days, n=38). All patients underwent angiography which showed total occlusion or stenosis ≥70% in the pertinent limb artery. Among biomarkers evaluated (median; 1st quartile, 3rd quartile), significantly higher concentrations were found in patients with acute compared with chronic limb symptoms for Cyr61 600 (467; 908) ng/l vs. 460 (399; 595) ng/l (p=0.02) and sFlt-1 2740 (1275; 3719) ng/l vs. 179 (102; 2816) ng/l (p<0.001). In contrast, concentrations were not different between the two groups for PIGF 27.1 (22.5; 30.7) ng/l vs. 21.3 (17.2; 27.9) ng/l (p=0.08), hsCRP 2.70 (1.55; 3.70) mg/l vs. 2.30 (1.43; 4.08) mg/l (p=0.74), hsTnT 0.014 (0.008; 0.024) μg/l vs. 0.013 (0.009; 0.017) μg/l (p=0.83) and NT-proBNP 248 (111; 896) ng/l vs. 182 (79; 282) ng/l (p=0.10). Diagnostic accuracy for Cyr61 to discriminate acute from stable PAD was adequate as indicated by an AUC of 0.65 (95% CI: 0.53–0.77). Univariate logistic regression analysis identified Cyr61 to be significantly associated with acute limb ischemia at an odds ratio of 2.71 (95% CI 1.06–7.60, p=0.045).

Conclusion: The novel biomarker cysteine-rich angiogenic inducer 61 provides useful information to discriminate acute from stable PAD in support of its role as an ischaemic biomarker – beyond myocardial ischemia as previously demonstrated.

Acknowledgement/Funding: Zurich Heart House Foundation

P1413 | BEDSIDE
Diabetic foot: the role of vascular function and inflammation

A.S. Antonopoulos, G. Siasos, N. Tentolouris, T. Konsola, E. Oikonomou, C. Kollia, G. Vogiatzi, S. Tsalamandris, E. Zacharia, D. Tousoulis. *Hippokration General Hospital, 1st Cardiology Department, Athens Medical School, Athens, Greece*

Background: Diabetic foot (DF) is a complication of diabetes mellitus (DM) which is developed among others as a consequence of microvascular and macrovascular impairment. Endothelial dysfunction and arterial stiffness are closed related to atherosclerosis progression. Moreover, inflammatory cytokines contributes to atherosclerosis progression.

Purpose: To investigate the role of endothelial dysfunction, arterial stiffness and inflammation in the clinical manifestation of DF in subjects with DM type 2.

Methods: In this cohort study we enrolled 309 consecutive subjects with DM type 2 presented in the diabetic department of our hospital. From the study population 214 were in stable condition without evidence of DF (NDF), 69 have been diagnosed with stage A or B (non-infection-ischemia or infection only respectively) (abDF) and 26 were diagnosed with stage C or D (ischemia or infection with ischemia respectively) (cdDF). Specialized pathologists have made the diagnosis of DF by clinical examination and specific vascular and neurological tests according to Texas diabetic wound classification system. Endothelial function was evaluated by flow mediated dilation (FMD) in the brachial artery and pulse wave velocity (PWV) was measured as an index of arterial stiffness. Glycosylate hemoglobin (HbA1c) was measured to evaluate adherence to treatment. Intereleukin-6 (IL-6) levels were measured as a well-established inflammatory marker.

Results: Patients with cdDF compared to subjects with abDF and NDF were younger (p=0.03), had increase Body mass index (p=0.05) and were more often males (p=0.01) while there was no difference in HbA1c levels (7.3±0.99% vs. 7.27±1.3% vs. 7.01±1.12%, p=0.31) and creatinine levels (1.07±0.62 mg/dl vs. 1.02±0.38 mg/dl vs. 0.96±0.32, p=0.29). Interestingly, subjects with cdDF compared toab DF and NDF subjects had impaired FMD (5.97±3.06% vs. 4.75±2.10% vs. 5.00±2.39%, p=0.005), impaired PWV (10.21±2.61 m/sec vs. 12.06±3.11 m/sec vs. 12.24±2.15 m/sec, p=0.004) and IL-6 levels [0.85 (0.52–1.33) pg/ml vs. 0.51 (0.41–0.70) pg/ml vs. 0.50 (0.36–0.78) pg/ml, p=0.02]. As many confounders exists analysis of covariance revealed that even after adjustment for age, sex, BMI and HbA1c, FMD and IL-6 levels differ significantly (p<0.05 for both) in patients with cdDF compared to the rest study groups.

