ASSOCIATED PROTEIN YAP

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Objectives: To investigate the functional role of the microRNA (miR)-15/16 in vascular smooth muscle phenotypic modulation and its underlying mechanism.
Background: In response to vascular injury, vascular smooth muscle cells (VSMCs) undergo phenotypic modulation from contractile phenotype to synthetic phenotype that is characterized with the elevation of VSMC proliferation and migration while reduction of muscle contractile genes. This phenotypic switching leads to neointima formation that can cause many occlusive vascular diseases such as restenosis. Previous studies have shown that miRs encoded by the miR-15/16 clusters act as tumor suppressors, but the functional role of miR-15/16 in VSMCs is unknown.
Methods and Results: By using quantitative reverse-transcription polymerase chain reaction, we found that miR-15/16 is the one of most abundant microRNAs expressed in contractile VSMCs. However, when contractile VSMCs convert to synthetic phenotype in vitro and in vivo miR-15/16 expression is significantly reduced. By loss-of-function assays, knocking-down endogenous miR-15/16 in VSMCs attenuates smooth muscle gene expression but promotes VSMC proliferation and migration. Conversely, over-expression of miR-15/16 promotes smooth muscle contractile gene expression while attenuating SMC migration and proliferation. Consistent with this, over-expression of miR-15/16 in a rat carotid balloon injury model markedly attenuates injury-induced smooth muscle dedifferentiation and neointima formation. Mechanistically, we identified the potent oncoprotein yes-associated protein YAP as a downstream target of miR-15b/16 in human VSMCs. Reporter assays validated that miR-15/16 targets YAP 3'-untranslated region through an evolutionarily conserved binding site. Furthermore, over-expression of miR-15/16 significantly represses YAP expression, whereas conversely, depletion of endogenous miR-15/16 results in up-regulation of YAP expression.
Conclusions: These results indicate that miR-15/16 plays a critical role in smooth muscle phenotypic modulation by targeting YAP. Promoting expression of miR-15/16 would be a potential therapeutic approach for treatment of proliferative vascular diseases.

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IS THERE A RELATIONSHIP BETWEEN ADVANCED GLYCATION END-PRODUCTS AND SOLUBLE RECEPTORS OF ADVANCED GLYCATION END-PRODUCTS WITH THE ETIOLOGY AND SEVERITY OF CONGESTIVE HEART FAILURE?

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Background: Advanced glycation end-products (AGEs) and the soluble receptor for advanced glycation end products (sRAGEs) came up with the recent researches regarding new biomarkers for the diagnosis of congestive heart failure (CHF). Although it has been known that AGEs and sRAGEs have a role in the pathogenesis of CHF, information regarding their role and their pathogenetic mechanism is very limited. The aim of this study was to find any relationship between AGEs and sRAGEs with the etiology and severity of CHF.
Methods and Material: This study was a prospective cross sectional study that enrolled 85 patients with chronic CHF. Measurement of left ventricle ejection fraction (LVEF) was done by echocardiography. Blood samples were collected for measuring AGEs and sRAGEs just before or after echocardiography assessment (in the same session). Measurement of AGEs, sRAGEs and NT-pro BNP were done by ELISA method. The relationship between AGEs and sRAGEs with the severity and as well as the etiology of CHF were evaluated via SPSS-15.
Results: Of 85 patients 48 (56.5%) were male; Mean±SD of their ages was 55.8±13.4 years old (ranges from 27 to 84 years). Correlation coefficient between LVEF and sRAGEs was 0.196 (P=0.072) and between LVEF and AGES was 0.269 (P=0.013). Mean of sRAGEs in the patients with and without ischemic etiology was 3.4±2.2 microgram/ml and 2.8±4.2 microgram/ml, respectively (P=0.141). Mean of AGES in the patients with and without ischemic etiology was 16.8±9.8 microgram/ml and 11.6±7.3 microgram/ml, respectively (P=0.141). Although there was trend in favor of ischemic heart failure, the difference between two groups was not statistically significant.
Conclusion: According to this study the rate of AGES and sRAGEs could be helpful in the diagnosis and assessment of severity of CHF and may be used for etiologic differentiation of heart failure syndrome.

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THE ROLE OF SIRT6 IN ENDOTHELIAL CELL SENESCENCE AND CYTOPROTECTION

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The wear and tear processes that contribute to human ageing are being increasingly implicated in the development of cardiovascular pathologies. One such process is telomere damage, which leads to the onset of cellular senescence. Although the occurrence of senescence in the vascular endothelium is now clearly established (reviewed in Erusalimsky, J. Appl. Physiol. 2009;106:326), the mechanisms of its regulation have not been extensively investigated. SIRT6 is a member of a family of NAD-dependent protein deacylases known to influence metabolism, stress tolerance and ageing. SIRT6 participates in DNA repair, telomere maintenance, and transcriptional repression of genes that regulate glucose homeostasis and inflammation. Since these processes may be relevant to cardiovascular pathologies, we are investigating the function of SIRT6 in endothelial cells (Cardus et al, Cardiovascular Res. 2013;97:571). In this presentation I will show evidence that SIRT6 is present in mature endothelial cells and that its levels decrease upon senescence. I will also show that knock down of SIRT6 by RNA interference increases global DNA damage as well as telomere damage, resulting in the activation of a DNA damage response, which leads to the inhibition of cell proliferation and the establishment of a senescent phenotype. These effects are accompanied by an increase in the expression of pro-inflammatory and pro-thrombotic markers, by a reduction in endothelial nitric oxide synthase expression, and by impairment in the formation of capillary-like networks. Our findings highlight the role of SIRT6 as an important regulator of endothelial cell homeostatic functions and suggest that its modulation may affect the evolution of vascular ageing.

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INCIDENCE AND ELECTROGRAM CHARACTERISTICS OF NON-SUSTAINED VENTRICULAR FIBRILLATION IN PATIENTS WITH PRIMARY ELECTRICAL DISORDERS

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Background: Implantable cardioverter defibrillator (ICD) is frequently indicated in high risk patients with primary electrical disorders (Brugada syndrome [BrS], early repolarization syndrome [ERS], and idiopathic ventricular fibrillation [IVF]). Some patients present with ventricular fibrillation (VF) that terminates spontaneously. But limited information is available on non-sustained VF.

Objectives: The aim of the present study was to compare non-sustained VF and VF terminated by electrical shock and to investigate the difference of fluctuation in ventricular cycle length (CL) that could predict the self-termination of arrhythmia before electrical shock delivery.

Methods: We enrolled consecutive 27 patients (41.5+¾13.2 years; 22 males) with primary electrical disorders (BrS 16, ERS 7, IVF 4 patients) who experienced VF on ICD interrogation between April, 1996 and April, 2014. A total of 228 episodes were reviewed by two independent cardiac electrophysiologists.

Results: (1) Of 228 episodes, 193 (84.6%), 35 (15.4%) episodes were VF terminated by electrical shock and non-sustained VF, respectively. (2) Mean VFCL in non-sustained VF was longer than in VF terminated by electrical shock (193±¾35 vs. 179+¾28 ms)(P=0.036). (3) In each episode, VFCL became longer or did not change in non-sustained VF (187¡¾31 vs. 196¡¾38 ms)(first vs. last CL)(P=0.276) in contrast with progressively shorter VFCL in VF terminated by electrical shock (180+¾25 vs. 160+¾29)(first vs. last VFCL before electrical shock)(P<0.001).

Conclusion: Non-sustained VF in primary electrical disorders was not infrequent. VFCL was longer and progressively increased or did not change in non-sustained VF compared with VF terminated by electrical shock. Whether ICD programming reflecting this characteristic shortening of VFCL could decrease frequency of ICD shock awaits further study.

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EARLY EMERGENCY CALLS BEFORE PATIENT COLLAPSE AND SURVIVAL FROM OUT-OF-HOSPITAL CARDIAC ARREST

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Aim: Some out-of-hospital cardiac arrests (OHCAs) are witnessed after emergency calls. This study aimed to confirm the benefit of early emergency calls before patient collapse on survival after OHCAs witnessed by bystanders and/or emergency medical technicians (EMTs).
Methods: We analysed 278,310 witnessed OHCAs [EMT-witnessed cases (n = 54,172), bystander-witnessed cases (n = 224,138)] without pre-hospital physician involvement from all Japanese OHCA data prospectively collected between 2006 and 2012. The data were analysed for the correlation between neurologically favourable 1-month survival and the time interval between the emergency call and patient collapse.
Results: When emergency calls were placed earlier before patient collapse, the proportion of EMT-witnessed cases and survival rate after OHCAs witnessed by bystanders and EMTs were higher. When analysed only for bystander-witnessed cases, for earlier emergency calls placed before patient collapse, survival rate and incidences of bystander cardiopulmonary resuscitation (CPR) and dispatcher-assisted CPR decreased: 2.9%, 33.6% and 24.4%, respectively, for emergency calls placed >6 min before collapse and 5.5%, 48.8% and 48.5%, respectively, for those placed 1–2 min after collapse. Multivariable logistic regression showed that short call-to-collapse interval (adjusted odds ratio; 95% confidence interval) (0.92; 0.90–0.94) and EMT response time after collapse (0.84; 0.82–0.86) were associated with survival after bystander-witnessed OHCAs with emergency calls before collapse.
Conclusion: Early emergency calls before patient collapse efficiently increase the proportion of EMT-witnessed cases and promotes survival after OHCAs witnessed by EMTs and bystanders. However, early emergency call before collapse may interfere with the detection and recognition of cardiac arrest by dispatchers and may worsen the outcome when the patient's condition deteriorates to cardiac arrest before EMT arrival.

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COMPONENT ANALYSIS FOR EFFECTIVENESS OF VENTILATIONS AND COMPRESSIONS IN BYSTANDER CARDIOPULMONARY RESUSCITATION

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Aim: To determine the effectiveness of ventilations and compressions in bystander cardiopulmonary resuscitation (BCPR).
Methods: From out-of-hospital cardiac arrest (OHCA) data prospectively collected from 2005 to 2011 in Japan, we extracted data for 210,134 bystander-witnessed OHCAs with complete datasets but no prehospital involvement of physician [no BCPR, 115,733; ventilation-only, 2,093; compression-only, 61,075; and conventional (compressions + ventilations) BCPR, 31,233] and performed univariable component analyses of ventilation and compression for 1-month neurologically favourable using simple multinominal and multivariable logistic regression analysis.
Results: The rate of survival in the no BCPR, ventilation-only, compression-only and conventional group was 2.8%, 3.9%, 4.5% and 5.0%, respectively. The unadjusted OR (95% CI) for survival after dividing BCPR into ventilation and compression components were 1.13 (1.06–1.20) and 1.64 (1.56–1.72), respectively. When adjusted by other factors known to be associated with survival, the adjusted OR (95% CI) were 1.19 (1.11-1.27) and 1.60 (1.51-1.69), respectively. The adjusted OR of ventilation component was high in the OHCA subgroup of non-cardiac etiology (1.38; 1.19-1.59) and very high in the pediatric OHCA subgroup (1.56; 1.13-2.15).
Conclusions: Ventilation is a significant component of BCPR, but alone is less effective than compression in improving neurologically favourable survival after OHCAs.

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EARLY HEMODYNAMIC CHANGES OF TILT TABLE TESTING PREDICTS NEUROCARDIOGENIC RESPONSE IN AFRICAN AMERICAN POPULATION

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Background: Head up tilt table test (HUTT) is both time consuming and has an associated morbidity. Hemodynamic changes that occur during the early phase of HUTT may allow for prediction of neurocardiogenic syncope, without vasoactive stimulation thus, reducing protocol time and any associated morbidity.
Methods: 119 consecutive African Americans (AA) (57±19, male 44%) underwent a HUTT for evaluation of syncope of unknown etiology (8/2011-12/2013). A positive response was defined as the development of symptoms linked with an SBP < 90 mm Hg, HR < 50 beats/min, or sinus arrest > 3 seconds. Hemodynamic variables during the passive phase of HUTT were analyzed, and results were then classified into groups (positive vs. negative), as a function of various predictors (age, early changes in HR, SBP and DBP) and a decision tree was generated.
Results: 62 subjects (52%) had positive HUTT and 57 (48%) had negative HUTT. Early changes in HR from baseline (up to 9 minutes) did not predict HUTT response. Early changes in BP variables from baseline significantly predicted HUTT response ($p<0.05$). There was significant interaction between age and BP; SBP for age>60 but DBP for age<60. An algorithm (Fig 1) based on age and BP had a positive predictive and negative predictive value of 68 and 93 %, respectively, with an accuracy of 80%.
Conclusion: A novel algorithm using age and BP allows for the early prediction of HUTT results without need for vasoactive stimulation which allows for rapid diagnosis, lower morbidity and a reduction in cost.

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QUANTITATIVE SUDOMOTOR AXON REFLEX TEST (QSART) STUDY IN POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS)

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Objectives: The aim of this study is to determine the association of QSART deformities in Postural Orthostatic Tachycardia Syndrome (POTS) patients.
Background: The Postural Orthostatic Tachycardia Syndrome (POTS) affects primarily young women. POTS is a form of dysautonomia that is estimated to impact between 1,000,000 and 3,000,000 Americans, and millions more around the world. Quantitative Sudomotor axon reflex test (QSART) is used to evaluate postganglionic sympathetic cholinergic Sudomotor function by measuring the axon-reflex mediated sweat response over time.
Methods: 192 patients were selected randomly from our clinic with POTS who underwent QSART test .Patients Sudomotor Evaluation results were reviewed from electronic medical records and performed data analysis
Results: Out of 192 patients, 181 patients are female (94%, n=181, age 33.78±11.46), 11 patients are male (6%, n=11, age 27.88±9.29).QSART was abnormal in 129/192(67%) patients in which 83 patients had excessive sweating, 46 patients had Loss of sweating. 62/192(32%) patients had normal QSART.
Conclusion: Our research results demonstrated that POTS patients have a higher percentage of QSART abnormalities (67%).

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WHAT'S COMMON IS COMMON!

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Objectives/Background: Syncope is a common health problem encountered by internists and cardiologists. Here we describe a case of a young woman with multiple syncopal episodes.
Description: 33 year old lady with PMH of syncopal episodes and hypothyroidism was admitted to CCU after experiencing presyncope and hypotension during an EEG session as part of outpatient syncope evaluation. In the previous 6 months, she had an unremarkable but an exhaustive cardiac and neurologic workup including Holter monitoring, MRI/MRA of brain, EEG, thermoregulatory sweat test, quantitative axon reflex sweat test and a 10 minute 70° angle tilt table study. History taking revealed that her syncopal episodes would generally occur after prolonged standing with a prodrome of presyncope, tunneling vision and palpitations followed by loss of consciousness for ~30 seconds and complete recovery. A 70° angle tilt table study was abnormal after 45 minutes as patient had syncope associated with BP 84/71 and HR 49 suggesting vasovagal syncope. She was discharged with Midodrine and compression stockings.
Results/Discussion: It's important to clinically differentiate syncope from vertigo or seizure before embarking on a workup. Important clues from history like prodrome, provocative factors, associated symptoms, pre-existing medical conditions etc. and from physical exam like orthostatic hypotension, cardiac murmurs etc. can often point to an etiology. Three main etiologies of syncope are reflex/neurally mediated (including vasovagal), orthostatic hypotension and cardiac with the former two being more common and cardiac syncope being the most worrisome.
Conclusion: A good history and physical are essential for a cost-effective yet safe evaluation of syncope.

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CURIOSYNCOPY

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Although the usual causes of syncope such as vaso-vagal, orthostatic and obstructive types are well recognized, the associated symptoms of unusual causes may be confusing and the management less obvious.

We present some rare types of syncope managed in our facility, where the cause was not immediately apparent.

Swallow (Bagel) syncope. A patient presented with several episodes syncope and a normal examination. Further history indicated a relationship to meals and EKG monitoring revealed paroxysmal AV block in which reduced cerebral blood flow corresponded to eating solid foods.

Subclavian steal syncope.

A patient complained of pain when raising the left arm. There was also blurring of vision, vertigo, and episodes of syncope. Arm muscle and joint examination was normal but blood pressure was 30mmHg lower in the left arm. Arteriography demonstrated subclavian steal diminishing cerebral blood flow during arm raising.

Systemic mastocytosis syncope

A patient presenting with multiple syncope episodes, each associated with flushing, palpitation, itching and hypotension. The history suggested histamine reaction episodes. Examination was normal but bone marrow biopsy revealed increased mast cells.

Pan-dysautonomia neuropathy.

A patient was admitted with recurrent syncope after standing, associated with dry mouth, decreased sweating and constipation. Examination was normal but Tilt-table testing showed immediate blood pressure drop of 70mmHg.

Laugh syncope

A barber presented with shoulder pain after falling at work. Only bruising was found but further questioning revealed that immediately before falling unconscious, he had broken out in very hearty laughter at a joke told him by a customer.

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PRO-ARRHYTHMIC EFFECTS OF CALMODULIN KINASE II (CAMKII) IN TIMOTHY SYNDROME ARISING FROM A NEW CACNA1C MUTATION

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Background: Timothy syndrome (TS) is a disease of excessive cellular Ca2+ entry and life-threatening arrhythmias caused by a mutation in the primary cardiac L-type Ca2+ channel. Recently, a novel TS mutation (G1911R) was identified. While its genetic basis has become well-understood, the cellular mechanisms (especially the role of CaMKII) by which the mutation translates to arrhythmia susceptibility remain unclear.
Objectives: This study aims at exploring mechanisms by which CaMKII modulates arrhythmogenesis and identifying potential targeted sites of antiarrhythmic therapy in TS.
Methods: A human ventricular cell model incorporated with a CaMKII activation module was used. Effects of CaMKII on L-type Ca2+ channel, RyR2 receptor and SERCA2a were considered. Parameters in the equations of ICaL were modified to incorporate experimental data on G1911R mutation.
Results: Our results indicate that: 1) In intracellular ionic simulations, TS myocytes had excessive ICaL(155%), more activated CaMKII(10-fold), higher SR Ca2+ load (133%), larger amplitude Ca2+ transients(183%), and augmented frequency of Ca2+ waves(300%). The large SR Ca2+ release in TS had a profound effect on the kinetics of ICaL, increasing the rate of inactivation to a high level resulted from larger fraction of CaMKII activation. 2) In action potential simulations, CaMKII-dependent ICaL facilitation contributes to excessive action potential prolongation(from 413.6 to 1133.9 ms) which favors the generation of early afterdepolarizations (EADs); CaMKII-dependent SR overload results in SR Ca2+ leak for triggering delayed afterdepolarizations (DADs). 3) In CaMKII inhibition simulations, CaMKII inhibition reversed an increase in intracellular Ca2+, normalized action potential and prevented afterdepolarizations.
Conclusions: TS-mediated Ca2+ influx is an upstream initiating event for arrhythmia phenotypes that are ultimately dependent on CaMKII activation. Thus, ICaL block in combination with partial CaMKII inhibition may be potentially a new therapeutic target to treat TS patients.

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GASTROINTESTINAL DISTURBANCES IN POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS)

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Objectives: The aim of this study is to determine the Gastrointestinal disturbances in Postural Orthostatic Tachycardia Syndrome (POTS) patients.
Background: The Postural Orthostatic Tachycardia Syndrome (POTS) affects primarily young women. POTS is a form of dysautonomia that is estimated to impact between 1,000,000 and 3,000,000 Americans, and millions more around the world. POTS is a form of orthostatic intolerance that is associated with many Gastrointestinal disturbances.
Methods: 249 patients are referred to our clinic from January to November with POTS. Reviewed the medical records of 249 POTS patients and gastrointestinal symptoms
Results: Out of 249 patients, 226 patients are female (90.76%; average age 32.69), 23 patients are male (9.24%; average age 27.91). Out of 249 patients 189 patients (76%) had vomiting or nausea, 150 patients (60%) had irritable bowel syndrome ,128 patients (51%) had bloating, 125 patients (50%) had constipation , 80 patients (32%) had abdominal pain , 56 patients (22 %) had delayed gastric emptying, 24 patients (10%) had lactose intolerance, 8 patients (3 %) had Gastroesophageal reflux disease, 5 patients (2 %) had Iron deficiency anemia, 6 patients (2 %) had Peptic ulcer disease, 4 patients (2 %) had Celiac Disease.
Conclusion: Patients with POTS have a very high prevalence of gastrointestinal symptoms however the majority of abnormalities appear to be motility related. Motility testing should be performed in POTS patients. The diagnostic yield of endoscopic procedures appears to be low.

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VITAMIN B12 DEFICIENCY IN POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS)

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Objective: The aim of this study is to investigate the association between vitamin B12 levels and Postural orthostatic tachycardia syndrome (POTS).
Background: The Postural Orthostatic Tachycardia Syndrome (POTS) affects primarily young women. POTS is a form of dysautonomia that is estimated to impact between 1,000,000 and 3,000,000 Americans, and millions more around the world. We frequently find vitamin B12 deficiency in patients who present with POTS. Vitamin B12 is involved in the production of adrenaline from noradrenaline. It is the cofactor involved in catecholamine degradation.
Methods: 155 patients were selected randomly from our clinic with POTS. Patients Vitamin b12 levels charts were reviewed from electronic medical records, Vitamin b12 deficiency status was defined as serum level <200 pg/mL.
Results: Out of 155 patients, 146 patients are female (94%, n=146, age 33.68±7.26), 9 patients are male (6% ,n=9 ,age 24.73±4.39). 89/155(57%) patients had Vitamin B12 serum level <200 pg/mL, 66(43%) patients had Vitamin B12 serum level >200 pg/mL.
Conclusion: Our research results demonstrated that Postural Orthostatic Tachycardia Syndrome (POTS) patients have significantly lower vitamin B12 levels (57% have Vitamin B12 deficiency serum level <200 pg/mL).

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AN UNUSUAL TYPE OF SHORT V-V TAHCYCARDIA

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Case and Discussion: 42 year-old male with coronary artery disease and ischemic cardiomyopathy who underwent right-sided single chamber Implantable Cardioverter-Defibrillator placement by cardiothoracic surgery in August 2012. On device interrogation, he was found to have multiple asymptomatic tachycardia episodes. The device intracardiac electrograms were reviewed and showed short V-V tachycardia, which was interpreted as non-sustained ventricular tachycardia (NSVT). 12-lead EKG and Chest X-ray were not remarkable. However, when we compared the ventricular signal during the short V-V interval seen in device interrogation to the ventricular signal during sinus rhythm, they looked similar except for further separation of the two components of the ventricular signal during the short V-V interval on the EMG.

Pacing the ICD lead at the maximum output as part of work up to evaluate the possible diagnosis, which resulted in atrial capture only and morphology of the P wave was consistent with left atrial capture. This finding raised the possibility of lead misplacement. Chest x-ray with lateral projection was obtained and demonstrated ICD lead misplacement into the coronary sinus (CS) or left atrium. Echocardiography was done and confirmed lead misplacement in the CS and not in the left atrium. The two components were basically both near field A and V (not far field) and the episodes reported as NSVT were actually atrial tachycardia episodes with further separation of the A and V due to the AV nodal delay during the tachycardia. The fact that the tachycardia episodes terminated with V each time, rules out ventricular tachycardia with one to one retrograde conduction.

Patient was seen during follow up at 1 and 6 months, and ICD interrogation showed normal sensing, pacing and no more episodes of short V-V tachycardia.

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EFFECTS OF ANESTHESIA ON INDUCIBILITY DURING PEDIATRIC ELECTROPHYSIOLOGY STUDIES

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Background and introduction: Anesthesia has become an important part of pediatric electrophysiology studies (PEP). The purpose was to determine, (1) the prevalence of supraventricular tachycardia (SVT) and sinus tachycardia (Stach) during anesthesia induction, and (2) lack of inducibility of SVT during PEP under anesthesia.
Methods: IRB approved, retrospective review of PEP (1/99-1/14). Inclusion criteria: Less than 21 years, documented SVT prior to PEP, anesthesia. Data review: demographics, EP and anesthesia records. Two groups identified, Intravenous (IV) and inhalational anesthesia (I). Induction of SVT and Stach prior to initiating EP study was recorded as was failure to induce SVT during PEP.
Results: Inclusion criteria was met by 378 patients, 57% males, median age 14 years. IV anesthesia in 72% . During induction, only 1 patient from IV group developed SVT, (WPW patient), 10% of patients developed Stach and patients with WPW are twice at risk of developing Stach (16.19% vs. 8.06%; $p = 0.02$). Stach was seen more commonly with I induction (59% Vs 41%; $p < 0.0001$). The most common drug for I was sevoflurane (89%); and no differences were identified between drugs. Failure to induce SVT during PEP was 13 % and no differences seen between groups.
Conclusion: Route of anesthesia induction, inhaled or intravenous do not increase the risk of developing SVT. Sinus tachycardia is a common occurrence, and failure to induce SVT was not affected route of anesthesia.