Conclusion: These findings highlight the important role of inflammation and vascular dysfunction in the development of both macrovascular and microvascular impairment in diabetic subjects and stress the importance of preventive measures in these patients

P1414 | BEDSIDE
Analysis of the novel cardiac biomarkers sST2, Galectin-3, GDF-15 and Fetuin-A in patients with peripheral artery disease

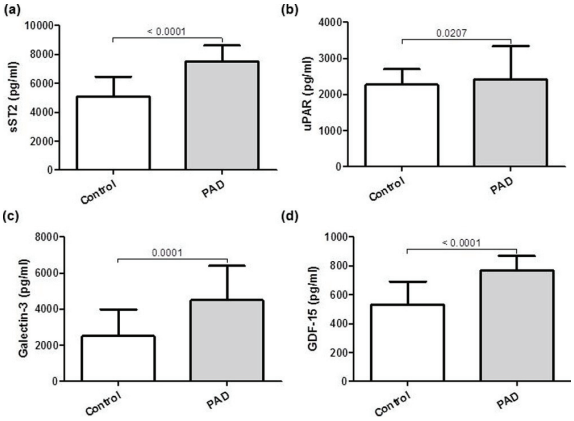
P. Jirak[1], M. Lichtenauer[1], C. Prodinger[2], V. Paar[1], B. Wernly[1], R. Pistulli[3], I. Rohm[3], C. Jung[4], U.C. Hoppe[1], P.C. Schulze[3], D. Kretzschmar[3]. *[1]Paracelsus Private Medical University, Internal Medicine II, Cardiology, Salzburg, Austria; [2]Paracelsus Private Medical University, Dermatology, Salzburg, Austria; [3]University Hospital of Jena, Clinic of Internal Medicine I, Jena, Germany; [4]Medical Faculty, University Duesseldorf, Division of Cardiology, Pulmonology, and Vascular Medicine, Duesseldorf, Germany*

Background: Peripheral artery disease (PAD) is a common form of manifestation of atherosclerosis, mainly triggered by classical cardiovascular risk factors and inflammatory processes. Affecting over 10% of people over 50 years of age, PAD has an considerable impact on morbidity, hospitalisation rates and health-care costs. Biomarkers have been introduced in many cardiovascular diesease entities over the last years. However, an analysis on the correlation of biomarker levels and PAD is still lacking, giving rise to further investigations.

Purpose: Aim of this study was to investigate the role of four novel cardiac biomarkers, namely sST2, Galectin-3, GDF-15 and Fetuin-A in patients suffering from PAD.

Methods: A total of 106 patients were enrolled in this current study, 51 that were diagnosed with PAD and 55 with excluded coronary and peripheral artery disease as controls. During outpatient visits, plasma samples of all patients were obtained and analyzed for sST2 (hemodynamics and inflammation), Galectin-3 (fibrosis and remodeling), GDF-15 (remodeling and inflammation), uPAR (inflammation), and Fetuin-A (vascular calcification) by use of ELISA after informed consent. Additionally, Rutherford stages and CRP levels as surrogate for inflammatory processes were analyzed and correlated with biomarker levels.

Results: Compared with controls, patients with PAD showed significantly higher levels of sST2 (5248 vs. 7503 pg/ml, p<0.0001), uPAR (2267 vs. 2414 pg/ml, p=0.0207), Galectin-3 (2795 vs. 4494 pg/ml, p<0.0001) and GDF-15 (549 vs. 767 pg/ml, p<0.0001). Fetuin-A showed lower levels in patients with PAD (117 vs. 100 ng/ml, p=0.119) in trend. A positive correlation with Rutherford Stages was found for sST2 (r=0.36, p<0.0001), Galectin-3 (r=0.27, p=0.019) and GDF-15 (r=0.34, p<0.0001). In contrast, Fetuin-A showed no correlation with Rutherford stages (r=0.12, p=0.26). CRP levels correlated with sST2 (p=0.02) and GDF-15 (p=0.009), while Galectin-3 (p=0.135) and Fetuin-A (p=0.20) were not associated with elevated CRP levels.



Conclusion: Circulating levels of sST2, uPAR, Galectin-3 and GDF-15 were significantly elevated in PAD patients and correlated with Rutherford stages. In contrast, Fetuin-A levels showed a decrease in PAD patients indicating increased vascular calcification. Thus, by incorporating different pathophysiological processes present in PAD, tested novel biomarkers facilitate a more precise diagnosis as well as a more accurate evaluation of disease severity and progression.

P1415 | BEDSIDE
Wall shear rate in patients with hypertension at different stages of atherosclerosis

V. Genkel[1], A.O. Salashenko[1], L.R. Toropova[2], E.I. Ilinykh[2], V.A. Sumerkina[2], I.I. Shaposhnik[1]. *[1]South-Ural State Medical University, Internal Medicine, Chelyabinsk, Russian Federation; [2]South-Ural State Medical University, Central research laboratory, Chelyabinsk, Russian Federation*

Introduction: Biomechanical forces have numerous functions in endothelial physiology. Wall shear rate (WSR) and wall shear stress plays an important role in the pathogenesis of the atherosclerosis.

Purpose: To investigate the WSR at the area of common carotid artery in patients with different ultrasound morphology of atherosclerotic peripheral vascular disease.

Methods: The study involved 85 hypertensive subjects. Patients underwent duplex ultrasound scanning of the carotid and lower limb arteries. We evaluated the carotid intima-media thickness (CIMT), the presence of atherosclerotic plaques and degree of luminal stenosis. Carotid WSR was measured in the right common carotid artery (CCA). We performed measurement of the systolic diameter of the right CCA 1 cm proximal to the carotid bifurcation and peak systolic blood flow velocity. According to the Poiseuille's Law WSR was calculated by the formula: WSR = (4 × peak blood flow velocity) ÷ CCA diameter.

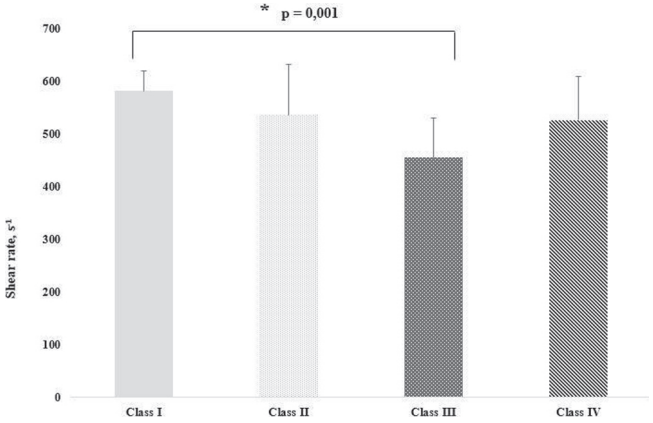
Duplex ultrasound was performed by high-resolution B-mode ultrasonography using an 8-MHz linear probe (Samsung Medison EKO7, Korea).

In accordance with ultrasound morphology classification of the arterial wall (G. Belcaro, 1996) patients were divided into four classes. The first class included patients with normal morphology of the vascular wall, the second class - patients with intima-media thickness ≥1.0 mm. Patients with plaques without hemodynamic disturbance were included in the third class. Subjects with greater than 50% stenosis belonged to the fourth class. Serum concentrations of high-sensitivity C-reactive protein (hsCRP), serum lipids and creatinine with calculation of estimated glomerular filtration rate (eGFR) were measured by standard procedures.

Results: WSR in patients of different classes are shown in Figure.

In patients of third class the WSR values were significantly lower, than in patients of the first class – 402±107 s^{-1} and 538±123 s^{-1} accordingly (p=0,001). In

patients with greater than 50% stenosis an increase in the WSR was observed, which was not statistically significant. The low WSR in the carotid artery was associated with CIMT (r = -0,299; p=0,006), high carotid stenosis (r = -0,334; p=0,002), elevated hsCRP (r = -0,321; p=0,023) and decrease eGFR (r = -0,321; p=0,023).



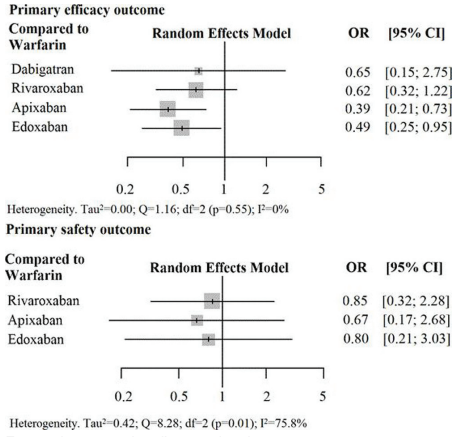
WSR in patients of different classes

Conclusion: In patients with hypertension the severity of peripheral arterial disease was associated with a marked decrease in carotid WSR. The low WSR was associated with elevated hsCRP and decreased eGFR.

P1416 | BEDSIDE
Safety and efficacy of direct oral anticoagulants in elderly patients undergoing treatment for venous thromboembolism: systemic review and network meta-analysis

R. Chaudhary[1], K. Bliden[2], U. Tantry[2], P.A. Gurbel[2]. *[1]Sinai Center of Baltimore, Baltimore, United States of America; [2]Inova Heart and Vascular Institute, Inova Center for Thrombosis Research and Drug Devlopment, Falls Church, United States of America*