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RELATIONSHIP OF BODY MASS INDEX (BMI) AND POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS)

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Objective: The purpose of this study is to determine the relationship of body mass index (BMI) and Postural Orthostatic Tachycardia Syndrome (POTS).
Background: The Postural Orthostatic Tachycardia Syndrome (POTS) affects primarily young women. POTS is a form of dysautonomia that is estimated to impact between 1,000,000 and 3,000,000 Americans, and millions more around the world. Body mass index (BMI) is a measure of relative size based on the mass and height of an individual.
Method: 169 patients were selected randomly from our clinic with POTS; Patients BMI charts were reviewed from electronic medical records. Patients were categorized as normal weight (BMI 18.5 to 24.9 kg/m2), overweight (BMI 25.0 to 29.9 kg/m2) or obese (BMI ≥30.0 kg/m2).
Results: Out of 169 patients (n=169), 97% are females (n=164; age 30.88±9.36), 3% are males (n=5; age 25.93±6.19), 51 Patients (30%) have normal weight (20.37±3.29kg/m2), 86 Patients (51%) have overweight (25.46±3.10 kg/m2), 32 Patients (19%) have Obesity (30.11±6.3 kg/m2).
Conclusion: Our results, for the first time, demonstrated the POTS and BMI relationship. In POTS patients higher percentage (51%) have overweight BMI (25.0 to 29.9 kg/m2), more than half of POTS patients (70%) have BMI (≥25.0 kg/m2).

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RECURRENT VENTRICULAR TACHYCARDIA IN A METHADONE DEPENDENT PATIENT WITH NON-COMPACTION CARDIOMYOPATHY

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Background: Methadone is a commonly used drug for opioid dependence and chronic pain. Cardiac side effects, especially QT interval prolongation and ventricular arrhythmias have recently become a concern, even though it rarely causes ventricular arrhythmias.
Case Report: In this report, we describe a case report of a 41 year-old female on chronic methadone who used cocaine 3 days before a syncopal episode, which was due to polymorphic ventricular tachycardia. The patient was also noted to have a non-compaction cardiomyopathy. The patient was treated with an amiodarone infusion, tapered off the methadone and underwent VT ablation. However, the ventricular tachycardia continued to be easily inducible and a dual chamber implantable cardioverter-defibrillator (ICD) was placed. This report highlights the interaction of methadone and structural heart disease and the role each plays in complex ventricular ectopy. Discussion: Even though methadone can cause QT interval prolongation, it is rarely the sole cause of ventricular arrhythmia and other risk factor are usually associated with the ventricular arrhythmia in patients on a steady dose of methadone, such as hypokalemia, hypomagnesaemia, structural heart disease, administration of other drug that can cause QT interval prolongation like including cocaine, haloperidol, erythromycin.
Conclusion: Methadone is known to cause acquired QT interval prolongation but it is rarely a sole cause of ventricular arrhythmias. Around 50% of patients with non-compaction cardiomyopathy developed ventricular arrhythmias, usually in the setting of other risk factors. Cocaine, hypokalemia, hypomagnesemia and non-compaction cardiomyopathy all contributed in ventricular arrhythmias in this patient with chronic methadone use and QT interval prolongation.

ARRHYTHMIAS: DIAGNOSIS AND TREATMENT – BASIC AND CLINICAL

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WIDE COMPLEX TACHYCARDIA IN A YOUNG PATIENT

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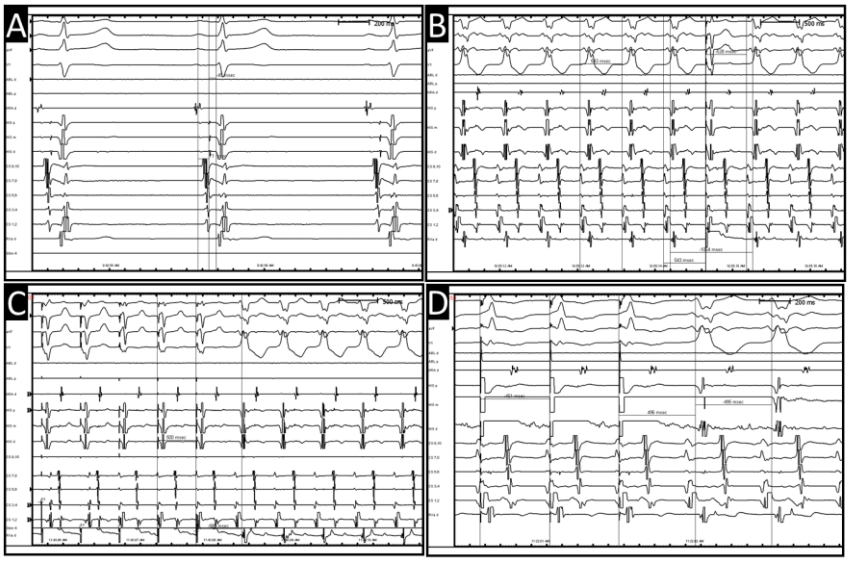
Introduction: A 19 year old female with symptomatic palpitations was found to have sustained wide complex tachycardia
Methods: N/A
Results: Echo was completely normal. She underwent EP study. She has normal interval measurements at the baseline with no pre-excitation (A). During tachycardia the shortest AV interval was 152 msec. During the tachycardia a premature ventricular contraction (PVC) delivered at a perfect time showed fusion with resetting consistent with macro re-entry tachycardia (B). Burst right ventricle apex pacing initiated the tachycardia with fusion present confirmed again the tachycardia mechanism. The post pacing interval (PPI) tachycardia cycle length (TCL) confirmed that it is far from the circuit (C). Entrainment from pacing at His showed perfect PPI-TCL which will not be expected if this was ventricular tachycardia with such morphology. The previous findings were due to antidromic re-entry tachycardia using left lateral antegrade only, decremental accessory pathway (AP). This was confirmed with premature atrial contraction during tachycardia and delivered during refractory septal A and showed advancement of the next V and the next A, consistent with an antegrade AP participating in the tachycardia. In image (B) the findings were due to advancing the next A from the PVC which advanced the next V. In image (D) the findings were due to His capture since His is part of the circuit. Two interesting findings were seen as well: The AP was adenosine sensitive. RFA was done during tachycardia and with significant wobbling in TCL (450-730 msec) as typically seen in accelerated junctional rhythm and terminated with A.
Conclusion: Patient did well, with no recurrence.



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A RARE CASE OF PLATYPNEA-ORTHODEOXIA IN A PATIENT WITH PFO

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Background: Platypnea-Orthodeoxia (POS) is a rare syndrome of hypoxia and dyspnea worsened by assuming the upright position. The most common etiology is intracardiac right to left shunting of blood across a Patent Foramen Ovale (PFO) or ASD. With modern interventional techniques, treatment can be done through minimally invasive trans-catheter closures.
Case: 72-year-old woman with prior ischemic stroke and PFO presented with POS causing functional decline over 4 months and inability to tolerate any activity during this time. On examination, she was tachycardic and dyspneic, with oxygen saturation of 75 in the upright and leaning forward position while on 3L oxygen. Saturation rebounded to 88-89 with recumbency. Laboratory evaluation was unremarkable. Chest X-Ray was normal. CT Chest ruled out pulmonary embolism. Given her history of stroke along with platypnea-orthodeoxia causing significant functional impairment, trans-catheter closure of PFO was performed resulting in complete resolution of symptoms.
Discussion: This case demonstrates an exceedingly rare syndrome in a patient with a PFO presenting with classical symptoms of POS- dyspnea and hypoxia that worsened in the upright position. After ruling out other causes for postural accentuation of right to left shunt, PFO closure was performed, completely resolving her symptoms. Development of POS requires two conditions: an anatomical defect leading to inter-atrial communication and a functional component causing shunt redirection with normal pulmonary or right atrial pressures. This syndrome is most frequently attributed to major pulmonary disorders, but may also be seen with cirrhotic vascular abnormalities. Closure of the PFO reverses the orthostatic hypoxia and often permanently resolves symptoms as in our patient's case. Less than 200 cases of this uncommon syndrome have been described to date in literature. As percutaneous closure of PFOs result in a favorable prognosis, alternate treatment modalities have not been explored adequately due to the relative rarity of this interesting phenomenon.

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CHYLOUS TAMPONADE DUE TO CATHETER INDUCED SUPERIOR VENA CAVAL OBSTRUCTION IN A PREMATURE INFANT

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Pediatric chylopericardium is a rare complication of thoracic duct injury during cardiothoracic surgeries. It could also be a potential complication of superior vena cava (SVC) obstruction. We report a rare case of chylous tamponade in a premature infant as a complication of prolonged central venous catheterization. A thirty-six week gestation premature female infant was born with congenital diaphragmatic hernia. She developed severe pulmonary hypertension that required ECMO for the first 8 days of life. Surgical repair was performed at 2 weeks of age. The patient required central venous catheterization in the SVC via the right internal jugular vein for administration of medications and hyper-alimentation. At 3 months of age, she developed respiratory distress and edema of the upper chest, head and neck. Chest X-ray showed enlarged cardiac silhouette. Echocardiogram showed normal cardiac anatomy and a large pericardial effusion causing diastolic collapse of the right atrium consistent with cardiac tamponade. Urgent pericardiocentesis was performed with aspiration of 50 cc of milky fluid that had triglycerides 413 mg/dl, protein 4.2 g/dl, WBC 6963/dl with 89% lymphocytes, suggestive of chylous pericardial effusion. A pigtail catheter was placed for continuous drainage of the fluid. A magnetic resonance venogram showed no clear flow related enhancement in both internal jugular vein and SVC with small collaterals visualized in the neck. This indicated complete obstruction of both veins. The patient continued to accumulate a significant amount of fluid despite being on octreotide. A surgical pericardial window was created with gradual clinical improvement. There was complete resolution of the swelling by 4 months of age. This is a rare case of SVC obstruction in a premature infant causing massive chylous pericardial effusion without surgical injury of the thoracic duct. This obstruction was likely caused by thrombus formation or vessel wall smooth muscle proliferation due to catheter-induced injury.

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HYPERALDOSTERONISM COMPLICATING CONGESTIVE HEART FAILURE DUE TO A LEFT TO RIGHT SHUNT IN A PREMATURE INFANT

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Congestive heart failure (CHF) develops in infants with significant left to right shunt lesions as the pulmonary vascular resistance drops after birth. The medical management includes diuretics and angiotensin converting enzyme inhibitors (ACEI) as afterload reducing agents. We report a 31 week gestation premature male infant who presented with a heart murmur in the NICU shortly after birth. An echocardiogram showed a large membranous VSD and a moderate size PDA. He had normal serum electrolytes on day 5 of life. At 2 weeks of age, he developed respiratory distress that required mechanical ventilation. A CXR showed cardiomegaly and pulmonary edema consistent with CHF. He was initially treated with furosemide and captopril without any significant improvement in 3 days. Routine basic labs showed severe hypokalemia (1.9 mmol/L) that did not respond to IV KCL supplementation. Other positive labs included elevated NT-proBNP to 22,700 pg/ml (nl <125 pg/ml), hypernatremia (149 mmol/L), increased urinary potassium excretion to 111.8 mmol/L (nl <10 mmol/L) and decreased urinary sodium excretion to <5 mmol/L (nl 20-40 mmol/L). These results were suggestive of hyperaldosteronism which was confirmed with serum aldosterone of 547.5 ng/dl (nl 7-99 ng/dl). The addition of spironolactone (an aldosterone antagonist) had a dramatic effect within 2 days as CHF symptoms improved clinically and the patient was extubated. The serum aldosterone level dropped to 109.3 ng/dl other lab values became normal. In this patient, the decreased renal perfusion due to CHF led to activation of the renin-angiotensin-aldosterone system and eventually the development of hyperaldosteronism and hypokalemia which was resistant to IV KCL infusion. The addition of an aldosterone antagonist to diuretics and ACEI was shown to be helpful in this situation. Also, NT-proBNP seems to be a useful biochemical marker for CHF that correlates well with the clinical picture.

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WATCHFUL OBSERVATION VERSUS EARLY AORTIC VALVE REPLACEMENT FOR SYMPTOMATIC LOW-GRADIENT SEVERE AORTIC STENOSIS

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Background: The timing of aortic valve replacement (AVR) remains controversial in symptomatic patients with normal flow, low-gradient severe aortic stenosis (AS) and preserved left ventricular ejection fraction (LVEF). We sought to compare long-term mortality of early AVR versus a watchful observation strategy.
Methods: From 2000 to 2011, we prospectively evaluated 284 consecutive symptomatic patients (136 men, age; 68±10 years) with normal flow, low-gradient severe AS and preserved LVEF who were potential candidates for early AVR. Low-gradient severe AS was defined as indexed aortic valve area < 0.6 cm^2/m^2 with mean gradient < 40 mmHg. Early AVR was performed on 98 patients (early AVR group) while the watchful observation strategy was selected for 186 patients (watchful observation group). Patients in the watchful observation group were referred for AVR if mean gradient ≥ 40 mmHg during follow-up.
Results: There were no significant differences between the early AVR and the watchful observation group in the risk of overall mortality (HR 0.94 for the early AVR; 95% CI, 0.51 to 1.73; P = 0.84) or in the estimated actuarial 10-year mortality rates (28 ± 8% vs. 29 ± 5%, P = 0.84) in the overall cohort. Lower STS score, lower comorbidity index, female gender and performance of AVR were independently associated with overall survival on multivariable Cox analysis. For 80 propensity-score matched pairs, the risk overall death was not significantly different between the two groups (HR 1.62 for the early AVR; 95% CI, 0.71 to 3.67; P = 0.25).
Conclusions: The early AVR does not improve survival in symptomatic patients with normal flow, low-gradient severe AS and preserved LVEF. Watchful observation with timely performance of AVR should be considered a therapeutic option.

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USE OF CONDUITS IN PATIENTS WITH PROHIBITIVE ILIO-FEMORAL ARTERY ANATOMY FOR TRANSCATHETER AORTIC VALVE REPLACEMENT

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Introduction: The FDA has approved transcatheter aortic valve replacement (TAVR) for the treatment of severe aortic stenosis. Large bore sheaths are required for delivery of the prosthetic valve, which limits the patient population to whom TAVR may be offered. We present our initial experience with iliac conduits to expand the patient selection criteria for TAVR Aortic. Charts and imaging of 28 consecutive patients who underwent TAVR between 7/8/2012 and 8/7/13 at the hospital were reviewed. Data on iliac arterial anatomy and postoperative complications were collected. Among these, 5 patients with complex iliac anatomy had an iliac conduit placed. The conduits were 10 mm polyester grafts sewn proximally onto the common iliac artery to provide unobstructed access to the aorta. After the procedure the conduit was partially removed to leave a patch angioplasty on the artery.
Results: Vascular complications occurred in 0 number of patients. 1 patient had transient paresthesia over upper thigh which resolved at 4 weeks follow up. Beside the 5 patients with iliac conduits, 15 underwent a regular TF approach with surgical exposure of the common femoral artery, and 3 underwent a TA approach.
Conclusion: There are only few case reports of iliac conduits being used to bypass severe iliofemoral disease. Our case series include only 5 patients. In patients with severe iliofemoral disease and with localized iliofemoral disease, and centers were TAVR are in the initial phase and attempts to reduce the complications rates, conduit approach might be a better choice. Other alternatives like retroperitoneal exposure, followed by direct aorta or iliac artery access avoiding the use of prosthetic conduit and eliminating the need for more extensive retro- peritoneal dissection, which has been used for endovascular aortic repair, yet need to be studied and applied for difficult iliac anatomy in TAVR.

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LEFT ATRIAL APPENDAGE VELOCITY IMPROVEMENT POST TRANSCATHEER AORTIC VALVE REPLACEMENT RESULTS IN BETTER OUTCOMES

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Objectives: To assess whether better improvement in left atrial appendage (LAA) emptying velocity (LAAEV) after transcatheter aortic valve replacement (TAVR) are associated with better outcomes.
Background: LAAEV is reflective of LAA function.
Methods: LAA velocities were consecutively recorded before and after TAVR with transesophageal echocardiography between 2012-2015 at a single center. Patients were categorized into two groups; group 1: LAAEV improvement more than 5cm/sec, group 2: LAAEV improvement less than 5 cm/sec. Primary endpoint was composite of death, admission for heart failure, stroke and acute coronary syndrome within 12 months. Patients with persistent atrial fibrillation and patients with TAVR related complications were excluded.
Results: Forty-three consecutive patients were included in the study. Mean age was 80 ± 8 years and male was (22/43, 49%). LAAEV before and after TAVR was 34.8 ± 17.4 (cm/sec) and 38.9 ± 22.6 (p=0.05). During median follow up of 31 (3-555) days, 9 patients had reached primary endpoints. Kaplan-Meier curve showed lower event rates for group 1 (Log-lank p=0.046, Figure 1).
Conclusions: Better improvement in LAAEV was associated with better outcome after TAVR in this pilot study. This measurement may serve as simple markers for TAVR prognosis.

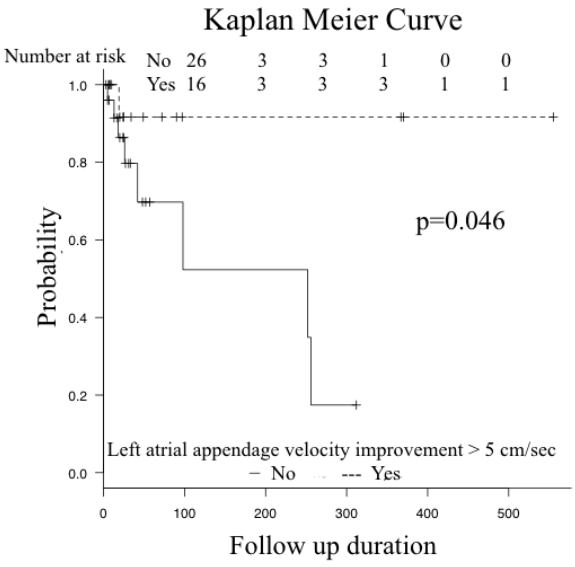

Figure 1

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BALLOON MITRAL VALVULOPLASTY IN MIRROR IMAGE DEXTROCARDIA WITH RHEUMATIC MITRAL STENOSIS

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Objective: To demonstrate the safety of balloon mitral valvuloplasty in patients of rheumatic mitral stenosis and situs inversus with dextrocardia
Background: Distorted cardiac anatomy and cardiac malpositions increase the complications of interatrial septal puncture and left ventricular entry during balloon mitral valvuloplasty.
Methods: Five patients with rheumatic mitral stenosis and situs inversus with dextrocardia were included in this study .Mean transmitral gradient before balloon mitral valvuloplasty (18 +/- 6 mmHg) was significantly higher, while mitral valve area (MVA) (0.68 +/- 0.4 cm2) was significantly lower All the five patients were young (mean age of 32 years) and symptomatic (mean pulmonary artery pressure 60 +/- 10 mmHg). Left femoral venous and arterial approach was used. Fluoroscopic imaging was performed without inverting the images although the software for the same was available. The interatrial septum was approached using fluoroscopy guide with needle directed towards the spine and keeping the pointer of Brockenbrough needle at seven to eight o' clock position followed by transatrial puncture in left lateral view. The transit across the mitral valve was done in left anterior oblique view without using pseudo right anterior oblique imaging with just clockwise or counterclockwise guidewire movement. Simultaneous transthoracic echocardiography guidance was used
Results: Pre and post balloon mitral valvuloplasty hemodynamic parameters were compared. After balloon mitral valvuloplasty, mean PA pressure was significantly reduced– [33.5 +/- 12 mmhg], with a significant reduction in transmitral gradient (8.2 +/- 3.5 mmHg), with an increase in mitral valve area (2.1 +/- 0.6cm2).
Conclusion: This case series demonstrates the safety and efficacy of balloon mitral valvuloplasty without inverting the images on fluoroscopy.

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SEVERE BICUSPID AORTIC VALVE (BAV) REGURGITATION IN A DYSFUNCTIONAL AND DILATED NON-COMPACTED LEFT VENTRICLE: A CASE REPORT

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Background: Bicuspid aortic valve (BAV) is the most common congenital heart disease. Up to 20% of asymptomatic adults with BAV present with moderate to severe valve insufficiency. Limited data exists regarding surgical indications and outcomes in the setting of BAV with severe LV dilatation, LV systolic dysfunction or LVNC.
Methods: We present a case report about a 32 year old male with a severe case of dilated cardiomyopathy in the setting of severe BAV regurgitation and LVNC syndrome. This patient upon presentation had no prior cardiac history and presented with a chief complaint of dyspnea on exertion and chest pain. Echocardiogram revealed the aortic valve as bicuspid with an eccentric, posteriorly-directed, severe aortic regurgitation originating between the right and non-coronary cusps. There were mild mitral and moderate pulmonic regurgitations. The decision to undergo surgical aortic valve replacement was made after extensive cardiac assessment, including stress testing, cardiac catheterization and cardiac MRI with good early outcomes.
Discussion: Our case represented the most extreme, documented presentation in the spectrum of BAV with dilated and dysfunctional, non-compacted LV. The case was complicated by the presence of left ventricle (apical and lateral wall) non-compaction; a common distribution in patients with BAV. Overall, LVNC patients with larger LVEDD, NYHA III-IV or chronic atrial fibrillation carry worse prognoses. Management reports of patients with LVNC requiring cardiac surgery are limited, and the impact of LVNC on myocardial protection strategies is not known. Delineation of the myocardial function, presence of ventricular thrombi, and inducible arrhythmias must be known when considering surgery.
Conclusion: There exists uncertainty in the management of the patient with regurgitant BAV with severe left ventricular dilatation, due to a lack of specific guidelines. Therefore, further research is warranted to provide guidelines for the care of such patients.

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HEPARIN VERSUS BIVALIRUDIN IN TRANSCATHETER AORTIC VALVE IMPLANTATION

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Background: We aimed to compare safety and efficacy of direct thrombin inhibitor bivalirudin to unfractionated heparin during transcatheter aortic valve implantation (TAVI).
Methods: In this retrospective analysis, 459 patients underwent TAVI between 2007 and 2012, 338 patients received bivalirudin, and 121 patients received UFH. In the bivalirudin group, the Sapien XT valve was implanted in 158 (46.9%) patients, while 179 (53.1%) received a Medtronic CoreValve. In the heparin group, only Medtronic CoreValve was implanted. The primary outcome of interest was the incidence of any bleeding. Secondary outcomes of interest were all cause mortality and cardiovascular mortality at 72 h post-procedure and 30 days.
Results: No significant difference between the groups was observed for life-threatening bleeding (2.4% for bivalirudin vs. 3.3% for heparin, p=0.59), major bleeding (8.3% vs. 8.2%, respectively, p=0.98) and minor bleeding (8.3% vs. 7.4%, respectively, p=0.76). At 72 h post-procedure, all-cause mortality was 3.0% in the bivalirudin group and 3.3% for the heparin group (p=0.88), whereas cardiovascular mortality was 3.0% in the bivalirudin group and 2.5% in the heparin group (p=0.77). At 30 days, all-cause mortality was 5.3% vs. 4.1% in the bivalirudin and heparin groups (p=0.57) and cardiovascular mortality was 4.4% vs. 2.5% (p=0.33). Device success (VARC-2 composite endpoint) was 94.0% in bivalirudin-treated and 92.6% in heparin-treated patients (p=0.60). The Early Safety at 30 days was 85.3% in the bivalirudin treated group compared to 83.6% in the heparin group (p=0.65).
Conclusions: Bivalirudin has a similar safety and efficacy profile as weight adjusted UFH during TAVI procedure.

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IMPACT OF LVH BY ECG VOLTAGE CRITERIA ON TRANS-CATHETER AORTIC VALVE REPLACEMENT OUTCOMES

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Background and hypothesis: The association of Left Ventricular Hypertrophy (LVH) by electrographic voltage criteria and trans-catheter aortic valve replacement (TAVR) outcomes has not been investigated. LVH is expected in patients with severe aortic valve stenosis undergoing TAVR. Absence of LVH by voltage criteria may be indicative of "burned-out" cardiomyopathy and portend a poor prognosis.

Methods: A retrospective chart review was conducted in 200 consecutive TAVR patients. ECG data was collected and stratified into LVH (yLVH n=51), and normal wall thickness (noLVH n=149). Outcomes were adjudicated according to the PARTNER trial definitions (NEJM 2010; 363: 1597-1607). Analyses of variation, correlation, chi-square, and logistic regression were used. The study was approved by the institutional IRB. *Results*: There was no association between any LVH and previous CVA, PVD, previous smoking history, hyperlipidemia, hypertension, or diagnosis of COPD. In addition, LVH was not associated with significant difference in age at time of procedure (83.0 +/- 1 vs. nLVH 81.8 +/- 0.6 years old; p=0.35), renal function (Cr 1.3 +/- 0.1 vs. noLVH: Cr 1.5 +/- 0.1 mg/dL; p=0.278), aortic valve area (0.746 +/- 0.025 vs. noLVH: 0.776 +/- 0.48 squared cm; p=0.672), aortic valve gradient (43.3 +/-2.2 vs. noLVH: 44.1 +/- 1.5 mmHg; p=0.788), LV ejection fraction (49.7 +/- 1.7 vs. noLVH 49.8 +/- 0.9%; p=0.95), and length of stay in ICU (146 +/- 33 vs nLVH: 117 +/- 7 hours; p = 0.203). Similarly, LVH was not associated with an increased incidence of post-TAVR death, re-hospitalizations, stroke, or acute renal failure.

Conclusion: Presence or absence of LVH by ECG voltage criteria in TAVR patients is not associated with significant differences in valve area, ejection fraction, or co-morbidities. And more importantly, it does not lead to inferior TAVR outcomes.

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ECHOCARDIOGRAPHIC EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION AFTER CLOSED MITRAL VALVOTOMY

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Background: Mitral stenosis is frequent valvular complication of rheumatic heart disease, leading to reduced LV filling during diastole, causing diastolic dysfunction. The aim of this study is 2D Echocardiographic Evaluation of left ventricular diastolic function after closed mitral valvotomy in rheumatic mitral stenosis.
Methods: This is a single centre one-year comparative study consisting of twenty nine patients of rheumatic severe mitral stenosis. We analyzed preoperative and post operative transthoracic 2D echocardiographic parameters of diastolic function and compared both data to evaluate improvement of diastolic function in all patients who underwent closed mitral valvotomy.
Results: 29 patients underwent successful operation; average age was 34.97 ± 9.74 with 62.1% females. Maximum patients were in NYHA grade 3 (69.0%) and 4 patients were in AF. Wilkins score ranged from 6 to 10. MVA increased from 0.77 ± 0.13 to 2.32 ± 0.26, EF increased from 61.38 ± 4.61 to 64.79 ± 3.22, DT (ms) decreased from 231.55 ± 49.31 to 168.28 ± 14.30, E/A ratio reverted to 1.70 ± 0.54 from 0.89 ± 0.39. TEI index improved from 0.50 ± 0.03 to 0.39 ± 0.06, MIPV (cm/sec) increased from 47.28 ± 3.71 to 57.86 ± 3.19. In peri-operative and follow up, there was no incidence of Mitral regurgitation and thrombo-embolic incident. There was no mortality.
Conclusion: Surgical closed mitral valvotomy produce excellent and comparable early hemodynamic improvement, significant improvement in clinical stage of disease and improvement in diastolic function.

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ROLE OF UNUSUAL PREDICTORS OF PERIVALVULAR AORTIC REGURGITATION POST TRANS-CATHETER AORTIC VALVE REPLACEMENT

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Background: Clinical outcome in Trans-catheter aortic valve replacement (TAVR) is affected by presence of post-procedure peri-valvular aortic regurgitation (PAR). We studied the role of pre-procedural and intra-procedural factors in predicting PAR post TAVR.
Methods: Data for all patients who underwent TAVR from December 2012 to September 2014 were retrospectively studied. Predictors including age, gender, BMI, preexisting aortic regurgitation, pre-procedural left ventricular ejection fraction (LVEF) and size of the prosthetic valve (Edwards Sapien, Edwards Lifesciences, Irvine, California). were studied for their relation to the presence of PAR after TAVR. Patients were divided into Group A, having post-TAVR PAR and Group B without post-TAVR PAR. Statistical analysis was done using Fischer test.
Results: Of the total 54 patients who underwent TAVR, 37 patients were included in Group A and 17 patients in Group B with 56.8% versus 47% were males (p= 0.566)and 78.4% versus 76.5% had pre-existing AR(p= 1.0) respectively. See Table 1.
Conclusions: Pre-existing aortic regurgitation, LVEF and size of the implanted prosthetic valve at aortic position are not predictors of PAR post-TAVR procedure. The role of demographic factors like age, gender and BMI is also not significant in the pathogenesis of post –TAVR PAR. Further large studies will be needed to search other possible predictors.
Table 1.

Predictors	Group A (n=37) Mean± SD	Group B (n=17) Mean± SD	p-value
Age	83.2 ± 6.4	84.9 ± 4.3	.253
BMI	29.7±5.9	28.3±5.9	.411
LVEF	56.49±13.9	60.6±9.3	.209
Size of prosthetic valve	24.8±1.8	24.6±1.5	.684

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OUTCOMES OF PATIENTS UNDERGOING CONCOMITANT AORTIC AND MITRAL VALVE SURGERY IN THE PHILIPPINE HEART CENTER FROM YEAR 2000 - 2013

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Background: There has been a steady increase in cardiac valve surgery performed for concomitant aortic and mitral disease in the Philippine Heart Center. Although the frequency of double valve surgery (DVS) remains low compared to isolated valve surgery, more patients are undergoing the said procedure.
The main objective of this paper is to examine the outcome of patients undergoing DVS at the Philippine Heart Center in terms of in-hospital mortality and postoperative complications.
Methodology and Results: This is a report of a retrospective study of the 312 patients who underwent AV and MV surgery from 2000 to 2013 at the Philippine Heart Center. In-hospital mortality was 7.9% and was higher for men, patients with smaller BSA and those who had concomitant CABG. The most common post-operative complication was pulmonary for the majority of patients. The more common complication noted among those who died was renal failure requiring dialysis.
Conclusion: The in-hospital mortality for the Philippine Heart Center for DVS from 2000-2013 is 7.9%. The center's in-hospital rate was lower compared to those published by Hannan et al, Galloway et al, and Hellgren et al. Reports in these centers noted mortality ranging from 14-18%. The most common postoperative complication for all patients was pulmonary and the most common complication for those who died was acute renal failure requiring hemodialysis.

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AN UNUSUAL CAUSE OF HEMOPTYSIS DURING PREGNANCY

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A 25year old female, 27 weeks pregnant, presented to our institution for evaluation of two episodes of hemoptysis. She described the amount to be 4-5 tablespoons each time. In addition, she also reported feeling short of breath on exertion for a week prior to presentation. She denied any symptoms of cough, fever, chills, weight loss, pleuritic chest pain, asymmetric leg swelling, sick contacts, recent travel outside the country or similar symptoms in her previous pregnancy. Vitals were noted to be stable. Physical exam was significant for a diastolic murmur at the apex and trace pitting edema in bilateral lower extremities. Laboratory tests revealed normal hematocrit, platelets, coagulation factors and liver function tests. Chest x-ray was significant for mild pulmonary congestion. Transthoracic echocardiogram revealed a severely dilated left atrium and a large (4.5cmX2.4cm), pedunculated, mobile, left atrial mass, attached to the inter-atrial septum, causing obstruction to the left ventricular inflow. This was considered to be most consistent with an atrial myxoma. The mean transmitral gradient was calculated to be 18mmHg corresponding to severe mitral stenosis. An interdisciplinary meeting was called to decide on the optimal timing of tumor resection. After careful review of available options and patient consent, a decision was made to proceed with surgery with careful monitoring of fetus intra-operatively. The patient underwent open heart surgery and resection of the tumor successfully with no adverse events to the fetus. She was subsequently discharged with close follow up and delivered a healthy full term fetus at 39 weeks by repeat cesarean section. There is paucity of data to guide management of patients with left atrial myxoma causing functional mitral stenosis during pregnancy and this case is an example of a favorable outcome from early intervention in such cases.

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POST ORTHOTOPIC HEART TRANSPLANTATION COMPLICATED BY DISSEMINATED BLASTOMYCES

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Introduction: Post transplant immunosuppression is necessary to prevent organ rejection. This immunosuppression, however, can lead to a host of complications arising from opportunistic infections. We present a case of disseminated blastomycosis manifested only as a skin lesion in an asymptomatic patient post-orthotopic heart transplantation.
Case: A 64-year old female who had recently undergone orthotopic heart transplant for end-stage ischemic cardiomyopathy presented for a scheduled routine cardiac biopsy. A crusted plaque was observed at the nasal tip. This started six months after surgery as a pimple that she repeatedly tried to extract by squeezing, which resulted in redness and crust formation. Her immunosuppressive and prophylactic medications included: Mycophenolate, Tacrolimus, Prednisone, Bactrim, Acyclovir, Valganciclovir, Pyrimethamine/Sulfadiazine, and Fluconazole. On physical exam she was flushed, with a large and exquisitely tender crusted necrotic lesion involving almost the entire half of the nose anteriorly, the left forehead and right side of the neck. She had decreased air entry over the right lung field. Chest CT showed bilateral nodular pulmonary infiltrates with confluence in the posterior right upper lobe. Blood cultures for aerobes/ anaerobes were negative. Both Excisional biopsy of the nasal cutaneous ulcer and bronchial biopsy, demonstrated numerous fungal yeast forms morphologically consistent with Blastomyces. Cultures of both specimens grew Blastomyces dermatitidis, with MRSA superinfection of the nose. She received 14 days of IV Amphotericin B for disseminated blastomycosis and 7 days of IV Vancomycin for MRSA. Her symptoms and cutaneous lesions improved and she was maintained on Itraconazole treatment for one year.
Discussion: This case illustrates a delicate balance that must be struck between suppressing the immune response to prevent graft rejection and avoiding over-immunosuppression that can lead to susceptibility to infection. Thus, in any post transplant patient, clinicians should watch out for any signs of infection even if the patient is asymptomatic.

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LEFT ATRIAL MYXOMA PRESENTING AS PAROXYSMAL ATRIAL FIBRILLATION

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Introduction: We present a case of large left atrial myxoma causing functional mitral stenosis with initial presentation of new onset atrial fibrillation.
Case Presentation: 55 year old female with past medical history significant for hypertension and diabetes presented with generalized weakness, fatigue, lightheadedness, shortness of breath and palpitations for the past two weeks. In the ER, she was found to be in atrial fibrillation and subsequently converted to normal sinus rhythm. Physical examination revealed a diastolic flow sound in the apical region. Echocardiogram revealed a moderately dilated left atrium with a large (2.5 x 4.7) myxoma attached to the interatrial septum which was prolapsing into the left ventricular cavity with irregular borders creating a functional mitral stenosis with valve area estimated at 1.1. Surgical opinion was sought and patient underwent minimally invasive atrial myxoma resection through anterior minithoracotomy. The patient tolerated the procedure well and her symptoms resolved. She has been doing well since then.
Discussion: Myxomas are the most common primary cardiac tumors and about 75% are in the left atrium. Initial suspicion for myxomas is reported to be as low as 5.7%. Systemic embolization is present in about 30% of patients and valvular obstruction can sometimes result in sudden cardiac death. Left ventricular failure caused by partial obstruction of the mitral valve orifice by the myxoma can also be observed. Myxomas might be initially misdiagnosed as mitral stenosis, but severe mitral stenosis, as seen in our patient has been described in only 14% of cases. A diastolic murmur on auscultation is found in 64-67% of cases while classical tumor plop sound is found in 15% of cases. Myxomas are benign and have excellent long term prognosis with low recurrence rate after surgical resection. Myxomas should be considered in the differential diagnosis in patients with suspected mitral valve disease.

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PREGNANCY RELATED SPONTANEOUS CORONARY ARTERY DISSECTION: WHEN PCI WAS NOT ENOUGH

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Introduction: We present a young otherwise healthy female with no cardiac risk factors with chest pain, initially normal EKG and elevated cardiac biomarkers with spontaneous LAD dissection.
Case Presentation: A 28 year old female who had an uncomplicated vaginal delivery 5 days ago, presented to the ER with sudden onset of chest pain. This was associated with shortness of breath and diaphoresis. Her cardiopulmonary exam was benign. Initial set of cardiac enzymes revealed CK-MB of 76 and Troponin 0.08. Cardiac enzymes were progressively elevated. A stat bedside echocardiogram revealed anteroseptal and apical akinesis. Emergent cardiac catheterization revealed an acute spirally dissected LAD through the proximal mid-segment, with 90% stenosis. The lesion was successfully stented using three drug eluding stents. Within an hour of the procedure, her chest pain recurred, and the EKG showed ST elevations, with non sustained ventricular tachycardia. A second catheterization revealed retrograde propagation of the dissection into the proximal LAD and back into the left main trunk. She underwent emergent CABG, from which she recovered well.
Discussion: Spontaneous coronary dissection should be considered in any young female patient without a previous cardiac history or risk factors, who presents with cardiac arrest or an acute coronary syndrome. The optimal management is unclear because of the limited clinical experience. Emergent coronary angiography followed by PCI or CABG is likely to offer the best survival. In pregnant women, dissection may be a consequence of increased hemodynamic stress or of hormonal effects on the arterial wall. Postpartum status is present in 18% women with mean postpartum period of 38 days.ST-elevation myocardial infarction (STEMI) is present in 49% of cases. The left anterior descending coronary artery is the most frequently affected vessel. Specific guidelines still need to be established.

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BODY MASS INDEX AND MORTALITY IN A VERY LARGE COHORT: IS IT REALLY HEALTHIER TO BE OVERWEIGHT?

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Purpose: To study risk of death in relation to body mass index (BMI) in 273,843 free-living persons.
Background: Despite substantial published literature controversy persists about the optimal level of body weight. The overall BMI-mortality risk is J-shaped, with underweight persons and obese persons at increased risk. Many experts define "normal" BMI as 18.5-24.9 kg/m^2, with 25-29.9 kg/m^2 as "overweight" and ≥30 kg/m^2 as "obese". Obesity is subdivided into 30-34.9 kg/m^2 (grade I), 35-39.9 kg/m^2 (grade II) and ≥40kg/m^2 (grade III). Studies consistently show higher mortality for grade II-III obesity, but results conflict for the "overweight" category and even grade I obesity.
Methods: We used logistic regression with 8 covariates including smoking; the BMI referent was 18.5-24.9 kg/m^2.
Results: With average follow-up of >30 years, there were 103,218 deaths, 41,215 attributed to cardiovascular (CV) causes and 62,003 to non-CV causes. Hazard ratios (HR) and [95% confidence intervals] for all deaths in relation to BMI were: <18.5=1.1 [1.0-2.0], 25-29=1.1 [1.1-1.2], 30-34=1.5 [1.4-1.5], 35-39=2.1 [1.9-2.3], and ≥40=2.7 [2.4-3.0]. Increased risk of persons with BMI below 18.5 kg/m2 was concentrated in non-CV deaths; for CV deaths these persons had a HR of 0.7 (0.6-0.7). For the overweight and grade 1 obesity categories, the HRs were 1.4 and 1.8 for CV deaths; for non-CV deaths these HRs were 1.0.
Conclusions: These data show the importance of examining causes of death when considering risks associated with underweight, overweight and obesity. For risk of CV death it is better to be thin.

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MEDITERRANEAN DIET: FROM HISTORY TO CULTURE TO MEDICINE

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Cardiometabolic diseases and cancer dominate the health status of the majority of westernized populations. In the context of dietary control, Mediterranean diet has been proposed as a healthy eating dietary pattern based on evidence that greater adherence to this diet is associated with lower all-cause and disease-specific survival. Its origins begin thousands years ago, in Mediterranean basin, in the middle 1960s this dietary pattern came to surface. Although there is not one Mediterranean diet, a high consumption of foods of vegetable origin, such as fruits, vegetables, legumes, nuts, cereals and whole-grains; olive oil as the principal source of fat; fish and poultry consumed in low-to-moderate amounts; relatively low consumption of red meat; and moderate consumption of wine, normally with meals, could be considered the most dominant characteristics of this dietary pattern.

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STATE-OF-THE-ART CVD PREVENTION: LOOKING BEYOND AND INTERPRETING THE ACC/AHA PREVENTION OF CARDIOVASCULAR DISEASE GUIDELINES

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The ACC/AHA released evidence-based guidelines on cardiovascular disease (CVD) risk assessment, lifestyle, obesity, and cholesterol management. The risk assessment guideline recommended a new "Pooled Cohort Equations" calculator to estimate 10-year and lifetime risk of atherosclerotic CVD (ASCVD), and other measures-- premature family history of CVD, C-reactive protein, ankle brachial index, and coronary calcium scores to further stratify risk and inform the treatment decision. The lifestyle guideline focused on dietary patterns and physical activity for blood pressure and LDL-cholesterol reduction and the obesity guideline highlighted the importance of multiple intensive personalized sessions with lifestyle interventionalists and the value of moderate weight loss in control of risk factors. The cholesterol guideline focused on the identification of four statin eligible groups: ASCVD, diabetes, LDL-cholesterol >=190 mg/dl, and >=7.5% 10-year risk of ASCVD, but emphasizing the importance of the clinician-patient risk discussion when considering initiation or intensification of therapy. While the guideline does not support specific initiation or target LDL-C levels, emphasis is on therapeutic response, still requiring regular monitoring of LDL-C, and non-statin agents can be considered if needed response is not achieved. The IMPROVE-IT results as well as emerging data on newer agents provide promising opportunities to address lipid residual risk in persons not adequately tolerating or responding to statins. Other criteria to address residual risk such as consideration of non-HDL-C levels have been recommended by the recent National Lipid Association guideline. Finally, recent blood pressure guidelines have recommended revised cutpoints for blood pressure control where benefit has been shown. Coordinated efforts for composite risk factor control, electronic medical record adoption of risk assessment tools, identification of providers' patients not adhering to recommended therapies, and e-health-based personalized CVD management strategies will be important steps to implement these guidelines and achieve further progress in CVD prevention efforts.

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GENDER DIFFERENCES AND HEALTHY AGING

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Forty years ago, few cohort studies of cardiovascular disease (CVD) included women and fewer still included diabetes or glycemia as risk factors. I describe here the Rancho Bernardo Study (RBS), a single-site, >40-year cohort study of sex differences in heart disease and how diabetes modifies women's natural cardioprotection. More than 6,000 participants were followed for morbidity and mortality, with nearly 3,000 survivors (and death certificates for >85% of decedents). In RBS, more than one-half of diabetes cases were undiagnosed without an oral glucose tolerance test (OGTT); more women than men had isolated post-challenge hyperglycemia as their only glucose evidence of diabetes; men had more diabetes, with higher fasting but lower post-challenge glucose levels than did women; women with diabetes had more classic CVD risk factors than did men; and excess risk factor clustering partially explained how diabetes eradicates female cardioprotection. Post-challenge glucose was a stronger CVD risk factor than was fasting glucose. Endogenous insulin was not an independent CVD risk factor in women or men. Men with higher testosterone levels developed fewer cases of diabetes and had fewer metabolic syndrome components. In men, higher total testosterone levels predicted reduced risks for all-cause and CVD but not cancer mortality. In women, both extremes of bioavailable testosterone predicted fatal coronary heart disease but not all-cause mortality. Summary point estimates from large systematic reviews of individual data have replicated most RBS findings. Ongoing research can further clarify how diabetes modifies women's cardioprotection from mid-life to old age. Future research may also identify if and how lifestyle variables influence gender differences and healthy aging.

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CARDIOVASCULAR RESPONSES TO THREATFUL CHALLENGES IN PERSONS WITH HIGH TRAIT ANXIETY

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An optimal cardiovascular response to threatening challenges is indispensable for coping with the situation. Anxiety disorders and high anxiety as a personality trait have been expected to be associated with autonomic lability and hyperreactivity during stress. Data published on this topic are rather variable. We have performed a series of studies in healthy humans and patients to clarify the relationship between anxiety and cardiovascular activation under stress conditions. In a group of healthy volunteers with high trait anxiety, we have observed an exaggerated hear rate (HR) response during psychosocial stress compared to non-anxious individuals. However, in contrast to general expectations, plasma epinephrine and norepinephrine responses were lower in anxious subjects. Treatment of anxious subjects with a mixture of aminoacids lysine and arginine (10 days) was able to normalize stress-induced catecholamine responses. We have revealed that the influence of trait anxiety on cardiovascular activation is gender dependent. Anxious women in the follicular phase of the menstrual cycle exhibited a greater stress-induced rise in systolic blood pressure compared to anxious women in the luteal phase and to non-anxious women in both phases. Accordingly, we have brought evidence for a reduced neuroendocrine response to stressors in patients with an anxiety disorder or with immune dysfunction accompanied by anxiety. Patients with different types of allergy showed increased trait anxiety and attenuated heart rate response during psychosocial stress. Similarly, the activity of alpha-amylase, an enzyme activated by the sympathetic nervous system, was reduced in patients compared to controls. In conclusion, high trait anxiety appears to be associated with impaired coordination of the stress response, rather than global hypo- or hyper-responsiveness.
Supported by APVV-0496-12.

CARDIOVASCULAR DISEASE PREVENTION AND RISK FACTORS

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ASSOCIATION OF MODIFIABLE LIFESTYLE FACTORS AND RISK OF TOTAL AND CARDIOVASCULAR MORTALITY AMONG OLDER US MALE PHYSICIANS

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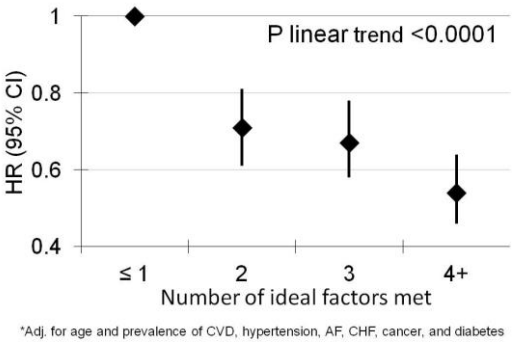
Background: While previous studies have reported beneficial effects of healthy lifestyle factors on the risk of major chronic diseases and mortality in younger adults, only limited data are available for older adults.
Objective: We sought to test the hypothesis that being ideal on few simple and modifiable factors (smoking, exercise, diet, body weight, and alcohol consumption) is associated with a lower incidence of total, cardiovascular disease, and cancer mortality among male physicians aged ≥65 years at baseline.
Methods: Prospective study of 8,321 male physicians from the Physicians' Health Study (PHS) who completed a food frequency questionnaire between 1999 and 2001. Information on lifestyle factors was self-reported at baseline and death was ascertained by the PHS endpoint committee. Ideal factors were current non-smokers, body mass index below 25 kg/m^2, vigorous exercise, alcohol intake of 1-2 drinks/d, and being in the top two quintiles of the alternate Healthy Eating Index. We used Cox proportional hazard model to estimate adjusted hazard ratios with 95% confidence intervals according to the number of prevalent ideal factors at baseline.
Results: Mean age was 73.2 years (range: 65.0 to 97.6 y) and 95% of study participants were Caucasian. During a mean follow up of 9 years, 1600 subjects died (including 444 CVD deaths and 505 cancer deaths). There was an inverse association between the number of ideal lifestyle factors met and the incidence of death (**Fig.1**). Compared to subjects meeting ≤ 1 factor, hazard ratios (95% CI) for CVD death were 0.79 (0.59-1.04), 0.80 (0.60-1.04), and 0.57 (0.41-0.79) for meeting 2, 3, and 4+ ideal factors, after adjustment for age and prevalence of CVD, hypertension, cancer, heart failure, atrial fibrillation, and diabetes at baseline, p trend 0.002. Corresponding values were 0.70 (0.55-0.90), 0.58 (0.45-0.74), and 0.51 (0.38-0.67), p trend <0.0001 for cancer deaths and 0.65 (0.52-0.82), 0.67 (0.54-0.84), and 0.55 (0.43-0.71), p trend <0.0001 for other causes of death. While no interaction was seen between number of ideal factors and prevalent diabetes, hypertension, cancer, or CVD on the risk of death, this relation was stronger in subjects <75 y [adjusted HR: 1.0 (ref), 0.60 (0.49-0.74), 0.55 (0.44-0.68), and 0.44 (0.34-0.57) for ≤ 1, 2, 3, and 4+ ideal factors, p trend <0.0001] than in subjects 75+ y [corresponding HRs: 1.0 (ref), 0.82 (0.67-1.00), 0.80 (0.66-0.97), and 0.65 (0.52-0.80), p trend 0.0001], p for interaction 0.02.
Conclusion: Even at older age, adherence to healthful lifestyle factors is associated with a lower incidence of total and cause-specific mortality in male physicians. These data suggest that even among older adults, it may still be important to recommend healthful behaviors to reduce mortality.

Fig.1. HR (95% CI) for total mortality *



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ASSESSMENT OF CARDIOVASCULAR PROGNOSIS IN DIABETIC PATIENTS. THE ROLE OF CARDIAC IMAGING

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Diabetes mellitus is major risk factor for cardiovascular disease and associated complications. Cardiovascular disease may be silent or presents with atypical symptoms due to autonomic neuropathy and therefore, many patients with minimal or no symptoms remain at high risk of morbidity and mortality. Cardiovascular imaging plays a major role in the diagnosis and risk stratification of coronary artery disease in diabetic patients. In patients who are able to exercise, a normal stress echocardiogram identifies patients at low risk. The pattern of multi-vessel abnormality is associated with a dramatic increase in cardiac events with approximately a third of these patients developing cardiac death and non -fatal myocardial infarction within a few years after the test. Myocardial contrast imaging during dobutamine stress test is a promising tool and offers improved sensitivity at submaximal heart rate and allows incremental risk assessment. Myocardial perfusion imaging with radionuclide techniques is widely used and has a well established diagnostic and prognostic value. However, even after a normal study, diabetic patients remain at higher of cardiac events compared to non diabetic patients with a normal imaging study. The low risk warrantee period after a normal imaging study is shorter in diabetic versus non diabetic patients which necessitate closer follow of high risk patients. Coronary calcium scoring is useful in detecting early phase of atherosclerosis and provides objective information to predict cardiac events. CT angiography may serve as a gate keeper for invasive angiography with a high sensitivity. Prognostic value is established, but information is largely influenced by early revascularization. Limitations include artifacts, irradiation and risk of contrast nephropathy. A careful understanding of the advantages and limitations of anatomical and functional imaging techniques allows better guide for risk assessment, implementation of aggressive preventive therapy and selection of patients who may benefit from revascularization.

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TIME OF ONSET OF CARDIAC EVENTS: DOES GENDER MATTER?

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Background: Various acute cardiovascular diseases exhibit predictable-in-time 24-hour, weekly or seasonal patterning in their nonfatal and fatal events, e.g., myocardial infarction, sudden cardiac death, abdominal, aortic, and thoracic dissections, venous thromboembolism, hemorrhagic and ischemic stroke.
Objective: Knowledge of these temporal patterns not only helps guide patient care, but research of their underlying endogenous mechanisms and external triggers aimed to the development and application of effective preventive and therapeutic strategies. However, no particular attention has been devoted to the existence of possible gender-related differences in the time of onset of life-threatening events.
Methods: We performed a systematic review of the literature of the last two decades dealing with temporal patterns of cardiovascular events.
Results: Two hundred and fourteen items were found. Eighty-four studies (total: ~1.640,000 people) focused on circadian aspects, 41 (total: ~2,040,000 people) focused on weekly aspects, and 89 (total: ~2,400,000 people) focused on seasonal aspects. Although the majority of studies (170 out of 214, 79%) provided information on number of cases in men/women subgroups, only less than one third (29%) performed separate analyses by gender and reported results for circadian (26/84, 31%), weekly (13/41, 32%), and seasonal (23/89, 26%) onset of events. For each disease, single patterns by gender will be presented.
Conclusions: Many different pathogenetic mechanisms may explain the existence of a temporal variation in the onset of acute cardiovascular diseases, and possible differences by gender.

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NEW INSIGHTS INTO SEX-BASED DIFFERENCES IN HEART DISEASE

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The role of coronary microvascular dysfunction (CMD) has now been more widely accepted as having a role in those with symptomatic non-obstructive coronary artery disease. However, the role of CMD in women compared to men is only recently being explored. Risk factors that predispose to CMD will be discussed. We will also discuss the sequela of CMD, including heart failure with preserved ejection fraction, Takasubo's cardiomyopathy, and sudden death. We will also discuss the role of stress in modulating endothelial dysfunction. Finally, both pharmacological and non-pharmacological treatment of CMD will be discussed.

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CARDIAC DYSFUNCTION SUBSEQUENT TO EXPOSRE TO OZONE; AN AIR POLLUTANT

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Even though a number of advancements have been made toward identifying the risks associated with cardiovascular disease (CVD), and these have resulted in a decline in mortality, many patients with cardiac disease show no established previous risk. It appears other unknown factors contribute to the pathophysiology of CVD. Out of 350,000 sudden cardiac deaths each year in the United States, 60,000 deaths have been linked to air pollution, suggesting a detrimental role of environmental pollutants in the development of CVD. The present study tested the hypothesis that chronic ozone (O3) exposure enhances the sensitivity to myocardial dysfunction. Sprague Dawley rats were continuously exposed for 8 hrs/day for 28 and 56 days to filtered air or 0.8 ppm O3. In-vivo cardiac function measured as LVDP, +dP/dt, –dP/dt and LVEDP after 24 hours of exposure, was significantly decreased and increased respectively in ozone exposed animals compared to rats exposed to filtered air. Attenuation of cardiac function subsequent to ozone exposure was associated with increased myocardial TNF alpha levels and lipid peroxidation as well as decreased myocardial activities of superoxidase dismutase (SOD) and IL-10. These data suggests an ozone-induced enhanced sensitivity to myocardial injury may be due to promoting levels of oxidative stress and increased activity of inflammatory mediators.

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ADJUDICATED VERSUS ADMINISTRATIVE HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Heart failure (HF) with preserved ejection fraction (HFpEF) is associated with readmission and mortality rates similar to HF with reduced ejection fraction (HFrEF). No disease-modifying therapy for HFpEF exists to date, partially because of the multifactorial pathophysiology of HFpEF and the heterogeneity of patients. Studies from administrative databases report that HFpEF represents 40%-60% of HF cases. However, limited prospective data suggest a lower proportion, and enrollment in recent HFpEF trials has been slower than anticipated, suggesting that (1) the proportion of HF patients fulfilling all clinical criteria for HFpEF may be considerably lower and (2) administrative data may not have been as specific to exclude patients with recovered ejection fraction (HFrecEF) or specific cardiomyopathies. Therefore, more detailed data are needed on HFpEF epidemiology in order to properly design clinical trials. In a study of 1752 outpatients who received care associated with designated ICD-9 codes between 01/01/2012 and 03/31/2012 in Emory Healthcare (Atlanta, GA), we confirmed the diagnosis of HF in 1652 patients (94.3%). After individual adjudication, we classified 19.4% as HFpEF, 16.2% as HFrecEF; and 60.0% as HFrEF, while 4.3% had HF due to special causes. In comparison, the proportion of HFpEF cases based of ICD-9 codes and last EF without adjudication would have been 39.0%. HFpEF patients were older, more likely to be female, and had a higher burden of comorbidities compared to HFrecEF. After 2 years, age- and gender- adjusted mortality was 10.2% in HFrEF, 8.6% in HFpEF, and 4.4% in HFrecEF patients (stratified log-rank P=0.005). We concluded that (1) the proportion of clinically verified HFpEF is considerably lower compared to administrative estimates; (2) many patients with preserved EF actually represent HFrecEF, which has a more favorable prognosis; and (3) a large number of HFpEF patients would not be eligible for clinical trials due to serious concomitant conditions.

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THE HEART FAILURE CLINIC: TAKING CENTER STAGE IN CHRONIC DISEASE MANAGEMENT

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Acute decompensated heart failure, because of its dramatic, albeit often insidious presentation, high intensity acute care requirement and relatively high in-patient mortality has dominated our focus on what "is" heart failure. The reality is that the major focus needs to shift towards viewing heart failure as a chronic disease, with often predictable (and preventable) exacerbations, that requires active, lifelong management and innovation. The heart failure clinic has been variably designed and implemented but often has been structured with parallel capabilities of in-patient care, focusing on acutely optimizing fluid and electrolyte status, normalizing filling pressures and augmentation of guideline driven medical strategies.

The heart failure clinic therefore finds itself with a broader mission for patients, families and providers. A reasonable structural framework for the topography of heart failure care include understanding the entire series of transitions for the patient, their physiology and the goals of care in various post-acute care periods including early and late transitions phases, a relative plateau phase and for most at some point an advanced heart failure and/or palliation phase.

Trained heart failure workers and standardized goals and approaches lead to improved outcomes, heart failure literacy and satisfaction with this chronic disease state.

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BEYOND THE GUIDELINES - NEW OPTIONS FOR TREATING HEART FAILURE IN 2015

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The updated ACCF/AHA Guideline for the Management of Heart Failure is not even 2 years old, however, trials have suggested new potential treatment options for heart failure with reduced ejection fraction (HFrEF). Two of these trials will be reviewed. Resting tachycardia is a poor prognostic factor in HFrEF pts. Indeed, beta-blockers may improve HFrEF outcomes in part by decreasing heart rate. The SHIFT trial evaluated ivabradine (inhibitor of If current in the sinoatrial node) in HFrEF pts with LVEF <35%, in sinus rhythm with heart rate >70, and a HF hospitalization in the previous year on guideline directed medical therapy (GDMT), including a beta-blocker if tolerated. At 22.9 months follow-up, 24% of ivabradine vs 29% of placebo pts reached the primary endpoint of cardiovascular death or HF hospitalization (HR 0.82, p<0.0001). Ivabradine caused fewer serious adverse events, but more bradycardia and visual side effects. SHIFT suggests that ivabradine is beneficial when the heart rate remains >70 in HFrEF pts on GDMT. The PARADIGM-HF Trial evaluated the combined angiotensin receptor-neprilysin inhibitor LCZ696 (valsartan-sacubitril) vs enalapril in class II-IV HFrEF pts with LVEF <40%. The trial was stopped after 27 months when the boundary for benefit with LCZ696 was crossed. The primary outcome (cardiovascular death or first HF hospitalization) occurred in 21.8% of LCZ696 vs 26.5% of enalapril pts (HR .80, P<0.001). LCZ696 also decreased mortality, cardiovascular death, and HF hospitalization. LCZ696 produced more hypotension, but less renal impairment, hyperkalemia and cough. Although the study was met with enthusiastic acclaim for the benefits of LCZ696, concerns have been raised about the trial's enalapril dose (10 mg bid) and the fact that 70% of pts had class II HF. The exact role of ivabradine and LCZ696 in future HFrEF therapy remains to be determined.

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LEFT VENTRICULAR VS. BIVENTRICULAR MECHANICAL SUPPORT FOR FAILING HEARTS: MAIN CHALLENGES BEFORE DECISION MAKING

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Left ventricular assist devices (LVADs) are safer and provide better survival and better quality of life than biventricular assist devices (BVADs) but end-stage heart failure often involves both ventricles, even if its initial cause was left-sided heart disease. Right ventricular failure (RVF) is also a severe complication in about 25% of patients receiving a LVAD, with high perioperative morbidity (renal, hepatic or multi-organ failure) and mortality. Patients who receive an RV assist device (RVAD) only days after LVAD insertion fare much worse than those who receive an RVAD simultaneously with LVAD implantation. Temporary RVAD support in LVAD recipients with high risk for postoperative RVF can avoid permanent BVAD support. Thus, patients who definitely need a BVAD should already be identified preoperatively or at least intra-operatively. However, although the initial biochemical, hemodynamic and echocardiographic patient profile at admission may suggest the need for a BVAD, many risk factors may be favorably modified by various strategies that may result in avoidance of RVF after LVAD implantation.

The lecture summarizes the knowledge of risk factors for irreversible RVF after LVAD implantation and strategies to optimize RV function (preoperatively, intra-operatively and post-operatively) aimed to reduce the number of BVAD implantations. Special attention is focused on assessment of RV size, geometry and function in relation to loading conditions with the goal of predicting preoperatively the RV changes which might be induced by RV afterload reduction with the LVAD. The lecture aimed also to provide a theoretical and practical basis for clinicians intending to be engaged in this field.

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BIVENTRICULAR SUPPORT - TOTAL ARTIFICIAL HEART

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The management of advanced HF has evolved over the last decades. With better understanding of HF pathophysiology, new pharmacological agents have been introduced that have resulted in improvements in survival. For those patients that fail to improve, mechanical circulatory support with LVADs and total artificial hearts (TAHs) have served as a beneficial bridge to transplantation (BTT). The TAH has continued to play a significant role as a BTT in patients with biventricular failure and more selected indications that could not be completely helped with LVADs. Improved survival with the TAH has resulted in more patients benefiting from this technology. Improvements will eventually lead to a totally implantable device that will permanently replace the failing human heart.

The majority of the experience is with the SynCardia TAH. The original series in 1992, showed survival of 62% (30 days). In 2004 the survival to transplantation was 79% versus 46% (control). A series in 2009 reported on 100 patients who received the TAH. Of these patients, 91% had an INTERMACS profile 1. Survival to transplantation was 68.3%, while the most common cause of death was multiple organ failure. Strokes occurred in 7.9% of the patients. The TAH continues to be used as BTT in patients with severe biventricular failure (i.e., INTERMACS profile 1 and profile 2) .However, the last few years has seen an increase in its use and a better understanding of the indications for its implementation. Newer indications for BTT include: hypertrophic and restrictive cardiomyopathies, chronic graft failure post heart transplantation, arrhythmias unresponsive to conventional therapies, congenital abnormalities, RV failure post LVAD implantation or failure, cardiogenic shock secondary to postinfarction VSD, amyloidosis, cardiac malignancies and Chagas' disease.

Newer TAH's include the Carmat TAH and BiVACOR TAH. The TAH continues to have an increasing role in the management of advance heart failure.

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INTERVENTIONS USING THE ELECTRONIC MEDICAL RECORD TO IMPROVE CARE OF PATIENTS WITH HEART DISEASE

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The increased use of electronic medical records has created an opportunity to impact clinical decisions through reminders or other clinical decision support. This presentation will discuss several randomized trials of interventions that use the medical record to impact provider prescribing practices for patients with heart disease. Several trials of heart failure care will be discussed with outcomes of increased use of angiotensin converting enzyme inhibitors, beta-blockers and implantable cardioverter defibrillators in appropriate patients. Recent, unpublished data will be presented from a trial testing an intervention to reduce inappropriate echocardiography. Specifically, I will discuss how a note to the physician at the end of the echocardiography report that recommended for or against a follow-up study had an impact on subsequent testing. Potential barriers to implementing these interventions will be discussed. Data on the cost and impact will demonstrate that these types of interventions have a small but significant impact on treatment and their very low cost makes them a good value (highly cost-effective).

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REDUCTION OF 30-DAY ALL-CAUSE READMISSION IN HEART FAILURE: CURRENT EVIDENCE AND FUTURE DIRECTIONS

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Heart failure is a leading cause of hospital readmission in older adults. About a quarter of all hospitalized heart failure patients are readmitted within 30 days of discharge. The Affordable Care Act, the new United States healthcare reform law, has created provisions for financial penalties for hospitals with higher than expected 30-day all-cause readmission rates older Medicare beneficiaries. Eager to avoid this penalty hospitals are adopting strategies for transitions of care based on variable and inconsistent associations with 30-day all-cause hospital readmission from single center reports, post hoc analyses, and observational studies. Data from our peer-reviewed publication demonstrated that digoxin reduces 30-day all-cause hospital admission in ambulatory older patients with chronic systolic heart failure and that in Medicare beneficiaries with systolic heart failure, a discharge prescription of digoxin was associated with lower 30-day all-cause hospital readmission, which was maintained at 12 months, and was not at the expense of higher mortality. We have also demonstrated that ACE inhibitors, but not beta blockers, may similarly reduce 30-day all-cause readmission in heart failure patients with reduced ejection fraction.

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COENZYME Q10 AS AN ADJUVANT THERAPY IN HEART FAILURE (HF)

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Congestive heart failure has become a global epidemic and its prevalence is increasing with the increasing longevity of life and improvements in management of acute coronary syndrome, hypertension and diabetes mellitus. It is the number one cardiac cause of hospitalizations in patients above 60 years and has a prognosis worse than most of malignancies. None of the conventional and newer treatments of HF have made any significant improvement in mortality and morbidity. Coenzyme Q10 (CoQ10) levels have been found to be consistently low in HF in most of reported studies. CoQ10 by improving oxidative phosphorylation at mitochondrial levels improves cellular bioenergetics of cardiac muscle cells and also by its antioxidant, vasodilatory and membrane stabilizing effects produces symptomatic improvement when added to the conventional treatment. In our own study, the addition of CoQ10 (100-200mg/day) to conventional decongestant therapy led to significant improvement in Quality Of Life and 6 Minutes Walk Test with reduced number of hospitalizations and reduction in development of refractory stage thereby decreasing the requirement for assisted cardiac devices and cardiac transplantations. Recent international Q SYMBIO trial has also shown improvement in symptoms and MACE with some mortality reduction with CoQ10 use in HF. Thus CoQ10 can be recommended as an important adjuvant therapy in HF.

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ULTRAFILTRATION THERAPY FOR ACUTE HEART FAILURE; WHERE ARE WE STANDING IN 2015?

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The negative prognostic impact of congestion and worsening renal function in patients with decompensated heart failure has been widely recognized. As diuretics are thought to contribute to deterioration of kidney function in this setting, attempts have been made to develop therapeutic strategies that are not fully based on diuretic use in this setting. Extracorporeal ultrafiltration represents an intriguing therapy for patients with heart failure that presumably lacks the adverse impact of diuretics on renal function while portending a number of biological advantages such as higher efficiency for sodium removal and restoration of diuretic responsiveness as observed in several clinical trials. However, conflicting data have recently emerged in relation to some of the previously proposed effects possibly due to counterbalance of the potential negative mechanisms and other less understood factors. In this talk, the existing evidence on the efficiency and safety of conventional therapy for acute decompensated heart failure is briefly reviewed. Then the potential role of ultrafiltration in this setting and the advantages of this therapeutic modality over conventional management strategies are discussed along with the results of the most recent trials. At the end, controversial aspects of ultrafiltration therapy for heart failure (e.g. indications for use and impact on mortality) are explained in detail.

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COGNITIVE IMPAIRMENT IN CHRONIC HEART FAILURE

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Heart Failure and Cognitive Impairment (CI) are medical conditions that are frequently seen in older adults. Heart failure has been shown to be associated with CI beyond that seen in normal aging, and indeed the risk of CI is four times higher in patients with heart failure when compared to age-matched controls. The spectrum of cognitive impairment includes delirium, isolated memory or non-memory related deficits and dementia. Both heart failure with reduced and preserved ejection fraction has been shown to be associated with defects in different domains of cognition. Various pathophysiological mechanisms related to heart failure can contribute to cognitive decline. In different studies, CI in heart failure has been associated with higher rates of functional impairment, mortality and interference with self-care. Poor adherence to medication regimens and self-care management of heart failure is possible in patient with cognitive problems and it could be a cause for readmissions. Validated tools and criteria should be used to differentiate acute cognitive decline or delirium from chronic cognitive decline or Mild Cognitive Impairment (MCI)/Dementia. These conditions are not routinely screened for in clinical practice settings with heart failure population and guidelines on optimal assessment strategies are lacking. Certain heart failure treatment approaches and strategies may help to reduce cognitive decline in these subjects. Early detection of CI may help to improve clinical outcomes in older adults with heart failure.

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INCREASING UTILIZATION OF THE BIOPROSTHETIC VALVE IN PATIENT UNDER 60- REAL WORLD EXPERIENCE CONTRARY TO GUIDELINE RECOMMENDATION

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Brigham and Women's Hospital, Boston, MA, USA

Objectives: To analyze increasing utilization of bioprosthetic aortic valves in patients under age 60.
Background: The 2014 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend mechanical valves for patients under age 60. Although bioprosthetic valves are preferred for ease of management, the risk of reoperation from deterioration is a major concern for young patients. We assessed this trend in our patients and compared outcomes by device type.
Methods: We analyzed 6,421 patients undergoing primary aortic valve replacement (AVR) from 1994 to 2014. Of these, 1297 were under age 60.
Results: The mean age was 49.7 (+/- 8.2) years, and 31% were women. Concomitant coronary bypass was performed in 21.7% and mitral valve procedures in 16.1%. Operative mortality was 2.2%. Before 2002, mechanical valves were implanted in 78% of patients while after 2003; mechanical valves were implanted in only 45% (Figure 1, P<0.001). Mechanical valves were implanted in younger patients (48.3±8.6 vs 51.4±7.5, p=0.001) and those on preoperative warfarin (2.9% vs 0.7%, p=0.004). The mechanical valve group trended toward higher operative mortality (2.9% vs 1.2%, p=0.054), but no long-term survival advantage.
Conclusions: Contrary to ACC/AHA recommended guidelines, our study showed increase use of bioprosthetic valves during AVR in patients under age 60 with similar long-term outcomes.

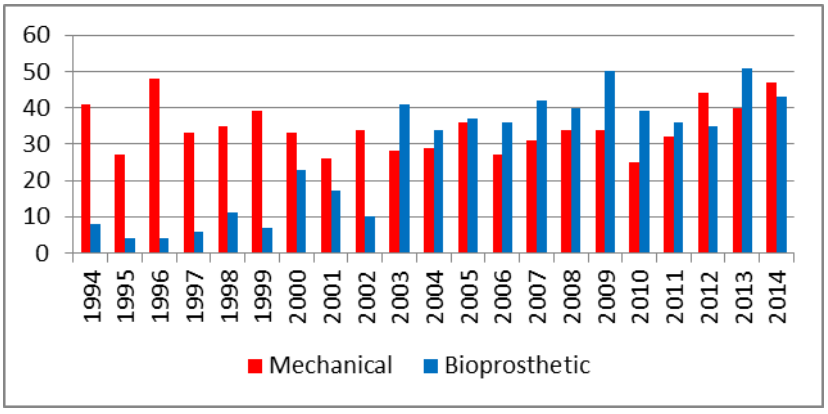

Figure 1: showing trend of valve type for patients <60 who underwent isolated AVR

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CIRCULAR SHAPE ASSUMPTION OF OVAL LVOT BY STANDARD 2D ECHOCARDIOGRAPHY (CONTINUITY METHOD) MAY RESULT IN SUBSTANTIAL UNDERESTIMATION OF AORTIC VALVE AREA

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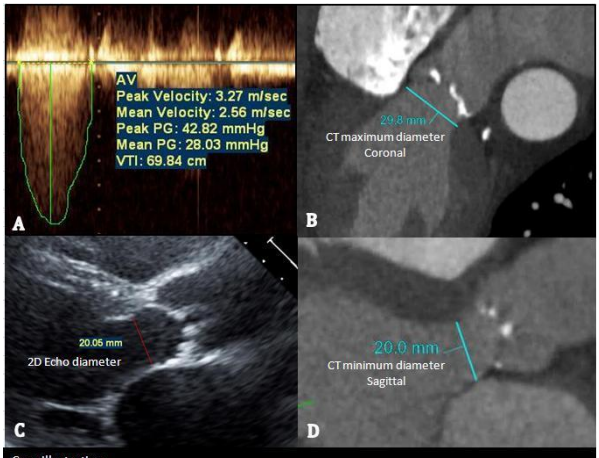
Objective: Our aim of the study is to estimate the degree of underestimation of the aortic valve area by standard 2D echocardiography continuity method.
Background: Currently by 2D echocardiography (echo) continuity method, we make circular assumption of oval shaped left ventricular outflow tract (LVOT) that may result in underestimating aortic valve area (AVA) and overestimating the degree of aortic stenosis (AS).
Methods: We retrospectively identified 46 AS patients with normal flow who underwent gated computed tomorgraphy (CT) and echo. We estimated AVA by echo (continuity method 1). We re-calculated the AVA by continuity method 2 in which echo derived Doppler flow is used in conjunction with CT derived LVOT diameter (average of minimum and maximum). We estimated the differences in AVA quantification between the two methods and their ability to distinguish severe from non-severe AS based on transvalvular gradients (figure) and dimensionless velocity index (DVI).
Results: AVA by continuity method 1 was significantly smaller compared to continuity method 2 ($p<0.01$). AVA estimation by continuity method 2 had a better diagnostic sensitivity (77%) with similar specificity (84%) compared to continuity method 1 (62% sensitivity; 84% specificity), in discriminating non-severe from severe AS, as determined by transvalvular gradients and DVI.
Conclusions: Standard echo may significantly underestimate the aortic valve area. Our study findings explain the discrepancy in AS severity we encounter when the stenosis is severe by valve area, however the transvalvular gradients are only moderately elevated (despite normal flow).



Case illustration .
Using the standard echo LVOT diameter (Frame C) by Continuity method 1, AVA is 0.72 cm^2. Re-calculated AVA by CT-derived average of minimim and maxiumum diameters (frames B & D) by continuity method 2 is 1.06 cm^2. AVA by Continuity method 2 is indicative of moderate AS, which is more reflective of the mean and peak gradients (Frame A).
AVA, aortic valve area; AS, aortic stensois; LVOT, left ventricular outflow tract

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PREDICTION OF NEW ONSET ATRIAL FIBRILLATION AFTER TRANSCATHETER AORTIC VALVE REPLACEMENT

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Objectives: To assess the role of left atrial appendage emptying and filling velocity (LAAEV and LAAFV, respectively) after transcatheter aortic valve replacement (TAVR) in predicting new onset atrial fibrillation (NOAF).
Background: NOAF after TAVR is a known risk factor for future adverse outcomes. Therefore it is important to identify patients at risk.
Methods: Medical records of 53 patients who had consecutive LAAEV and LAAFV measured before and after TAVR with transesophageal echocardiography were retrospectively reviewed. Those with history of permanent and paraoxymal atrial fibrillation were excluded.
Results: Thirty-five patients were included. Mean age was 79±9 (Male 15/35). Eight patients developed NOAF. NOAF was associated with longer hospital stay (median of 4 vs 13 day, p=0.001). Pre and post TAVR LAAEV and LAAFV was 35.2 ± 16.7 and 40.6 ± 23.1 (cm/sec), (p=0.041) and 30.8 ± 12.5 and 34.1 ± 13.9 (cm/sec), respectively (p= 0.167). Receiver operating characteristics curve analysis results are shown in table 1. Changes in LAAFV demonstrated better prediction of NOAF compared to left atrial volume index (AUC 0.789 vs 0.491, p=0.01)
Conclusions: Increase in LAAEV and LAAFV had good sensitivity and specificity, respectively. These may serve as simple marker to predict NOAF. Further study is warranted to verify these findings.

Table 1

Table 1
Result of receiver operating characteristics curve analysis

	Cut off value	AUC	95% CI	sensitivity	specificity
ΔLAAEV (cm/s)	4.9	0.70	0.53-0.88	88	63
ΔLAAFV (cm/s)	11.5	0.79	0.61-0.97	63	85
AVA index (cm^2/m^2)	0.38	0.63	0.41-0.86	75	59
LAVI (ml/m^2)	43.8	0.49	0.21-0.69	63	41

TAVR: transcatheter aortic valve replacement, ΔLAAEV: changes in left atrial appendage emptying velocity, ΔLAAFV: changes in left atrial appendage filling velocity, AUC: area under the curve, CI: confidential interval, AVA; aortic valve area, LAVI; left atrial volume index

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OUTCOMES OF MITRAL VALVE SURGERY FOR MITRAL STENOSIS

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Objectives and Background: Mitral valve replacement procedures with either a bioprosthetic or a mechanical valve are used to treat mitral stenosis. This study aimed to evaluate the outcomes of these two procedures.
Methods: A retrospective cohort involving a total of 195 mitral stenosis patients who have undergone mitral valve replacement with either bioprosthetic (n=50) or mechanical (n=145) valves in our institute from 1999 to 2012. Data were analyzed for mortality, functional class, echocardiographic findings, valve-related complications, and survival. Chi Square test, logistic regression, Kaplan Meier curve, and dependent proportions tests were some of the tests employed in the analysis.
Results: Out of 195 patients, 104 (53%) patients could be reached by telephone calls for collecting long-term outcome information. Twelve patients had late mortality, six in the bioprosthesis group and six in the mechanical. One patient had perioperative mortality. The Late mortality had significant association with post-op stroke (P<0.001) and post-op NYHA classes III and IV (P=0.002). Post-op NYHA class was significantly associated with age (P=0.003), pulmonary disease (P=0.017), mitral valve type (P=0.011, mechanical valves better), hypertension (P=0.01), and post-op stroke (P=0.017). NYHA classes were significantly better after the replacement surgeries (P<0.001). Bioprosthetic valves were significantly associated with worse survival (P=0.03), worse NYHA post-op (P=0.011), and more re-operations (P=0.006); and borderline association with late mortality.
Conclusion: Mechanical mitral valve replacement in mitral stenosis patients is associated with less late mortality, better functional classes, less re-operations, and better survival as compared to bioprosthetic valves. Stroke occurrence is associated with late mortality and worse functional classes.

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INFECTIOUS ENDOCARDITIS PREVALENCE HAS BEEN INCREASING OVER THE YEARS WITH PERSISTENTLY HIGHER PREVALENCE IN MALE GENDER

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Background: With better preventive care, we hypostatize that incidence of infectious endocarditis should decline over the years. The goal of this study was to evaluate the incidence of infectious endocarditis over the years using a large data base.
Method: The Nationwide Inpatient Sample (NIS) database was utilized to calculate the age-adjusted prevalence rate of infectious endocarditis in hospitalized patient from 19988 until 2007 based on ICD-9 coding.
Results: We found gradual increase in the prevalence of age adjusted infectious endocarditis over the last 20 years. Total incidence of infectious endocarditis is also on rise. Furthermore, the age-adjusted incidence of infectious endocarditis is almost twice in male in comparison to female gender. Age adjusted in-hospital prevalence of infectious endocarditis was 6.6 per 100,000 in 1988 vs. 7.4 per 100,000 in 2007. Age adjusted in-hospital prevalence of infectious endocarditis was 4.2 per 100,000 in 1988 in female vs. 10.6 per 100,000 in male. For 2007, age adjusted prevalence of infectious endocarditis was 11.4 per 100,000 in male vs. 5.3 per 100,000 in female. ($p<0.01$).
Conclusion: Age adjusted prevalence of infectious endocarditis is on the rise over the last 20 years. Furthermore, men have infectious endocarditis rate twice the rate of females. The cause of this rise and gender difference in the prevalence of infectious endocarditis is not known warranting further investigation.

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ELEVATED SERUM OSTEOPROTEGERIN LEVELS ARE ASSOCIATED WITH AORTIC VALVULAR STENOSIS: A META-ANALYSIS

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Background: Aortic valve stenosis (AVS) is a progressive disease involving a cascade of inflammation and osteogenic abnormalities. Osteoprotegerin (OP) is a member of the tumor necrosis factor family with pleiotropic effects on bone metabolism, the immune system and endocrine function. Recent studies have linked elevated serum OP levels with diabetes and peripheral vascular disease. The association between serum OP and AVS remains obscure.
Objective: The aim of the present study is to conduct a meta-analysis to evaluate the relationship between circulating OP levels and AVS.
Methods: We searched MEDLINE, CINHAL and COCHRANE databases for studies reporting serum OP levels in the patients with AVS and control population. We included case controls, cohort and cross-sectional studies. We calculated the weighted standardized mean difference (SMD) in serum OP levels between the AVS and control groups.
Results: Our search strategy yielded 19 articles and we included 6 studies enrolling 626 participants. The median age of the AVS group was 69yrs. (IQR 69-70) compared to 66yrs. (IQR 63 -69) in the control group. The median female percentage in the AVS group was 45 % (IQR 44-51%) compared to 45 %(IQR 44-50%) in the control group. The unweighted median serum OP levels in the AVS group were 6.1 pmol/l (IQR 5.4 – 9) compared to 4.9 pmol/l (IQR 3.6 – 6.4) in the control group. The SMD of serum OP level was 2.037 (95% CI 0.636 – 3.437) $p<0.001$ comparing those in the AVS group and control group.
Conclusion: Elevated serum OP levels are significantly associated with presence of AVS. Current findings warrant the need to further clarify to the role of OP in the development of AVS.

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WHAT IS OPTIMAL THERAPY FOR STABLE ANGINA IN THE YEAR 2015?

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In the year 2015, optimal therapy for stable angina comprises of abolition or near abolition of symptoms, improved quality of life and reduction of the incidence of serious adverse cardiovascular outcomes (acute myocardial infarction, sudden ischemic cardiac death, unstable angina and heart failure). Lifestyle modifications (abstinence of smoking, regular exercise) and lipid modifying treatment with a potent and high dose statin, but not with niacin, or fibrates or with HLD raising drugs, reduce the incidence of serious adverse cardiovascular outcomes. Daily use of low dose aspirin, and adequate control of blood pressure also reduce the incidence of serious adverse outcomes. Older and new antianginal medications, as well as coronary artery revascularization (percutaneous or surgical) reduce the frequency of angina episodes, increase angina free exercise duration and improve quality of life, but have little impact on the incidence of serious adverse cardiovascular outcomes with a few exceptions (use of beta blockers and ACE inhibitors when left ventricular ejection fraction is reduced and coronary bypass surgery for left main CAD). Individualization of treatment strategy which takes into account patients' life style and presence of comorbidities is essential to achieve this goal. Treatment of refractory angina despite optimal therapy remains a challenge and newer non-invasive and invasive treatment strategies are currently under active investigation.

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EVOLUTION IN THE MANAGEMENT OF LOW RISK PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH CHEST PAIN

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The majority of patients presenting to the ED with chest pain comprise a low risk population who do not have acute coronary syndrome (ACS) or other life threatening condition. Therefore, most at are low risk for morbidity and mortality. Such low risk patients are usually identified by absence of a history of cardiovascular disease, normal or nonischemic ECG, normal initial troponin, and clinical stability. The utility of accelerated diagnostic protocols (ADP) has been established for further confirmation of low clinical risk and appropriateness for direct discharge from the ED versus detection of higher risk patients who require admission. At minimum, these protocols entail serial ECGs and measurement of cardiac injury markers, both of which can be performed in the ED or a chest pain observation unit. Negative results have usually been followed by a cardiac functional (treadmill test or stress imaging evaluation) or anatomic study (cardiac computed tomography angiography Card [cardiac CTA or MRI) to enhance the safety of early discharge. These ADPs have been associated with a negative predictive value at 30 days greater than 99% for ACS or other major cardiovascular event. Several recent protocols for evaluation of low risk patients have been reported, such as a 2hr evaluation comprising a TIMI risk score of 0, normal ECGs, and normal hs-TnI. Cardiac CTA has a very high negative predictive value and has been performed without prior measurement of troponin. Currently, the ADP is in evolution with recent reports indicating excessive testing of low risk patients and more reliance on physician discretion for functional or anatomic testing with maintenance of safety and negative predictive value. This approach has also resulted in shorter length of stay in the ED or observation unit (<6 hr) and lower cost.

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CT ASSESSMENT OF CORONARY FLOW PHYSIOLOGY

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Coronary CT angiography (CCTA) is widely accepted as the most sensitive method for detecting coronary stenosis seen on invasive coronary angiography (ICA). However, the specificity of the abnormal CCTA for ischemia is low. Three methods for assessing ischemia with CCTA have been evaluated. CT perfusion (CTP) is performed by adding a CT acquisition during vasodilator stress. Two multicenter trials have shown good correlation between CT perfusion and evidence of ischemia by the combination of invasive coronary angiography and SPECT myocardial perfusion imaging (MPI) or SPECT-MPI alone. A second method evaluates the transluminal attenuation gradient (TAG) along the length of a coronary artery. A drop in attenuation correlates with the presence of an ischemic abnormality. This approach has been less completely validated than the other approaches. Fractional flow reserve by CT (FFR-CT) has recently been developed for estimating invasive FFR, the current gold standard for lesion-specific ischemia. FFR-CT applies computational fluid dynamics to a standardly acquired CCTA study. It requires no additional image acquisition, no additional radiation, and no administration of pharmacologic stress. Three large multicenter trials have evaluated the accuracy of FFR-CT in predicting invasive FFR. The most recent trial (NXT) evaluated 484 patients and demonstrated high accuracy (81%) in prediction of abnormal invasive FFR (≤8 0). The accuracy FFR-CT was higher than that of stenosis by CCTA or by ICA. The feasibility of using FFR-CT for planning PCI has been recently demonstrated. Overall, the early data with the various methods of assessing coronary flow physiology with CCTA suggests that the combination of anatomic and physiologic assessment with the methods for assessing ischemia as well as coronary plaque--will provide incremental information in evaluating patients with known or suspected coronary artery disease and may become part of routine clinical approach to its application.

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MYOCARDIAL VIABILITY IN CORONARY ARTERY CHRONIC TOTAL OCCLUSION

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Coronary artery chronic total occlusion (CTO) has rapidly become a popular target of percutaneous coronary intervention (PCI). Technical and technological advances required for approaching these anatomically complex and challenging lesions have progressed at an extraordinary pace and have led to amazing success rates. Undoubtedly, many patients with disabling symptoms and failed medical therapy have been served well with these novel procedures in recent years. Patient selection, however, has primarily focused on patient symptoms, lesion characteristics, as well as the state of collateral circulation. Multiple national and international registries have been established to follow the progress of percutaneous CTO recanalization and have provided valuable information. Concern, however, exists that this challenging procedure will become the "standard of care" before its effectiveness and appropriateness is tested in prospective controlled trials. This presentation will review the current state of patient selection and the need for careful assessment of the presence and extent of myocardial viability prior to these lengthy, resource intensive and potentially high risk procedures.

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CHOOSING WISELY: WHAT WORKS AND WHAT DOESN'T

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Background: Contemporary medical care includes numerous practices that are duplicative, unnecessary and/or potentially harmful. It has been estimated that up to 30% of care activities may not directly improve patient health or well-being. In this context, the American Board of Internal Medicine (ABIM) Foundation has developed the Choosing Wisely campaign, an initiative to help providers and patients engage in conversations about effective care choices. In collaboration with ABIM, participating provider organizations, including the Critical Care Societies Collaborative, each created separate lists of "Things to Question," providing specific, evidence-based recommendations for providers and patients to use as a framework to discuss care decisions.
Methods and Results: The Critical Care Societies Collaborative, involving the American Association of Critical Care Nurses, the American College of Chest Physicians, the American Thoracic Society and the Society of Critical Care Medicine, has identified "Five Things Physicians and Patients Should Question." This list centers on methods to reduce excessive ICU testing, limiting unnecessary blood transfusions and parenteral nutrition, avoiding inappropriately aggressive sedation in intubated patients, and enhancing end-of-life care and supportive decision-making. In addition to this list of questionable practices, there are several potentially underutilized strategies that can contribute positively to patient outcome, including team-based initiatives such as infection surveillance and control, as well as integrated efforts to improve patient adherence.
Conclusion: Physician and patient awareness of Choosing Wisely recommendations may result in enhanced ICU healthcare quality through preservation of increasingly limited healthcare resources while promoting improved patient outcome.

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ENDOTHELIAL DYSFUNCTION FOLLOWING IMPLANTATION OF CORONARY DRUG-ELUTING STENTS AND MEDICAL THERAPIES

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Drug-eluting stents (DES) are widely used for the treatment of coronary artery disease to reduce the rate of restenosis. However, several studies reported endothelial dysfunction following DES implantation. Togni et al. reported endothelial dysfunction following sirolimus-eluting stent (SES) implantation using a bicycle ergometer. Intracoronary administration of acetylcholine (ACh) has been most frequently used for evaluation of coronary endothelial function. Hofma et al. compared endothelial dysfunction at 6 months following implantation of SES and bare metal stent (BMS). They reported that, although no significant change in the vascular diameter was observed in the BMS group in response to ACh load, lumen diameter reduction was observed after administration of ACh in the SES group. Kim et al. also demonstrated endothelial dysfunction in patients treated with SES or paclitaxel-eluting stent (PES) implantation. Moreover, they compared endothelial function following implantation of BMS, SES, and so-called second generation DES, zotarolimus-eluting stent (ZES). As a result, both SES and ZES groups had significant endothelial dysfunction compared to BMS group. Furthermore, its degree was significantly milder in the ZES group compared to that in the SES group. In addition, endothelial dysfunction may contribute to the development of severe adverse cardiac events including late/very late stent thrombosis, severe coronary artery spasms, and neo-atherosclerosis after DES implantation. Therefore, amelioration of endothelial dysfunction after DES implantation might improve prognosis. At present, several studies suggested that ACE inhibitors and peroxisome proliferator-activated receptor-gamma (PPAR gamma) agonists, pioglitazone, may improve endothelial function in the patients with coronary artery disease. Telmisartan, which has PPAR gamma-mediated effects in addition to its renin-angiotensin system inhibition effects, has favorable effects on endothelial function. We previously reported that telmisartan significantly ameliorated endothelial dysfunction after DES implantation. For the future issues, it is necessary to investigate the impact of these drugs on the long-term clinical prognoses after DES implantation.

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RESPIRATORY MANEUVERS THAT CAN BE USEFUL DURING CARDIAC CAUTERIZATION OR CORONARY INTERVENTIONS

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Respiratory maneuvers have been used during invasive cardiac catheterization for improvement in diagnosis and recently treatment of cardiac disease. These maneuvers are integral part of invasive assessment and treatment of cardiac patients. It can be divided to maneuvers that can be performed during right or left heart catheterization. The focus of this lecture are maneuvers that can be useful mostly during left heart catheterization and interventions. One of the most important maneuver is performing deep inspiration during catheter advancement into the ascending aorta using right radial artery access during left heart catheterization. This can facilitated catheter advancement in to the ascending aorta. The same maneuver can be used when coronary ostia engagement is difficult during right radial access. The most two important interventional maneuvers that are recently described by Movahed et al will be discussed in this lecture. One is deep inspiration maneuver during stent delivery in tortuous native coronary lesions. By instructing a patient to take deep breath right before stent advancement in difficult cases, stent deliverability can be facilitated by reducing tortuosity of coronary tree. Opposite maneuver described as reverse Movahed's maneuver can be used in tortuous vein graft interventions. As opposed to native coronaries, vein graft tortuosity is reduced by performing expiration maneuver that can lead to facilitated stent delivery in difficult vein graft cases by reducing tortuosity in the vein grafts using this maneuver. These two maneuvers will be extensively discussed in this lecture.

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EVOLVING ROLE OF PLATELET FUNCTION TESTING IN ACUTE CORONARY SYNDROMES

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The reduction in ischemic events provided by the dual anti-platelet regimen with aspirin and clopidogrel is extensively published in patients with acute coronary syndrome and patient's undergoing percutaneous coronary intervention (PCI). However, there have been several "boxed warning" on clopidogrel and its variable response which lead to intense controversy on pharmaokokinetic and pharmacodynamic and pharmacogenomic issues of anti- platelet drugs especially clopidogrel. Research use of platelet function testing has been successfully validated in identifying the new anti-platelet drugs like prasugrel and ticagrelor. These platelet function tests are not regarded as just a laboratory phenomenon anymore; rather a tool shown to predict mortality in several clinical trials. It is believed that sub optimal pharmacodynamic response to anti platelet regimen may be associated with cardiovascular, cerebrovascular events. The role of platelet function testing to guide anti platelet therapy has been controversial. However updated American and European practice guidelines have issued a Class 11b recommendation for platelet function testing to facilitate the choice of anti-platelet regimen in high risk patients undergoing PCI such as diabetes mellitus, diffuse three vessels coronary artery disease, left main stenosis, diffuse atherosclerotic disease and chronic renal failure, and in patients with suspected pharmacodynamic interaction with other drugs to assure the adequacy of platelet inhibition.

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STABLE ISCHEMIC HEART DISEASE: THE PRESENT AND THE FUTURE

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As has been well-established, patients with acute coronary syndromes, severe multi-vessel or left main coronary artery disease, have better outcomes when prompt revascularization is performed in addition to optimal medical therapy (OMT). However, in stable ischemic heart disease (SIHD) patients, comparative effectiveness research has revealed equipoise between initial strategies of OMT alone and OMT plus revascularization. Conducted in diverse SIHD patient populations and throughout the spectrum of atherosclerotic and ischemic burden, the RITA-2, MASS II, COURAGE, BARI 2D, and FAME 2 trials demonstrate that an initial conservative strategy of OMT alone is associated with similar major cardiovascular outcomes (i.e., mortality, myocardial infarction, or long-term angina relief), as with an initial invasive approach. What remains unclear is whether there may be one or more subsets of patients with SIHD in whom revascularization may be associated with a reduction in the rate of mortality or myocardial infarction, which is to be addressed in the ongoing ISCHEMIA trial

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DECLINING TRENDS IN CARDIOGENIC SHOCK DEVELOPING DURING HOSPITALIZATION FOR ACUTE MYOCARDIAL INFARCTION (AMI): INSIGHTS FROM A POPULATION BASED CORONARY HEART DISEASE REGISTRY

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Background: Cardiogenic shock (CS) is a serious and often fatal complication of AMI. The impact of aggressive medical and procedural interventions for both prevention and management of CS due to AMI is less clear, however. The purpose of the present study is to examine decade long trends in the incidence and in-hospital death rates associated with CS that develops during hospitalization for AMI as compared with CS that is present at the time of hospital admission.
Methods and Results: We studied 5,782 patients with AMI who were admitted to all 11 hospitals in central MA on a biennial basis between 2001-2011 There was a marked decline in the frequency of CS developing during hospitalization from 3.6% in 2001/2003 to 2.7% in 2009/2011 ($p<0.05$) while the frequency of CS at admission did not change over time (1.5% in 2001/2003; 1.8% in 2009/2011). The in-hospital case fatality rate (CFR) among those who developed CS during hospitalization declined from 47.1% in 2001/2003 to 28.6% in 2009/2011, whereas the hospital CFRs associated with CS on admission worsened from 38.9% in 2001/2003 to 53.6% in 2009/2011
Conclusions: Over the past decade, significant declines have been observed in both the incidence and in-hospital CFRs due to CS developing during AMI hospitalization. Early reperfusion and/or revascularization interventions in patients hospitalized with AMI are potentially related to a reduced incidence of CS developing during hospitalization for AMI, while the aggressive management of CS which develops during hospitalization likely contributed to the improved short-term survival of these high risk patients. The reasons for the stable incidence of CS that is present on hospital admission and the worsening short term outcomes of these patients is less clear and requires further examination

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RENAL BIOMARKERS PREDICT ADVERSE OUTCOMES IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Objectives: We sought to identify predictors of heart failure (HF) hospitalization in heart failure with preserved ejection fraction (HFpEF) patients by evaluating biomarkers and transthoracic echocardiogram (TTE) parameters.
Background: HFpEF is an increasingly recognised clinical entity that accounts for approximately half of all HF diagnoses, yet remains challenging to prognosticate.
Methods: This was an observational prospective study of patients admitted in 2013 for HFpEF. One-year follow-up data on HF admissions was obtained.
Results: Our HFpEF population (n=48) was 47.9% female, with a mean age of 71.9 ± 15.3 years. Mean serum urea, creatinine, and estimated glomerular filtration rate (eGFR) were 13.9 ± 12.8 mmol/L, 185 ± 131.3 umol/L and 40.8 ± 27.2 ml/min per 1.73m2 respectively. Serum urea and creatinine levels, along with a lower eGFR, correlated with more HF admissions (r=0.365 p=0.011, r=0.411 p=0.004 and r=-0.452 p=0.001 respectively). The same biomarkers correlated with longer hospital stays for HF (urea r=0.404 p=004, creatinine r=0.450 p=0.001 and eGFR r=-0.517 p<0.001). Predictably, higher serum N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and higher TTE ratio of mitral velocity to mitral annulus early diastolic velocity (E/E') also both correlated with increased HF admissions (r=0.411, p=0.004 and r=0.463, p=0.001 respectively). Patients' age, serum HbA1c and LDL-C levels showed no significant correlation with HF hospitalization. Multiple regression analysis showed E/E', eGFR, NT-proBNP and age were all statistically significant (p<0.05) predictors of HF admissions.
Conclusion: Renal biomarkers are useful prognostic factors in predicting readmissions for HFpEF, along with the mainstays of serum NT-proBNP and E/E'.

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PREDICTORS OF RESPONSE IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE REQUIRING MILRINONE

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Objectives: To determine predictors of improved short term clinical outcomes in decompensated heart failure with reduced ejection fraction (HFrEF) requiring milrinone.
Background: Milrinone is a phosphodiesterase-3 inhibitor (PDE-3) which improves cardiac output and hemodynamics in patients with decompensated HFrEF. Inotropes such as milrinone, however, have been associated with increased mortality, and predictors of which patients may have the best hemodynamic response are not clearly understood.
Methods: We prospectively observed 49 patients with decompensated HFrEF requiring milrinone. Baseline clinical and hemodynamic parameters obtained at milrinone initiation were compared using Pearson product-moment correlation coefficients with response to milrinone measured by net 72 hour diuresis (72HD), length of inotrope use, and length of stay (LOS).
Results: Lower pulmonary artery saturation was associated with increased 72HD (R2=0.39, p=0.03) but longer duration of inotrope use (R2=-0.50, p=0.003) and increased LOS (R2=-0.46, p=0.008). Elevated right atrial pressure was associated with lower 72HD (R2=0.52, p=0.002) and an increased LOS (R2=0.37, p=0.04). Increased serum creatinine (R2=0.40, p=0.005) and reduced serum sodium (R2=0.38, p=0.007) were associated with increased LOS. Increased heart rate was also associated with lower 72HD (R2=-0.33, p=0.02) and increased LOS (R2=0.33, p=0.02). Chronic stable dose of outpatient beta-blocker, ejection fraction, and mean arterial pressure had no significant correlation with outcomes.
Conclusions: Markers of advanced heart failure (elevated right atrial pressure, increased serum creatinine, reduced serum sodium, increased heart rate) may predict resistance to milrinone. In patients who present with these signs, close attention to inotrope resistance and early consideration of mechanical circulatory support should be considered.

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CORRELATION BETWEEN AORTIC ROOT DILATION AND DIASTOLIC DYSFUNCTION AND RELATIONSHIP WITH OTHER PARAMETERS

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Background: Consensus is lacking about the clinical importance of aortic root dilatation in assessment of the risk of development of Diastolic Dysfunction (DD).
Objective: The aim of this study was to assess the aortic root dilatation in patients with Diastolic Dysfunction (DD).
Methods: We retrospectively reviewed 2,262 medical records of patients receiving Echocardiograms at a University hospital between 2008 year and 2012 year. The patients were divided in two groups according to presence or absence of diastolic dysfunction. Aortic root diameter was measured by M-mode echocardiography, and LV diastolic function was evaluated by measuring the peak velocity of early (E) and late (A) diastolic transmitral blood flow, peak early diastolic mitral annular velocity (E') by Tissue Doppler echocardiography, and pulmonary venous sampling. Aortic dilation was assessed by measurement of aortic root diameter <3.7mm vs. ≥ 3.7mm
Results: Bivariate analysis between Aortic dilation (AD) and DD showed that AD was present in 15.2% of patients with DD vs. 11.3% without DD (chi-square p= 0.0173). A multivariable logistic regression analysis indicated that age (OR=1.041, 95% CI=1.014-1.068, p=0.0030) and hypertension (OR=3.269, 95% CI=1.273-8.391, p=0.0138) were associated with the presence of DD. None of the other predictor variables showed any statistically significant association (AO dilation, Pro BNP, BMI and DM).
Conclusions: Aortic root dilation is strongly associated with DD in bivariate analyses, but this association does not persist when entered into a model adjusting for other parameters.

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EFFECTS OF LIBERAL VERSUS RESTRICTIVE BLOOD TRANSFUSION STRATEGIES IN CONGESTIVE HEART FAILURE

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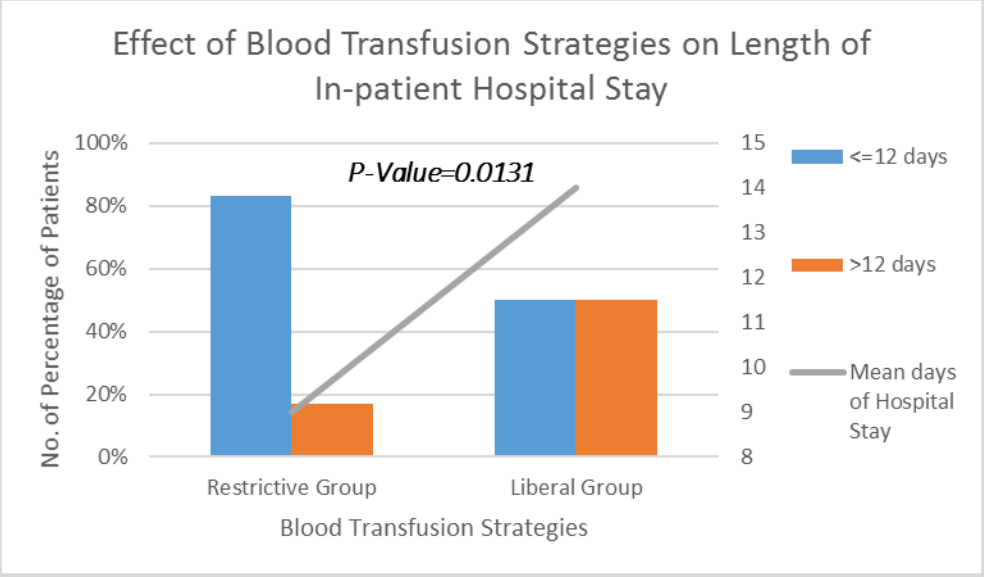
Objectives: The aim of this study was to ascertain proper use of blood transfusion in congestive heart failure (CHF).
Background: Anemia is one of major comorbidities and an important prognostic factor, which is almost 30% prevalent in CHF. Blood transfusion (BT) is primary standard of care for anemia. No clear data is available regarding BT strategies in CHF regarding when to transfuse and what should be the goal of hemoglobin (Hb).
Methods: We conducted a retrospective-chart review study in our hospital after obtaining IRB approval. After excluding patients who had recent surgery, acute bleeding episode and acute coronary event, we found 56 patients who received BT during in-patient hospital stay regarding CHF. We divided them into 2 groups: Restrictive (RBT) vs Liberal (LBT) blood transfusion strategies (12 vs 44 patients; Transfusion Hb threshold <7 vs <9 with a goal set >9 vs >10-12 gm/dl, respectively).
Results: The mean age of sample was 75 ± 2 years, 50% were females, and 54 % had chronic kidney disease. Results shown in RBT vs LBT group, baseline Hb was 10.5 vs 10.6 gm/dl; numbers of BT were used 2.4 vs 1.5 with p-value=0.003 and length of stay: <=12 days: 83% vs 50%; >12 days: 17% vs 50%; p-value=0.0131, respectively. No BT reactions were found in any patients.
Conclusions: We report significantly lower length of stay in RBT than LBT group. As this is a small pilot study, we are suggesting a need for larger study to reproduce similar findings.



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PREDICTING READMISSION IN A HEART FAILURE POPULATION AT A RURAL TERTIARY CARE HOSPITAL

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*Background***:** Heart Failure (HF) remains the primary cause of admission to hospital in the United States.
Methods: 405 patients' charts admitted with a diagnosis of acute systolic HF or acute on chronic systolic HF with a LVEF ≤ 40%. 21 data elements from the medical record available at the time closest to the initial follow up visit were abstracted. These data elements are as presented in tables I and II.
Scoring Equation for the Log Odds of 30-Day Readmission
Log Odds of 30-Day Readmission = -0.7193 – 0.0434 *Age + 0.0864*[maximum (0,Age-63)] + 0.0312*Weight – 0.0690*[maximum(0,Weight-95)] - 0.00795*Cholesterol + 0.0302*[maximum(0,Cholesterol-175)]
Results: Tables I and II report the descriptive statistics stratified by readmission status. One year all-cause mortality rates were 19.5 % reflecting advanced heart failure population. Among all the variables analyzed, age (>63 yrs), weight (< 95 kg), and total cholesterol (>175 mg/dl) were found to be associated with 30 day readmission. Patients in the readmission groups were seen in outpatient clinic within 2 weeks from the discharge from the hospital.
Conclusion: In a rural tertiary care setting, these data suggest that the clinical milieu of older age, lower weight and elevated cholesterol play a role in the risk of readmission for heart failure.

Table I: Descriptive Statistics by Readmission Status: Continuous Variables

Variable	Readmission within 30 Days (n=92)	No Readmission within 30 Days (n=302)	P-Value
Age	75.3 (13.3)	73.5 (12.2)	0.0736
Weight (kg)	89.7 (15.0)	91.1 (25.6)	0.4043
EF	28.5 (9.2)	29.0 (9.4)	0.5419
SBP	122.7 (19.3)	121.4 (17.3)	0.8624
HG	12.0 (2.3)	12.2 (2.0)	0.4084
Total Cholesterol	150.4 (52.7)	144.9 (39.1)	0.9550
Creatinine	1.5 (0.8)	1.6 (0.9)	0.6003
NA	137.9 (4.7)	137.9 (4.0)	0.6733
K	4.3 (0.5)	4.3 (0.5)	0.4325
QRS	126.6 (36.6)	123.1 (37.1)	0.3761

Table II: Descriptive Statistics by Readmission Status: Categorical Variables

Variable	Readmission within 30 days (n=92)	No Readmission within 30 Days (n=302)	P-value
Male	56 (60.9%)	184 (60.9)	0.9921
Ischemic	57 (62.0%)	206 (68.2%)	0.2648
ACEI/ARB	66 (71.7%)	231 (76.5%)	0.3544
Beta Blockers	81 (88.0%)	262 (86.8%)	0.7472
Statins	50 (54.4%)	183 (60.6%)	0.2858
Aldo Blocker	29 (31.5%)	93 (30.8%)	0.8949
Diuretics	75 (81.5%)	264 (87.4%)	0.1531
ICD			0.6614
No	45 (48.9%)	143 (47.3%)	
Yes	18 (19.6%)	50 (16.6%)	
BIV-ICD			0.7138
No	39 (42.4%)	117 (38.7%)	
Yes	32 (34.8%)	104 (34.4%)	

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FACTORS ASSOCIATED WITH HEART FAILURE READMISSIONS FROM SKILLED NURSING FACILITIES

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Background: Despite guideline-driven pharmacological therapies and careful transitional care, the rates of preventable hospital re-admission of heart failure patients and associated costs remain unacceptably high in the SNF populations. Transfer to SNF is one strategy to limit hospitalizations. As such, 25% of patients are still symptomatic at time of discharge**.**
Purpose: The objective of this study is to identify patient factors affecting re-admissions of HF patients residing in SNF within 30-days.
Methods: A retrospective electronic chart review was completed on patients >65 years with HF who were admitted into large medical center between 2012 and 2014. Descriptive statistics and univariate analyses using the chi-square test or Fisher's exact test for categorical variables and the Mann-Whitney test for continuous data was used to compare patients readmitted within 30 days vs. those who were not readmitted within 30 days. Significant factors associated with readmission in the univariate analysis ($p<0.10$) were included for a multivariate logistic regression model. A receiver operating characteristic (ROC) curve was constructed to look at the final model's ability to predict the outcome. A numerical measure of the accuracy of the model was obtained from the area under the curve (AUC), where an area of 1.0 signifies near perfect accuracy. The analysis of LOS was accomplished by applying standard methods of survival analysis, i.e., computing the Kaplan-Meier product limit curves, where the data were stratified by readmission within 30 days (Yes vs. No). No data were considered 'censored'. The groups were compared using the log-rank test. The median rates for each group were obtained from the Kaplan-Meier/Product-Limit Estimates and their corresponding 95% confidence intervals were computed, using Greenwood's formula to calculate the standard error. Unless otherwise specified, a result was considered statistically significant at the $p<0.05$ level of significance.
Results: Fifteen variables: creatinine, weight difference, CKD, Angina, Arrhythmia, VHD, Tobacco, ADL, independent in bathing, independent in the toilet, S3 Heart sounds present, HJR, AF, Nitrates, and Hydralazine, were identified for the multivariate logistic regression as potential risk factors associated with "readmission within 30 days". Based on 23 readmissions within 30 days, our final model included only 2 predictor variables. Creatinine and ADLs were included in the final model as this subset of predictors was found to be the best for prediction of "readmission within 30 days". Creatinine ($p<0.0087$) and ADLs ($p<0.0077$) were both significantly associated with readmission within 30 days in the final logistic regression model. Every 1-unit increase in creatinine is associated with an 87% increase in the odds of being readmitted within 30 days (OR = 1.87). Those patients who require assistance with ADLs are over 9 times more likely to be readmitted within 30 days (OR=9.25) as compared to patients who are independent.

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DISCHARGE HOME HEALTH VS. HOSPICE REFERRAL AND 30-DAY ALL-CAUSE READMISSION IN MEDICARE BENEFICIARIES HOSPITALIZED FOR HEART FAILURE

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Background: Heart failure (HF) is the leading cause for 30-day all-cause hospital readmission, a target for reduction in the new U.S. healthcare reform law. Discharge hospice referral has been shown to be associated with lower readmission. Sicker HF patients are often referred to home health (HH) care. However, 30-day all-cause hospital readmission for patients receiving these two referrals have not been compared before.
Methods: In the Alabama HF Project, of the 6549 HF patients who were discharged alive home, 129 received hospice referral and 1369 received HH referral during hospital discharge. Of the 1369 receiving HH referral, 359 died within six months after discharge and were considered hospice-eligible. Thus, our pre-match cohort consisted 488 (129+359) patients. Propensity scores for hospice referral were estimated for each of the 488 patients and were used to match 124 of the 129 patients in the hospice group with 124 patients in the HH group who had similar propensity scores, thus assembling a matched cohort of 248 patients balanced on 22 baseline characteristics (mean age, 79 years, 54% women and 19% African American).
Results: 30-day all-cause readmission occurred in 5% and 46% of matched patients receiving discharge hospice and HH referrals, respectively (HR for hospice referral, 0.10; 95% CI, 0.04-0.23). There was similar reduction in 30-day HF readmission (HR, 0.15; 95% CI, 0.05-0.44). Although 30-day mortality was higher in the hospice group (44% vs. 32%; HR, 1.57; 95% CI, 1.05-2.36), it was similar at 90 days post-discharge (66% vs. 63%; HR, 1.10; 95% CI, 0.80-1.49).
Conclusions: Medicare beneficiaries hospitalized for HF receiving discharge hospice referral had lower 30-day all-cause readmission rates than those receiving discharge home health referral that died within 6 months of hospital discharge.

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READMISSIONS: HOW MANY ARE ACTUALLY PREVENTABLE?

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Objective: To analyze 30 day readmission data for an acute cardiology service and determine the percentage of preventable readmissions.
Introduction: Readmissions are an important issue for patients, physicians, payers, and policymakers. The all-cause readmission rate in 2010 was about 19.2% among Medicare beneficiaries costing the US economy approximately 17.5 billion dollars. Some believe the majority of readmissions are preventable and thus, payers should penalize hospitals and providers for readmission. However, root cause analyses of readmissions from the provider perspective have not been performed. It may be unfair to penalize readmissions if the majority is not preventable.
Methods: Retrospective review of the electronic medical record was performed on all 30 day readmissions where the index admission was on the acute cardiology service at a single, academic medical center. The population was a total of 152 patients readmitted from 7/1/2013 – 11/16/14. Root cause analysis was performed by two independent physicians and readmissions were deemed 'preventable', 'maybe preventable', or 'not preventable' based on review of the medical record. Disagreements were settled by an additional reviewer and inter-rater agreement was determined by a weighted kappa analysis.
Results: Of 152 readmissions, only 32 (21%) were considered 'preventable' or 'maybe preventable'. The reviewers agreed on 81.3% of cases and the weighted kappa was 0.41 indicating moderate agreement. Fifty-nine (59%) of 'preventable' and 'maybe preventable' readmissions were considered medication related and thirty-one (31%) were considered management related.
Conclusions: Preventable readmissions account for a small percentage of total readmissions. Payment policies aimed at penalizing readmission are thus, unlikely to improve quality and may disincentivize providers from appropriately readmitting patients for necessary and appropriate medical care. Other mechanisms to reduce health care cost growth such as finding ways to reduce preference-sensitive, low-value medical care would be more appropriate than penalizing providers and hospitals for readmission.

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FRACTIONAL EXCRETION OF UREA AS A PROGNOSTIC INDICATOR IN PATIENTS WITH LOW CARDIAC INDEX

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Background: There is a tremendous amount of difficulty in predicting which patients with acutely decompensated heart failure will have a poor prognosis in the near future. None of the published markers associated with advanced heart failure are very sensitive in their prognostic values. A fractional excretion of urea is a measurement used by nephrologists to determine the state of renal perfusion. We evaluated the prognostic value of the fractional excretion of urea in patients with low cardiac indices.
Methods and Results: A retrospective chart review spanning 6 months was performed. Those patients with low cardiac indices of less than 2L/min/m2 and had a fractional excretion of urea measured during the hospitalization were analyzed. There was a 100% negative predictive value (95% CI: 73.35-100%) associated with a normal fractional excretion of urea. The odds ratio of having an adverse event associated with an abnormal fractional excretion of urea was 17.9 (95% CI: 0.91-350.9, p-value=0.0578).
Conclusion: Based upon the results of this study, there is a suggestion that the fractional excretion of urea can be a very sensitive prognostic indicator in patients with compromised cardiac function.

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COMPARATIVE PROGNOSTIC VALUE OF DIFFERENT AMBULATORY BLOOD PRESSURE PARAMETERS AS PREDICTORS OF STROKE: THE HYGIA PROJECT

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Objectives: Several features of blood pressure (BP) patterning determined by ambulatory monitoring (ABPM) have been explored as potential predictors of stroke. Some, but not all, studies have concluded that elevated morning BP surge or increased BP variability might be significant markers of stroke. We evaluated the comparative prognostic value for stroke of clinic BP and multiple ABPM-derived characteristics, including asleep and awake BP means, morning surge, and indices of BP variability among the participants in the Hygia Project, designed to evaluate prospectively CVD risk by ABPM in primary care centers of Northwest Spain.
Methods: This study involved 11255 subjects, 6028 men/5227 women, 58.9±14.5 years of age, prospectively evaluated throughout a 4.0-year median follow-up. BP was measured at 20-min intervals from 07:00 to 23:00h and at 30-min intervals at night for 48h.
Results: We documented 147 ischemic and 29 hemorrhagic strokes. When each ABPM-derived parameter was analyzed separately, the asleep systolic BP mean was the most significant predictor of stroke (adjusted hazard ratio 1.35; 95%CI [1.20-1.52] for each 1-SD increase; P<0.001). A greater morning BP surge was significantly associated with lower, not higher, stroke risk (0.87 [0.76-0.99], P=0.042). After adjustment by asleep systolic BP mean, neither clinic BP nor any other ABPM-derived parameter, including awake and 48h means, sleep-time relative BP decline, morning surge, and indices of awake, asleep and 24h BP variability, was significantly associated with increased/decreased risk of stroke.
Conclusions: Progressively elevated sleep-time systolic BP mean is the only significant and independent prognostic marker of stroke. Contrary to current believe, neither a greater morning BP surge, morning hypertension, or extreme-dipper BP patterning increase the risk of stroke after adjusting by asleep BP level. On the basis of the null prognostic value of clinic BP here corroborated, ABPM should be considered a clinical requirement for proper risk stratification.

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FETUIN-B IMPAIRS CARDIAC INSULIN SIGNALING AND CONTRIBUTES TO INCREASED CARDIAC ISCHEMIA/REPERFUSION INJURY SUSCEPTIBILITY IN DIABETES

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Objectives: This study was aim to investigate the role of fetuin-B in diabetic myocardial ischemia/reperfusion (MI/R) injury and its underlying mechanisms.
Background: Diabetes mellitus (DM) increases morbidity/mortality of ischemic heart disease. Accumulating evidence suggests that elevated serum fetuin-A level causes impaired glycemic control. However, the role of fetuin-A and its paralogue fetuin-B in diabetic MI/R injury is poorly understood.
Methods: The high-fat diet-fed streptozotocin (HFD-STZ) diabetic mice were subjected to MI/R. In vitro, H9c2 cardiomyocytes were subjected to hypoxia/reoxygenation (H/R).
Results: Compared with the normal animals, diabetic mice showed more severe MI/R injury and cardiac functional impairment. The diabetic heart exhibited increased fetuin-B (but not fetuin-A) expression and impaired insulin signaling as evidenced by decreased insulin-stimulated threonine phosphorylation of IRS-1 and reduced insulin-stimulated Akt phosphorylation and GLUT4 membrane translocation. Cardiac-specific knockdown of fetuin-B restored cardiac insulin signaling. Meanwhile, knocking down fetuin-B reduced MI/R injury in diabetic mice as evidenced by decreased infarct size and increased cardiac function. Moreover, overexpression of fetuin-B in H9c2 cardiomyocytes (adenoviral vector) impaired insulin signaling and increased H/R injury (cardiomyocyte apoptosis and viability). Increased fetuin-B expression was associated with enhanced FoxO1 activation in diabetic hearts. ChIP showed that FoxO1 binds the fetuin-B promoter. FoxO1 siRNA significantly decreased fetuin-B expression in diabetic mice. Adenoviral vector-mediated overexpression of FoxO1 in H9c2 cardiomyocytes induced increased fetuin-B expression and blunted insulin signaling.
Conclusions: Our results demonstrate that increased fetuin-B expression induced by FoxO1 activation inhibits cardiac insulin signaling and renders diabetic hearts more susceptible to MI/R injury.

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MORNING SURGE AND SLEEP-TIME BLOOD PRESSURE AS PROGNOSTIC MARKERS OF CARDIOVASCULAR RISK: THE HYGIA PROYECT

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Objectives: The extent of blood pressure (BP) surge upon waking has been associated with increased cardiovascular (CVD) risk in some, but not all, studies. Numerous studies, however, have consistently shown the association between elevated sleep-time BP mean and the rising BP pattern with markedly increased CVD risk, leading to a paradox, as patients with sleep-time hypertension or non-dipper/riser BP pattern have attenuated morning BP surge.
Methods: This study involved 11255 subjects, 6028 men/5227 women, 58.9±14.5 years of age, prospectively evaluated throughout a 4.0-year median follow-up. BP was measured at 20-min intervals from 07:00 to 23:00h and at 30-min intervals at night for 48h.
Results: We documented 1539 total events, including 400 deaths, 176 strokes, 144 myocardial infarctions, 147 coronary revascularizations, and 193 heart failures. A greater prewaking systolic BP surge was associated with significantly lower, not higher, CVD risk in a Cox proportional-hazard model adjusted for the significant influential characteristics of age, sex, diabetes, chronic kidney disease, cigarette smoking, waist perimeter, and previous CVD event (hazard ratio [HR] 0.83 [95%CI 0.78-0.88] per each 1-SD increment; P<0.001). The HR was progressively and significantly higher in the first three than in the last two quintiles of increasing prewaking BP surge. The prognostic value of morning surge markedly decreased after correcting by the asleep BP mean, the single most significant prognostic marked of total CVD events (HR=1.37 [1.29-1.44], P<0.001).
Conclusions: Our findings document that, when properly analyzed as a continuous variable, a larger morning BP surge is associated with a significantly lower CVD risk, in line with the markedly greater risk associated with decreasing dipping of the BP pattern, and the most highly significant prognostic value of progressively elevated asleep BP, an independent prognostic marker of CVD risk that has also been prospectively validated as a relevant therapeutic target for CVD risk reduction.

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PATIENT CHARACTERISTICS ASSOCIATED WITH OBESITY RELATED HYPERTENSION IN OBESE AFRICAN AMERICANS AND HYPERTENSION NON RESOLUTION AFTER BARIATRIC SURGERY: A SINGLE CENTER STUDY

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Background: Obesity related hypertension (HTN) disproportionately affects African American (AA) population, reversing the declining trend of cardiovascular morbidity and mortality. Rou-en-Y gastric bypass (RYGB) surgery is the most effective bariatric surgery (BS) procedure to treat obesity and obesity related hypertension. We examined the clinical characteristics associated with obesity related HTN in an obese AA cohort presenting for BS and with one year HTN non resolution in obese AA patients who underwent RYGB surgery at the Howard University Center for Wellness and Weight Loss Surgery (HUCWWLS).
Methods: A retrospective review of a prospectively maintained database from January 2007 onwards at HUCWWLS was performed. Pre-operative clinical characteristics of obese AA patients with HTN undergoing BS were compared. Also, patient characteristics associated with one year HTN non resolution after RYGB were examined.
Results: Of 242 obese AA patients presenting for BS; 168 (69 %) had preoperative HTN. Patients with preoperative HTN were older than patients without HTN (47 years vs. 38.5 years; $p < .0001$); had higher prevalence of diabetes (45.83% vs. 9.46%; $p < .0001$) and dyslipidemia (42.3% vs. 10.8 %; $p < .0001$). In a subset of patients who underwent RYGB and had one year outcome data available (n= 57), higher body mass index (BMI) and taking 2 or more HTN medications were significantly associated with hypertension non resolution.
Conclusion: AA patients with obesity related hypertension presenting for BS are older; have higher prevalence of diabetes and dyslipidemia irrespective of body mass index (BMI) compared to normotensive AA obese patients. Obese AA hypertensive patients who have non resolution of hypertension, 1 year after RYGB have higher BMI and are on 2 or more HTN medications. Prospective studies are needed to further evaluate characteristics of obesity related HTN to guide primary and secondary prevention strategies.

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PREVENTION A POSSIBLE DRUG–DRUG INTERACTION: IS CONCURRENT ADMINISTRATION OF ORLISTAT AND PIOGLITAZONE INCREASE THE RISK OF DRUG-INDUCED HEPATOTOXICITY?

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Background: Drug–drug interactions (DDIs) are an emerging threat to public health and are difficult to detect. To prevent DDIs and their burden, the possible DDIs should be kept in mind. We know that obesity predisposes to the development of insulin resistance and type 2 diabetes as well as heart disease. Therefore, combinational uses of anti-obesity drugs and glucose-lowering drugs in a patient with cardiovascular problem are very common. As the hepatotoxicity of both pioglitazone (an anti-diabetic drug) and orlistat (an anti-obesity drug) has been shown in some cases, the aim of this study was to evaluate the interaction of pioglitazone and orlistat in human hepatocellular cell line HepG2 cells to determine their effect on liver toxicity.
Methods: HepG2 cells were treated with 25 microM Pioglitazon (Pio), 20 microM Orlistat (Orl) pioglitazone, orlistat or combination of them. The MTT assay was used to assess cell viability.
Results: Pioglitazone and orlistat combination caused a loss of HepG2 cell viability. While pioglitazone (25 microM) and orliatat (20 microM) alone decreased the cell viability around 91% and 85% respectively (not-significant, $p > 0.05$), the combination of these two drugs reduced the amount of viable cells to 55% which was significant as compared by each drug alone. ($p < 0.001$).
Conclusions: Revealing the significant loss of viability of HepG2 cells in the combination use of pioglitazone and orlistat indicates these two drugs should not be administered in the same time to prevent their hepatotoxic effects especially in patients with liver dysfunction.

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MIR-210 SUPPRESSES GLUCOCORTICOID RECEPTOR IN RAT CARDIOMYOCYTES IN RESPONSE TO FETAL HYPOXIA

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Objective: To determine the role of hypoxia-induced micro-RNA (miR)-210 in the regulation of glucocorticoid receptor (GR) in rat cardiomyocytes during fetal hypoxia.
Background: Studies by our lab and others have demonstrated that fetal hypoxia is a major contributor to fetal programming of adult heart disease, and that glucocorticoids play a cardioprotective role in adult rat ischemia/reperfusion injury. However, little is known concerning the mechanisms by which fetal hypoxia influences glucocorticoid signaling. miR-210 is a well-established hypoxia-sensitive miR that has been shown to modulate cardiomyocyte responses to hypoxia. The role of miR-210 in the regulation of GR remains undetermined.
Methods: Cardiomyocytes were isolated from fetal (E21) rats and cultured under normoxia (21% O2) or hypoxia (1% O2) for 24-48 hours. GR and nuclear HIF-1 alpha protein and GR mRNA expression were measured using Western blot and qPCR, respectively. miR-210 expression, measured using miScript qPCR, and GR protein levels were determined in the presence or absence of a HIF-1 alpha inhibitor 2-methoxyestradiol (2ME). miR-210-mediated suppression of GR expression was detected using a luciferase reporter assay. The miR-210 LNA-antimiR hsa-miR-210-3p was used to confirm a causative role for miR-210 in the regulation of GR expression.
Results and Conclusions: Fetal cardiomyocytes exposed to hypoxia had significantly lower GR protein, but not mRNA, expression. Nuclear HIF-1 alpha protein and miR-210 levels were significantly increased in response to hypoxia; these effects were abrogated by exposure to 2ME during hypoxia. miR-210 mimics suppressed GR expression through interaction with the 3' UTR of GR mRNA. Finally, hypoxia-induced reductions in GR were reversed by treatment with miR-210 inhibitors during hypoxic insult. These results indicate that a HIF-1 alpha-mediated increase in miR-210 plays a key role in hypoxia-induced reductions in GR expression in cardiomyocytes.
(Supported in part by NIH Grants HL118861 and HL118861S1)

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NEW VIEW OF THE CARDIAC RYANODINE RECEPTOR ARRANGEMENTS AND THEIR FUNCTIONAL CORRELATION

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Cardiac Ryanodine Receptor (RyR2) are integral membrane proteins that function as Calcium-activated Calcium ion channels as well as a scaffold for a large number of signaling molecules that modulate the release of Calcium through the channel. The relative position of the RyR2 tetramers is therefore a critical determinant of their function. We have used transmission electron tomography to map the position of the tetramers in myocytes sections and have used tissue obtained from both rat and human hearts. Biochemical and physiological techniques were also used to correlate structure with function. Dual-tilt electron tomography produced en face views of both rat and human dyads, enabling a direct examination of RyR2 arrangement. Both species showed that tetramer packing was non-uniform containing a mix of checkerboard and side-by-side arrangements as well as isolated tetramers. We have shown that the tetramers' arrangement depended on the Magnesium concentration and on their phosphorylation status; in low Magnesium and after phosphorylation RyR2s were positioned in largely checkerboard arrangements while in response to high Magnesium the tetramers were positioned largely side by side. These tetramer arrangements: side by side, mixed and checkerboard were associated with progressively increasing Calcium spark frequencies. We have also shown that FK506-binding proteins, a well-known regulators of RyR2, has a dramatic effect on tetramer arrangement. The correlation between tetramer arrangement and spark frequency suggests that tetramer rearrangement may be another mechanism whereby physiological processes operate and provides potential new mechanisms by which the activity of RYR2, the dyad and cardiac contractility may be regulated.

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CORRELATION ANALYSIS OF THE ALTERATIONS IN EPOXY- AND HYDROXY-ARACHIDONIC ACID METABOLITES WITH THE DEVELOPMENT OF CARDIAC HYPERTROPHY IN RATS

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Cardiac hypertrophy is an important risk factor for several heart diseases, most importantly heart failure and sudden cardiac death. The importance of a group of arachidonic acids (AA) metabolites, namely epoxy- and hydroxy-AA, has been reported during the development of cardiac hypertrophy, though their specific roles are still unknown. In the current study, our aim was to determine the association between epoxy- and hydroxy-AA and the alterations in heart dimensions and functions, activation of fetal gene program and fibrotic and oxidative stress markers during cardiac hypertrophy. Cardiac hypertrophy was developed in Sprague Dawley rats by inducing pressure overload on the heart through aortic constriction procedure. Epoxy- and hydroxy-AA formation during cardiac hypertrophy was measured by liquid chromatography-mass spectrometry. Heart dimensions and functions were measured by echocardiography, while fetal genes and fibrotic and oxidative stress markers were measured by real-time PCR. Pairwise correlation analysis was performed, and univariate statistical analysis was used to identify metabolites whose formation rate was statistically associated with each of the tested parameter. Thereafter, non-parametric Spearman rank correlation coefficients were calculated. We found that wall thickness and the decrease in heart volumes parameters were strongly correlated with epoxy-AA and 5- and 9-hydroxy-AA ($r=\sim0.75$; $p<0.001$), while, 19-hydroxy-AA showed inverse correlation ($r=-0.42$; $p<0.01$). Heart functions were not correlated with any of the tested metabolites. In contrast, all metabolites, except 19-hydroxy-AA, showed a strong correlation with fetal gene program activation, especially 8,9- and 11,12-epoxy-AA ($r=\sim0.68$; $p<0.001$). Fibrotic and oxidative stress markers were better correlated with hydroxy-AA ($r=\sim0.67$; $p<0.001$), except 19-hydroxy-AA, compared with epoxy-AA ($r=\sim0.51$; $p<0.05$). In conclusion, the significant and differential association between epoxy- and hydroxyl-AA and pathologies of cardiac hypertrophy indicates the specific roles of these metabolites in the hypertrophic response of the heart to noxious stimulus.

This work was supported by a grant from the CIHR to AOSE.

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IMPROVEMENT EFFECTS ON CARDIAC FUNCTION AFTER OSTEOPONTIN-DERIVED SVVYGLR PEPTIDE-SECRETING MYOBLAST SHEETS TRANSPLANTATION FOR ISCHEMIC CARDIOMYOPATHY

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Autologous skeletal myoblasts sheet transplantation has the effect to secret cytokines that improve heart function, and is applied in clinical practice as a successful therapy for failing hearts. Osteopontin-derived seven-amino acid sequence (Ser-Val-Val-Tyr-Gly-Leu-Arg; SV peptide) induces angiogenesis. In this study, we hypothesized that the gene modified functional myoblast sheet could enhance therapeutic effect of sheet implantation and evaluated the long-term therapeutic effects of SV peptide-secreting myoblast sheets in an ischemic cardiomyopathy model rat. The ischemic cardiomyopathy model rats were divided into three groups: a WT-rSkMs group (transplanted with wild-type myoblast sheets), a SV-rSkMs (transplanted with SV peptide-secreting myoblast sheets); and a control group (ligation only). We evaluated cardiac function, histological changes, and smooth muscle actin (SMA) expression via transforming growth factor (TGF)-beta/Smad signaling. Cardiac function was significantly improved in the SV-rSkMs group. The systolic function in the SV-rSkMs group especially showed a significant improvement. Left ventricular remodeling was also significantly attenuated in the SV-rSkMs group. Furthermore, many clusters of SMA-positive myofibroblasts were widely observed in the infarcted areas of the SV-rSkMs group. In vitro, SMA expression was increased when the SV peptide was added to the isolated cardiac fibroblasts (CFs). The SV peptide showed a high affinity for TGF-beta receptor, and activated TGF-beta/Smad signaling on the CFs. SV peptide-secreting myoblast sheets transplantation provided continuous improvement of cardiac function and left ventricular remodeling. SV peptide induced myofibroblast differentiation of fibroblasts via TGF-beta/Smad signaling, and increased muscle-like cells in infarcted area. The accumulation of SMA-positive cells induced by SV peptide confers contractility to the stiff left ventricular wall. SV could possibly be used as a new peptide drug for myocardial regeneration medicine and be expected future usefulness for cardiac regeneration therapy without cell transplantation.

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MITOCHONDRIAL CALCIUM REGULATION FOR CARDIOPROTECTION

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Preservation of mitochondrial function is essential to limit myocardial damage in ischaemic heart disease. We examined the protective effects and mechanism of a new compound, NecroX-5, on rat heart mitochondria in a hypoxia/reoxygenation (HR) model. NecroX-5 reduced mitochondrial oxidative stress, prevented the collapse in mitochondrial membrane potential, improved mitochondrial oxygen consumption, and suppressed mitochondrial Ca2+ overload during reoxygenation in an in vitro rat heart HR model. Furthermore, NecroX-5 reduced the ouabain- or histamine-induced increase in mitochondrial Ca2+. These findings suggest that NecroX-5 may act as a mitochondrial Ca2+ uniporter inhibitor to protect cardiac mitochondria against HR damage.

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CARDIAC ENDOTHELIAL CELL-DERIVED EXOSOMES INDUCE SPECIFIC REGULATORY B CELL

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The mechanism of immune tolerance is to be further understood. The present study aims to investigate the role of the Cardiac endothelial cell (CEC)-derived exosomes in the induction of regulatory B cells. In this study, CECs were isolated from the mouse heart. Exosomes were purified from the culture supernatant of the primary endothelial cells. The suppressor functions of the regulatory B cells were determined by flow cytometry. The results showed that the CEC-derived exosomes carried integrin avb6. Exposure to lipopolysaccharide (LPS) induced B cells to express the latent transforming growth factor (TGF)-b, the latter was converted to the active form, TGF-b, by the exosome-derived avb6. The B cells released TGF-b in response to re-exposure to the exosomes in the culture, which suppressed the effector T cell proliferation.
We conclude that CEC-derived exosomes have the capacity to induce B cells with immune suppressor functions.

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P66SHC-MEDIATES OXIDATIVE STRESS AND ENDOTHELIAL ACTIVATION INDUCED BY MITOCHONDRIAL DYSFUNCTION IN HUVECS

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Mitochondrial dysfunction is the underlying mechanism involved in the pathophysiology of various cardiovascular diseases like atherosclerosis. CRIF1 is a protein present in the mitochondria associated with large mitoribosomal subunits, and CRIF1 knockdown induces mitochondrial dysfunction and promotes ROS production. p66shc is a redox enzyme implicated in mitochondrial ROS generation and translation of oxidative signals and, therefore, is a key factor for oxidative stress in endothelial cells. In this study, we investigated whether mitochondrial dysfunction induced by CRIF1 knockdown induces p66shc stimulation and plays any role in mitochondrial dysfunction-induced endothelial activation. Knockdown of CRIF1 decreased the expression of mitochondrial oxidative phosphorylation (OXPHOS) complexes I, III and IV, leading to increased mitochondrial ROS (mtROS) and hyperpolarization of the mitochondrial membrane potential. Knockdown of CRIF1 also stimulated phosphorylation of p66shc and increased cytosolic ROS in endothelial cells. Furthermore, the expression of vascular cell adhesion molecule-1 and an endoplasmic reticulum stress protein were increased upon CRIF1 knockdown in endothelial cells. However, p66shc knockdown blunted the alteration in mitochondrial dynamics and ROS production in CRIF1 knockdown endothelial cells. In addition, p66shc knockdown reduced the CRIF1 knockdown-induced increases in adhesion between monocytes and endothelial cells. Taken together, these results suggest that CRIF1 knockdown partially induces endothelial activation via increased ROS production and phosphorylation of p66shc.

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ANTI-INFLAMMATORY FUNCTION OF APE1/REF-1 IN ENDOTHELIAL ACTIVATION

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Apurinic apyrimidinic endonuclease 1/Redox factor-1 (APE1/Ref-1) has a pleiotropic role in controlling cellular response to oxidative stress. APE1/Ref-1 is mainly localized in the nucleus, but cytoplasmic localization has also been reported. A trafficking of APE1/Ref-1 between cellular compartments is reflected to different types of stressors. N-terminal region contains the redox regulatory domain characterized by 2 critical cysteine residues, C65 and C93. However, the functional role of cytoplasmic APE1/Ref-1 and redox mutants (C65A/C93A) are still unknown. We investigated the role of APE1/Ref-1 or its mutants on tumor necrosis factor-alpha(TNF-alpha)-induced vascular cell adhesion molecule-1 (VCAM-1) expressions in endothelial cells. N-terminus deletion mutants (putative nuclear localization signals) of APE1/Ref-1 were generated by deleting 28 amino acids of the N-terminus (29–318). The exposure of TNF-alpha increased the cytoplasmic APE1/Ref-1, which was inhibited by NADPH oxidase inhibitor, not cycloheximide nor leptomycin, suggesting cytoplasmic translocations of APE1/Ref-1. Transfection of an N-terminus deletion mutant APE1/Ref-1(29-318) inhibited TNF-alpha-induced VCAM-1 expression, indicating an anti-inflammatory role for APE1/Ref-1 in the cytoplasm. In contrast, redox mutant of APE1/Ref-1 (C65A/C93A) transfection led to increased TNF-alpha-induced VCAM-1 expression. Our findings suggest cytoplasmic APE1/Ref-1 localization and redox cysteine residues of APE1/Ref-1 are involved in critical role for anti-inflammatory activity of APE1/Ref-1 in endothelial cells.

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HPLC-FLUORESCENCE METHOD FOR THE ENANTIOSELECTIVE ANALYSIS OF PROPRANOLOL IN RAT SERUM USING IMMOBILIZED POLYSACCHARIDE-BASED CHIRAL STATIONARY PHASE

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A stereoselective high-performance liquid chromatographic (HPLC) method was developed and validated to determine S-(−)- and R-(+)-propranolol in rat serum. Enantiomeric resolution was achieved on cellulose tris(3,5-dimethylphenylcarbamate) immobilized onto spherical porous silica chiral stationary phase (CSP) known as Chiralpak. A simple analytical method was validated using a mobile phase consisted of n-hexane-ethanol-triethylamine (95:5:0.4%, v/v/v) at a flow rate of 0.6 mL min-1 and fluorescence detection set at excitation/emission wavelengths 290/375 nm. The calibration curves were linear over the range of 10–400 ng mL-1 (R = 0.999) for each enantiomer with a detection limit of 3 ng mL-1. The proposed method was validated in compliance with ICH guidelines in terms of linearity, accuracy, precision, limits of detection and quantitation, and other aspects of analytical validation. Actual quantification could be made for propranolol isomers in serum obtained from rats that had been intraperitoneally (i.p.) administered a single dose of the drug. The proposed method established in this study is simple and sensitive enough to be adopted in the fields of clinical and forensic toxicology. Molecular modeling studies including energy minimization and docking studies were first performed to illustrate the mechanism by which the active enantiomer binds to the βeta-adrenergic receptor and second to find a suitable interpretation of how both enantiomers are interacting with cellulose tris(3,5-dimethylphenylcarbamate) CSP during the process of resolution. The latter interaction was demonstrated by calculating the binding affinities and interaction distances between propranolol enantiomers and chiral selector.

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SPECKLE TRACKING ECHOCARDIOGRAPHY IN THE ASSESSMENT OF CONSTRICTIVE PERICARDITIS

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Background: The aim of the present study was to assess the incremental value of Speckle Tracking Echocardiography (STE) for differentiation between CP and RCM. Although normal or exaggerated early diastolic mitral annular velocity provides high specificity for differentiating constrictive pericarditis (CP) from restrictive cardiomyopathy (RCM), its sensitivity has been shown to be lower.
Methods: Twelve patients with CP, 8 with RCM, and 12 healthy controls were studied. Standard mitral inflow Doppler and tissue Doppler echocardiography (TDI) were performed. LV TDI annular peak systolic and diastolic velocities (S', E') and time difference between onset of mitral inflow (E velocity) and onset of E' (E'-E time) were measured. LV longitudinal strain and systolic and diastolic strain rate were obtained in the basal, mid and apical segments of septal and lateral walls in apical 4-chamber view both by STE. Circumferential and radial strain and averaged LV rotation and rotational velocities from the base and apex were also obtained by STE.
Results: E' and S' were significantly higher in patients with CP than RCM (9.1 ± 1.4 vs 4.4 ± 1.6cm/s, and 7.8 ± 1.2 vs 4.2 ± 1.4cm/s respectively, $p < 0.001$). E'-E was significantly shorter in patients with CP (25.8 ± 21.6 vs 56.5 ± 24.4ms, $p < 0.005$). Impairment of longitudinal strain in the antero-lateral wall (ALWLS) was shown in CP patients compared to controls (-14.2 ± 2.9 vs -20.1 ± 2.8%, $p<0.001$) whereas circumferential and radial strain values did not change significantly. ROC curves suggested that the thresholds offering an adequate compromise between sensitivity and specificity for detection of CP were -15.2% for ALWLS (AUC 0.87), 32.8 ms for E'-E time (AUC 0.78), and -5.1 cm/sec for E' velocity (AUC 0.72).
Conclusions: STE indices provide incremental diagnostic information to conventional Doppler echocardiography and can be helpful to differentiate between CP and RCM.

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ATRIAL FLUTTER HAS LESS SPONTANEOUS ECHO CONTRAST AND HIGHER APPENDAGE EMPTYING VELOCITY THAN ATRIAL FIBRILLATION

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Objectives: We hypothesized that patients with atrial flutter (AFl) would have less incidence of thrombus formation and better prognostic indicators of thromboembolism risk than patients with atrial fibrillation (AF) on trans-esophageal echocardiography (TEE).
Background: The risk of stroke and thromboembolism in AF is established. The risk in patients with atrial flutter AFl is not as evident.
Methods: A retrospective analysis of 1,800 patients undergoing TEE was performed. Those with AF or AFl were reviewed. Exclusion criteria were chronic anticoagulation, prosthetic valve, mitral valve disease, congenital heart disease and heart transplantation. 73 with AF and 38 with AFl were included in the analysis. Patient demographics and TEEs were reviewed to obtain the data.
Results: Eight patients with thrombus were observed in the AF versus none in the AFl group, which was statistically significant (p=0.05). The prevalence of spontaneous contrast and LAAEV was significantly lower in AFl group (p <0.001). No spontaneous contrast was seen with LAAEV >60 cm/sec. All eight patients with thrombi in the AF group had spontaneous contrast.
Conclusion: Patients with AFl have lower incidence of LAA thrombi, higher LAAEV and less spontaneous contrast compared with AF patients, suggesting a lower risk for arterial thromboembolism in AFl patients.

	Atrial fibrillation (n=73)	Atrial flutter (n=38)	P value
Age (mean years)	63	63	0.890
Sex (female)	17/ 73 (23%)	8/38 (21%)	1.00
LVEF (mean%)	50.6	55.2	0.08
LAVI (mean)	31.6	29.8	0.257
Presence of Thrombus	8/73 (11%)	0/38 (0%)	0.05
Presence of Spontaneous contrast	38/73(52%)	5/38 (13%)	<0.001
LAAEV (mean)	44.11 cm/sec	62.02 cm/sec	<0.001
CHADS2 score	1.30	1.19	0.78

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THREE-DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY IN THE ASSESSMENT OF RIGHT VENTRICULAR DYSFUNCTION AFTER SURGICAL REPAIR OF TETRALOGY OF FALLOT

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Background: The combined effects of preoperative hypertrophy and hypoxia, possible intraoperative myocardial damage, type of reconstruction, and acquired postoperative lesions such as pulmonary regurgitation may result in impaired RV deformation in post-operative tetralogy of Fallot (TF). Recently 3D speckle tracking echocardiography (3DSTE) has been proposed to assess mechanical dyssynchrony in these patients but the role of electromechanical dysfunction is not completely clear.
Methods: Sixteen patients after TF repair (aged 17-53years) with dilated right ventricle, right bundle branch block (QRS >120ms), and NYHA class I or greater were studied with two-dimensional and three-dimensional speckle tracking echocardiography. Right ventricular end-diastolic and end-systolic volumes were measured from three-dimensional datasets and right ventricular ejection fraction (3D-RVEF) was obtained. Right intraventricular dyssynchrony was determined as the difference between the longest and shortest electromechanical coupling times in the basal septal and lateral RV segments. Interventricular dyssynchrony was determined as the difference between electromechanical coupling times in the basal lateral LV segment and the most delayed RV segment. Sixteeen age-matched healthy subjects were selected as controls.
Results: Right intraventricular dyssynchrony (77.1+/-24.2ms vs 13.1+/-8.9ms) and interventricular dyssynchrony (74.7+/-22.2ms vs 11.4+/-7.9ms) were shown in patients compared to normal controls. Right intraventricular dyssynchrony correlated with RV longitudinal strain ($r=0.62$, $p<0.005$), 3D RV end-systolic volume ($r=0.47$, $p=0.02$), and QRS duration ($r=0.39$, $p=0.03$). Interventricular dyssynchrony correlated with RV longitudinal strain ($r=0.73$, $p<0.001$), RV systolic pressure ($r=0.59$, $p<0.005$), 3D-RVEF ($r=0.53$, $p=0.003$), and QRS duration ($r=-0.44$, $p=0.031$). Reduced RV strain, 3D-RVEF and prolonged QRS duration were the main determinant factors predicting RV dyssynchrony by multivariate analysis. On ROC curves RV strain and 3D-RVEF had optimal predictive accuracy of the NYHA functional class and a larger area under the receiver operating characteristic curve than the QRS duration.
Conclusions: In patients with repaired TF RV dyssynchrony is associated with reduced 3D-RVEF and RV 3DSTE parameters.

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DOBUTAMINE-INDUCED ATRIAL FIBRILLATION DURING DOBUTAMINE STRESS ECHOCARDIOGRAPHY

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Objective and background: Endogenous catecholamines are implicates in initiation and maintenance of atrial fibrillation (AF). Synthetic catecholamines have also been rare inducers of AF.
The aim of this study was to determine the incidence and predictors of AF induced during dobutamine stress echocardiography (DSE) as reported in English literature.
Methods and Results: A total of 27 studies including 51,972 patients reported the incidence of AF during DSE from 1991 to 2011. The incidence of AF during DSE ranged from 0.3% to 2.2% (mean 0.9%). The dose of dobutamine used in these studies ranged from an initial dose of 2.5 to a peak dose of 50 microgram/kg/min usually in graded 3 or 5-minute stages. Three studies used an accelerated protocol for dobutamine infusion (fixed dose of 50 microgram/kg/min in 2 and two fixed doses of 20 and 40 microgram/kg/min in another). Intravenous atropine was included in DSE protocol in 24 (89%) studies with highest dose of 0.4 mg in 1, 1 mg in 15 and 2 mg in 8 studies. Independent predictors of dobutamine-induced AF were reported in only 3 studies (n=21,394, incidence of AF 1-1.9%) with a prior history of AF being the only consistently reported predictor (odds ratio for development of AF up to 3.7).
Conclusion: AF is a rare complication of DSE and occurs more frequently in those with prior history of AF.

PROGRESS IN ECHOCARDIOGRAPHY

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CORRELATE OF GLOBAL LONGITUDINAL, RADIAL AND AREA STRAIN IN SEVERE AORTIC STENOSIS WITH NORMAL LEFT VENTRICULAR EJECTION FRACTION: A THREE-DIMENSIONAL AND TWO-DIMENSIONAL MULTILAYER SPECKLE TRACKING ECHOCARDIOGRAPHY

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Background: The aim of this study was to the capability of real-time three-dimensional echocardiography (RT3DE) and two-dimensional multilayer speckle-tracking echocardiography(MSTE) in characterizing early abnormalities of left ventricular (LV) structure and function in patients with severe aortic stenosis (AS) and normal LV ejection fraction (EF±50%).
Methods: Conventional, 3D STE and MSTE were performed in 51 patients (mean age 68.9±9.0 yrs) with severe AS (aortic valve area <1 cm2, AV Vmax >4 m/sec or mean PG >40mmHg) and normal LVEF but without overt coronary artery and 64 healthy controls. Global longitudinal strain (GLS), global circumferential strain (GCS), global area strain (GAS), and global radial strain (GRS) were calculated by RT3DE and MSTE.
Results: Severe AS group had lower 3D GLS, GAS and 2D epicardium, midwall and endocardium GLS compared controls. But, 3D GCS, GRS was not significantly different between two groups. In MSTE analysis, 2D LS and CS values decreased from the endocardial layer toward the epicardial layer.
Conclusions: Three-dimensional and multilayer STE identifies early functional LV changes in severe AS patients with normal LVEF. GLS and GAS impaired, while circumferential strain is still preserved, supporting a normal LV chamber systolic function. Therefore, 3D and multilayer STE may give additional information in the decision-making process for severe AS patients with normal left ventricular function.

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PROGNOSTIC IMPLICATIONS OF RACE IN PATIENTS WITH NORMAL DOBUTAMINE STRESS ECHO

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Aim: Stress Echo is an effective investigative tool to assess coronary artery disease. Given the different risk factor profile for coronary artery disease between Asian and Caucasian populations, the aim of this study was to assess whether there was a difference in prognostic outcome of a normal Dobutamine stress echo (DSE) between the two population cohorts.
Method: A retrospective analysis was carried out on all patients that received a DSE between the periods of April 2011 to December 2012. The echo results, patient letters and patient information from a national electronic patient data system (System One) were reviewed retrospectively to collect demographic, morbidity and mortality data.
Results: 211 patients were identified as having had a normal DSE. 61 patients were Asian in origin and 148 were Caucasian with 2 described as another race. In this group, there were no cardiac mortalities within the year. In the One year period 5 Non ST elevation myocardial infarctions (NSTEMI's) occurred giving a cardiac event rate of 23 per 1000 patients. Of these NSTEMI patients 1 (1.6%) was Asian and 4 (2.7%) patients were Caucasian (p value=1.00).
Conclusion:
1. A normal DSE confers a good one year prognostic outcome in terms of cardiac mortality and morbidity.
2. There is no difference in prognostic outcome of a normal DSE between the Asian and Caucasian population.
3. Larger sample studies are required to confirm these findings.

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CORRELATION BETWEEN CARDIOVASCULAR AND LIVER MAGNETIC RESONANCE T2* AND TRANSTHORACIC ECHOCARDIOGRAPHIC STUDY IN THALASSEMIA PATIENTS

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Background and Objective: Heart failure is the most important reason of mortality and morbidity in thalassemia patients. Repeated blood transfusions, peripheral hemolysis and increased iron absorption from intestinal tissue in thalassemia patients resulting iron overload and accumulation of iron in tissues such as myocardium. Early detection of cardiac involvement is important to improvement of prognosis in these patients. Transthoracic Echocardiography has been known as a non-invasive technique for routine cardiac evaluation in thalassemia but left ventricular systolic function remains approximately normal until late in thalassemia.
Method: 130 thalassemia patients (38.5% intermedia, 61.5% major) were selected, 8 patient were excluded due to poor image quality in echocardiographic study. T2* cardiovascular and liver magnetic resonance was performed in the patients to assessment of liver and myocardial iron load. 2D and 3D echocardiography and tissue Doppler study were performed on all subjects.
Results: The mean value of LVEF in the thalassemia patients were 60% ± 0.6%. PAP was higher in thalassemia intermedia than thalassemia major (P = 0.014) and PAP correlated positively with age (P=0.003). There was a significant correlation between longitudinal global strain and MRI T2* of the liver (P = 0.02) and cardiac (P = 0.006). There was significant correlation between LVEF (by 3D method) and cardiac MRI T2*(P = 0.05).
Conclusions: Thalassemia patients with cardiac and liver iron overload had lower longitudinal global strain and LVEF therefore in unequipped centers which CMR is not available, evaluation of longitudinal global strain and LVEF with 3dimentional method can be replacing tools.

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IS THERE ANY CORRELATION BETWEEN CHA2DS2-VASC SCORE TO LEFT ATRIAL VOLUME INDEX?

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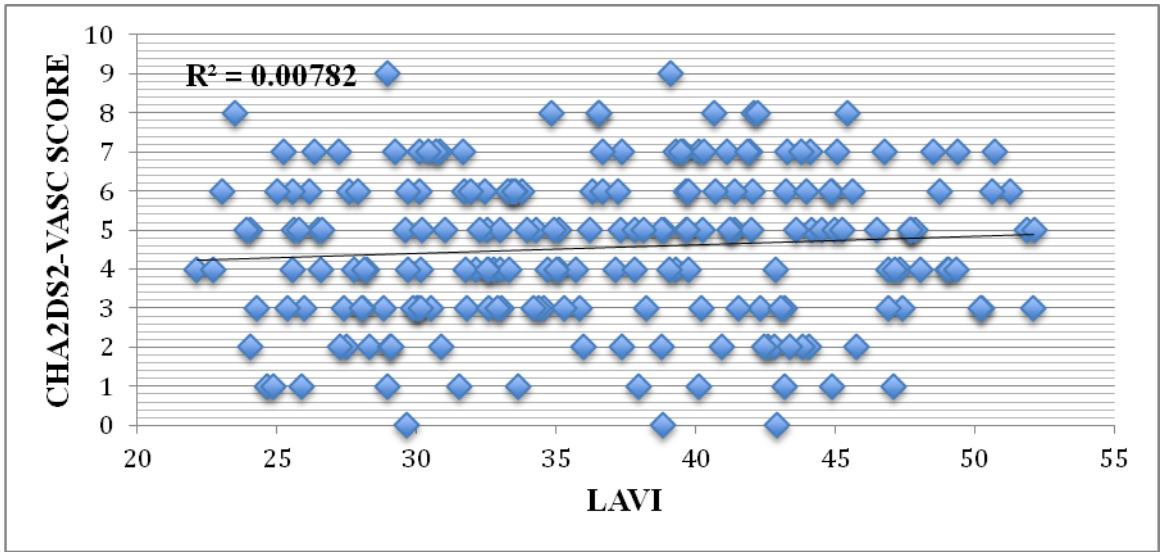
Background: Current guidelines recommend use of CHA2DS2-VASC score for risk stratification in prevention of thromboembolic events in patients with nonvalvular atrial fibrillation (AF). Left atrial dysfunction can increase the risk of thrombus formation in the left atrium and left atrial appendage, with left atrial remodeling and distortion as a precipitant for AF. Left atrial volume index (LAVI) has also been shown to predict strokes and mortality in non-AF patients. We sought to determine if there is any correlation between CHA2DS2-VASC score and LAVI.
Methods: A total of 813 patients were evaluated from June 2013 to June 2014; 207 patients met inclusion criteria for diagnosis of AF and had echocardiographic data for calculation of LAVI.
Results: Of the cohort, 47% (n=96) were female and 53% (n=111) were male, mean age of 71.39 ±11.91 years. The average CHA2DS2-VASC score was 4.56± 1.94. The mean LAVI was 36.68 ±7.36. The figure shows lack of correlation between the 2 clinical factors.
Conclusion: Although CHA2DS2-VASC score and LAVI have both been shown to predict strokes, we found no correlation in this observational study. Clinical risk factors and echocardiographic features are independent predictors and are both useful for predicting thromboembolic events in patients with AF.



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MAKING NOT-SO-OBVIOUS OBVIOUS; THE ROLE OF 2D ECHOCARDIOGRAPHY IN DIAGNOSIS OF AORTIC DISSECTION

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Clinical presentation
Case 1: A 52 year old female with history of hypertension (HTN) presented with left sided neck pain radiating to left jaw which resolved spontaneously. It was associated with transient difficulty in speech. Physical examination was unremarkable. After a negative CT scan of head, she was admitted. Transthoracic Echocardiogram (TTE) done for stroke workup showed dilated ascending aorta with dissecting flap extending from aortic root to the arch with mild aortic regurgitation. CT angiogram confirmed the findings of type A aortic dissection (AD). She underwent emergent surgery and recovered well.
Case 2: A 66 year old male with history of HTN presented with sudden onset chest pain. He was hypotensive and tachycardic at presentation. Cardiovascular exam revealed grade 2/6 diastolic murmur. EKG showed ST depression in anterolateral leads with ST elevation in AVR and V1. TTE performed prior to the transfer to cardiac catheterization lab showed dilatation of aortic root and ascending aorta with large intimal flap prolapsing into the left ventricle outflow tract during diastole with severe aortic regurgitation. CT angiogram confirmed the diagnosis of type A AD. Despite undergoing emergent surgery, his clinical status continued to worsen and died.
Clinical significance: The role of TTE is somewhat limited in diagnosis of AD. It has high positive predictive value, but it may be difficult to exclude the diagnosis if findings are negative. These two cases illustrate the role of TTE as a quick useful tool in diagnosis of aortic dissection in near miss scenarios.

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RUPTURED CASEOUS MITRAL ANNULAR CALCIFICATION PRESENTING AS A MOBILE MASS

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Introduction: The annulus of the mitral valve commonly becomes calcified in the elderly. Mitral valve annulus calcification (MAC) may be found in 10% of old patients and 40% of patients with end-stage renal disease (ESRD) referred for echocardiography. Caseous calcification of the mitral annulus (CCMA) may present as large intracavitary mass. Rupture of MAC has been reported as a fatal complication of transapical aortic valve implantation. We report a case of spontaneous rupture of mitral valve annular calcium with systemic embolism.
Case: A 63-year-old diabetic female with ESRD presented with purulent drainage from her left foot. Wound culture showed a rare strain of Enterococcus and ceftazoline was started. ECG and blood cultures were essentially unremarkable. MRI of the left foot showed no osteomyelitis or cellulitis. Transthoracic and transesophageal echocardiography showed a mobile echodensity measuring 0.9 x 0.6 cm attached to the atrial aspect of the posterior mitral valve annulus without any valve dysfunction. Abdominal aortography with runoff showed severe diffuse atherosclerosis involving distal vessels without evidence obvious evidence for thromboembolism. The patient was started on anticoagulation and will be followed up for further imaging and management.
Discussion: CCMA is an unfamiliar condition with a generally benign course and potential for rupture with complicating mitral valve dysfunction, conduction abnormalities and systemic embolization. It is unclear whether interventions aimed at lowering mechanical shear forces (beta-blockade), stabilizing atherosclerotic lesions (statins), or reducing phosphate overload would prevent this particular complication of CCMAC.

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CONTRIBUTION OF EPICARDIAL ADIPOSE TISSUE TO ATRIAL FIBRILLATION SUBSTRATE WITH HIGH DOMINANT FREQUENCY IN ABLATION

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Background: The peri-atrial epicardial adipose tissue (EAT) volume predicts the development of new-onset atrial fibrillation (AF), and is associated with the severity of AF. EAT is associated with the outcome after AF ablation. EAT is considered to induce electrical and structural remodeling of the atrium leading to AF. EAT is located adjacent to high dominant frequency (DF) sites. The relationship between the EAT location and efficacy of a combined high DF site and continuous complex fractionated activation electrogram (CFAE) site ablation is unclear.
Methods: Fifty-five non-paroxysmal AF patients (26 persistent and 29 longstanding) underwent pulmonary vein isolation (PVI) followed by a high DF site and continuous CFAE site ablation. High DF sites (DF ≥8Hz) and continuous CFAE sites (fractionated intervals ≤50ms) were targeted. The patients were divided into an AF-free group and AF-recurrent group.
Results: The AF freedom on antiarrhythmic drugs in persistent and longstanding persistent AF patients was 88.5% and 75.9% over a 12-month follow-up period, respectively. The total EAT, left atrial (LA)-EAT, and right atrial (RA)-EAT volumes did not indicate significant differences between the AF-free and AF-recurrent groups. In the LA, the overlap between the high DF sites and EAT was larger in the AF-free group than in the AF-recurrent group (57.0±33.3% vs. 22.6±23.3%, $p<0.01$). However, this overlap did not differ between the AF-free and AF-recurrent groups in the RA (20.4±28.2% vs. 19.0±24.4%, NS). The overlap between the continuous CFAE sites and EAT did not differ between the two groups in both the LA and RA. In addition, the overlap between the AF substrate and EAT did not differ between the persistent AF and longstanding persistent AF patients.
Conclusions: High DF sites that overlap with EAT may be important sources of AF.

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EFFECT OF AMIODARONE-WARFARIN INTERACTION ON ANTICOAGULATION QUALITY IN A SINGLE CENTER

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Background: Clinical trials have reported a low time in therapeutic range (TTR) in patients with atrial fibrillation treated with both warfarin and amiodarone. These trials included centers and countries with both high and low TTR's.
Objectives: To determine the impact of amiodarone on the TTR in a single, high-quality anticoagulation clinic.
Methods: TTR was assessed in amiodarone and non-amiodarone treated patients from a University Anticoagulation Clinic.
Results: Baseline characteristics between patients ever-taking or never-taking amiodarone were similar, except more amiodarone patients were smokers (19.5% vs. 6.1%, p=0.0031). The TTR calculated from 8,901 international normalized ratios (INR) in 249 non-amiodarone patients with a mean follow-up of 34 +/- 20 months (mean 36 +/- 18 INR's) was 66% +/- 16.6 compared with 61.3% +/- 16.2 (p=0.111) from 1,455 INR's in 41 amiodarone treated patients with a mean follow-up of 28 +/- 20 months (mean 35 +/- 22 INR's). Factors associated with a low TTR were male gender (p=0.0013), smoker (p=0.0048), and amiodarone use (p=0.0374). A second on-treatment analysis, in which the TTR was calculated only during amiodarone therapy, resulted in similar findings, however amiodarone did not emerge as a predictor of a low TTR. In 11 patients, the TTR prior to amiodarone (54.5% +/- 22.2) was not significantly different in the first 3 months (54.6% +/- 33.4) or after 3 months (67.2% +/- 33.7) of amiodarone.
Conclusion: In a single high-quality anticoagulation center, anticoagulation quality, as measured by the TTR, can be comparable in amiodarone and non-amiodarone treated patients.

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CLINICAL 1 YEAR EXPERIENCE WITH A NOVEL MULTIPOLAR IRRIGATED ABLATION CATHETER IN AF ABLATION PROCEDURES

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Introduction: Pulmonary vein isolation (PVI) is an established method to treat atrial fibrillation (AF). However, PVI is still a time consuming procedure. Thus, new methods are necessary to improve procedural parameters, e.g. shortening of procedure time (PT). A novel multipolar irrigated radiofrequency (RF) ablation catheter (nMARQ™) is a new tool trying to improve PVI procedures. In this study we investigated the influence on procedural parameters using a multipolar irrigated ablation catheter (MIAC).
Methods: 48 consecutive patients with paroxysmal AF were investigated undergoing PVI divided into 2 groups: 1.) n=24, standard ablation catheter (SAC, Thermocool Biosense Webster©), 2.) n=24, MIAC (nMARQ™ Biosense Webster©). Study endpoints included procedure time (PT), fluoroscopy time (FT), number of energy applications (EA) and clinical outcome (freedom from AF). All MIAC patients underwent phrenic nerve stimulation and esophagus temperature monitoring during PVI as well as endoscopy post PVI for safety assessment.
Results: Patient characteristics did not differ significantly between both groups. PE was reached in all patients in the SAC group. However, in the MIAC group complete PVI failed in 5/24 patients. Mean FT and LA PT were similar. However, number of EA (20±1 vs. 29±4, $p<0.05$) and cumulative RF time (16±1 vs. 24±5 min, $p<0.001$) to achieve PVI were significantly lower in MIAC group vs. SAC. Analysis of clinical outcome revealed no differences a mean follow-up (FU) of 263±131 days between both groups (MIAC: 85% vs. SAC: 76%). Regarding safety one catheter charring event, one thermal esophageal lesions and one phrenic nerve palsy, despite prophylactic stimulation, was observed in the MIAC group.
Conclusion: In our small cohort ablation with MIAC seems to still bear a potential for complications along with important device related limitations to successfully assess and achieve PV disconnection. Furthermore, ablation with MIAC failed to show significant benefits regarding relevant procedural parameters or clinical outcome compared to a SAC cohort.

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IMPACT OF REDUCED ABLATION TIME ON CLINICAL OUTCOMES IN PAF PATIENTS USING ARCTIC FRONT ADVANCE CRYOBALLOON (AFACA)

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Background: Cryoablation of paroxysmal atrial fibrillation (PAF) with the AFACA has technical advantages over the older system but its use has been associated with complications.
Objective: We proposed to study the impact of shortening ablation time on the outcomes of the AF ablation using AFACA.
Methods: We retrospectively studied 118 consecutive patients with PAF who underwent AFACA between 7/12 – 5/13. In the conventional group (83 pts; 7/12 – 2/13) we aimed for ablation time of 4-min/lesion and in the modified group (35 pts; 3/13-6/13), we aimed for 3 min/lesion. Ablation times and complications including selected indicators of 'collateral damage' (pericarditis, esophageal injury or fistula, transient phrenic nerve paralysis) with 3 and 6-month procedure success were compared.
Results: In the modified time group, the total ablation time and time/lesion were reduced by 24% ($p<0.001$) and 26% respectively ($p < 0.001$). 'Collateral damage' was reduced in the modified time group (8.6% versus 24.1%; $p = 0.05$), driven mostly by minor pericarditis. Only one major complication occurred in the conventional group (atrio-esophageal fistula). [Table1].
Conclusions: Shortening of ablation time using AFACA resulted in significantly less complication rate including reduced 'collateral damage' to mediastinal structures, while preserving optimal clinical outcomes of cryoablation in patients with PAF.

Table 1.

Parameters	Conventional (n=83)	Modified (n=35)	p-value
Age(years)	60.9±11	59.2±11.3	0.45
Male, n (%)	49(59)	26(74)	0.12
Number of pulmonary veins per patient, n	4.0±0.4	4.0±0.4	>0.999
Average no. of lesions per patient, n	9.9±2.0	10.0±1.8	0.8
Average no. of lesions per vein, n	2.5±0.6	2.6±0.6	0.41
Average ablation time (min),n	37.0± 6.7	28.2± 6.8	<0.001
Average ablation time/lesion (min)	3.8± 0.3	2.8± 0.6	<0.001
Average ablation time/vein (min)	9.2±1.9	7.4±2.3	<0.001
Complication Rate, n (%)	23(27.7)	3(8.6)	0.02
Transient Ischemic attack, n (%)	3(3.6)	0(0)	0.55
'Collateral damage' n (%)	20(24.1)	3 (8.6)	0.05
Minor pericarditis, n (%)	12 (14.5)	1 (2.9)	0.11
Transient phrenic nerve palsy, n (%)	5 (6)	1 (2.9)	0.67
Esophageal injury, n (%)	1 (1.2)	1(2.9)	0.51
Atrio-esophageal fistula n (%)	1 (1.2)	0 (0)	>0.999
Pulmonary vein stenosis	1(1.2)	0(0)	>0.999
Total Follow up, n (%)	81(97.6)	35(100)	>0.999
3-months success ±AAD, n (%)	61 (75.4)	25 (71.4)	0.82
3-6months true success (No AAD), n (%)	62 (76.5)	27 (77.1)	0.78

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MANAGEMENT OF GASTROINTESTINAL SYMPTOMS IN PATIENTS TREATED WITH DABIGATRAN ETEXILATE (PRADAXA®)

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Dabigatran etexilate (DE) is indicated to reduce risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF). Increased incidences of gastrointestinal symptoms (GIS) such as abdominal discomfort were seen in trials comparing DE to warfarin.
An exploratory study evaluated 2 strategies for GIS management with DE.DE-naïve NVAF patients with no GIS for > 2weeks were followed for 3 months taking DE. Patients reporting GIS were randomized (1:1) to either a strategy of taking DE within 30 min after a meal or added pantoprazole (40 mg daily). Patients whose GIS did not completely resolve with the initial strategy were to be assigned the other as add-on therapy. Management periods lasted 4 weeks. 1067 patients were enrolled and treated with DE. 117 patients (11%) self-reported GIS and were randomized: 58 to pantoprazole and 59 to DE + meal. In the pantoprazole group, 39 patients (67%) had complete symptom resolution, 11 (19%) partial resolution, and 8 (14%) no resolution. In the DE + meal group, 33 (56%) had complete resolution, 7 (12%) partial resolution, and 19 (32%) no resolution. A descriptive P value comparing strategies was <0.05 favoring pantoprazole. For the second (add-on) phase, 11 of 19 patients with partial or no GIS resolution taking pantoprazole added DE + meal: 2 had symptom resolution, 6 partial resolution, and 3 no resolution or withdrew consent. Alternatively, 14 out of 26 patients with partial or no response taking DE + meal added pantoprazole: 6 had symptom resolution, 6 partial resolution, and 2 no resolution.
Patients who developed GIS on DE had partial or complete resolution of symptoms more frequently on an initial management strategy that included pantoprazole. Overall, 90/117 (77%) of patients with GIS randomized experienced complete or partial resolution of symptoms when taking DE with a meal or concomitant pantoprazole.

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USEFULNESS OF DABIGATRAN IN JAPANESE PATIENTS WITH NON VALVULAR ATRIAL FIBRILLATION

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Background: Recently, several novel anticoagulants have been approved for the prevention of thromboembolic strokes as an alternative to warfarin in patients with non-valvular atrial fibrillation (AF). However, anticoagulant effects and bleeding risks of a direct thrombin inhibitor dabigatran have not been fully elucidated in Japan.
We studied adverse events in the dabigatran-treated group, and analyzed for risk factors of hemorrhagic adverse events.
Methods: We retrospectively examined patients taking dabigatran or warfarin with AF in Toho University Medical Center Sakura hospital. Anticoagulant effects were evaluated using Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT). CHADS2 score and HAS-BLED score were used for risk evaluation.
Results: Dabigatran was administered as anticoagulant in 70 patients and warfarin was administered in 230 patients. Thromboembolism was observed in 15 patients with warfarin, but was not observed with dabigatran. Bleeding complications were observed in 9 patients (12.9%) with dabigatran and 119 (51.7%) with warfarin. In patients with dabigatran, intracranial hemorrhage was not observed. APTT of bleeding group was 38.9±8.7 sec at trough, APTT of non-bleeding group was 38.6±6.1 sec (p=0.96).APTT of bleeding group was 53.48.3 sec at peak, APTT of non-bleeding group was 50.0±9.7 sec (p=0.25). PT of bleeding group was 12.6±1.3 sec, PT of non-bleeding group was 12.1±1.8 sec (p=0.13). PT and APTT were not correlated with creatinine level.CHADS2 score or HAS-BLED score was not correlated with bleeding. Gastric manifestations were observed in 19 patients (27.1%) with dabigatran.
Conclusions: Dabigatran may be a safe and effective drug for the patients with AF including the aged patients, and its anticoagulant effect is stable. However, minor bleeding may occur without marked prolongation of APTT.

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EVALUATING EJECTION FRACTION AND OBESITY IN A HEART FAILURE PROGRAM PREDOMINANTLY COMPOSED OF A BLACK AND HISPANIC POPULATION

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Objective: To relate the obesity paradox to ejection fraction and obesity.
Background: The obesity paradox remains controversial in the literatures. Obesity has detrimental effects on heart failure, but has been found to be paradoxically associated with improved survival.
Method: This is a cross-sectional study. We analyzed 732 patients who were enrolled in our heart failure program and excluded those who did not follow up or patients discharged from the cardiology clinic. 344 patients who have been followed since 2013 were included. Using ACC/AHA guidelines, heart failure is classified as a reduced ejection fraction (HFrEF, EF <40), preserved ejection fraction (HFpEF, EF>50) and heart failure with an improved ejection fraction (HFpEF(i),EF> =40). BMI (Body Mass Index) was classified according to NCEP-ATP III. All variables were analyzed by SAS Ver. 9.4.
Results: The number of normal weight (BMI <25kg/m2), overweight (30 kg/m2>BMI > =25kg/m2) and obesity (BMI > =30kg/m2) were 125(35.7%),121(35.1%) and 98(29.1%) respectively. The number of patients in our selected populations of HFrEF, HFpEF and HFpEF(i) were 228(67.9%),68(20.2%) and 40(11.9%) respectively. A preserved EF had a significant P-value associated with the overweight group compared to our normal weight group. In addition, the absence of diabetes mellitus, an ICD, no prior cardiac catheterization and age over 65 were associated with a preserved EF.
Conclusion: The obesity paradox applied to our study group. The overweight group had a higher percentage of patients with a preserved ejection fraction compared to the normal weight group. Factors favoring a preserved EF were different among our three BMI groups. Targeted management of related factors in heart failure could lead to different approaches in the future treatment of heart failure.