Background: Currently, four direct-acting oral anticoagulants (DOACs) are approved for the treatment of venous thromboembolism (VTE) – direct thrombin inhibitor dabigatran, and the activated factor X inhibitors rivaroxaban, apixaban, and edoxaban. Although DOACs are suggested to be used in the elderly population (≥75 years), data from clinical outcomes studies regarding the efficacy and safety of DOACs in these patients are limited.
Methods: We conducted a systematic review of randomized controlled trials (RCTs) published from inception through February 12, 2017, comparing DOACs with each other or warfarin for treatment of VTE in elderly patients (age ≥75 years). The primary efficacy endpoint was a combination of recurrent VTE or death, and primary safety endpoint was composite of major and clinically relevant nonmajor bleeding events (CRNM). We followed a Random Effects Frequentist network meta-analysis approach.
Results: Seven RCTs met criteria for inclusion: dabigatran (two RCT; n=788); rivaroxaban (two RCT; n=1,283); apixaban (two RCT; n=1,097); edoxaban (one RCT; n=1,104). Apixaban (0.39 [0.21, 0.73]) and edoxaban (0.49 [0.25, 0.95]) were associated with a more favorable efficacy profile and a statistically significant reduction in primary efficacy outcome compared to other DOACs. No significant heterogeneity was observed. There were no statistically significant differences between the DOACs regarding the primary safety endpoint. Data for bleeding events was not available for dabigatran.



Forest plot comparing direct oral antico

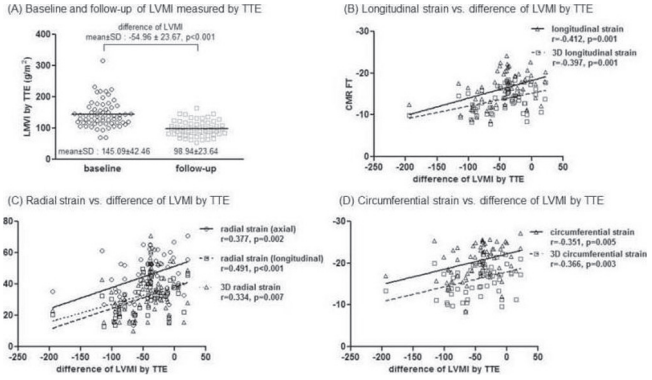
Conclusion: Based on network meta-analysis, a statistically significant reduction in the risk of VTE or VTE-related death was observed for apixaban and edoxaban in elderly patients with VTE. No significant reduction in major or CRNM bleed was observed between DOACs. In the absence of head-to-head treatment comparison, the confidence in these estimates is low. Future studies are warranted.

CARDIOVASCULAR MAGNETIC RESONANCE: VALVES AND VESSELS

P1417 | BEDSIDE
Assessment of reverse remodeling predicted by myocardial deformation on feature tracking as a new technique in patients with severe aortic stenosis: a cardiac magnetic resonance imaging study

J.-W. Hwang[1], S. Kim[2], S.-J. Park[1], S.-A. Chang[1], S.-C. Lee[1], Y. Choe[2], S.-W. Park[1]. *[1]Samsung Medical Center, Division of Cardiology, Seoul, Korea Republic of; [2]Samsung Medical Center, Department of Radiology, Seoul, Korea Republic of*

Background: The novel technique of feature tracking (FT) with balanced steady-state free precession cine sequences was introduced, and allowed myocardial strain to be derived directly, offering advantages over traditional myocardial tagging. The aim of this study was to evaluate the correlation between reverse remodeling as an outcome and left ventricular strain using cardiac magnetic resonance imaging (CMR) FT, and to evaluate prediction of reverse remodeling by myocardial deformation in patients with severe AS.
Methods: We enrolled 63 patients with severe AS and normal left ventricular (LV) systolic function (LV ejection fraction>60%), who underwent both CMR and transthoracic echocardiography (TTE) before surgical aortic valve replacement (AVR). CMR at 1.5T, including non-contrast T1 mapping, was carried out to define the amount of myocardial fibrosis. Cardiac Performance Analysis software was used to derive myocardial deformation as strain parameters from three short-axis cine views (basal, mid and apical levels) and apical 2, 3, 4 chamber views. The primary outcome was reverse remodeling, as evaluated by regression of left ventricular mass index (LVMI).
Results: Median follow-up was 28.77 months (interquartile range 11.27–38.33 months). As evaluated by LVMI between baseline and follow-up, mass regression was significantly improved after AVR (baseline 145.09±42.46 [g/m^2] vs. follow-up 98.94±23.67 [g/m^2], p<0.001). Statistically significant Pearson's correlations with LVMI regression were observed for longitudinal global strain (r=-0.412, p=0.001), axial radial strain (r=0.377, p=0.002), longitudinal radial strain (r=0.491, p<0.001), and circumferential strain (r=-0.351, p=0.005). A general linear model with multivariate analysis showed strain could independently predict the amount of LVMI regression in terms of longitudinal global strain (beta=3.15, p-value=0.049), 3D longitudinal global strain (beta=-4.36, p=0.042), and longitudinal radial strain (beta=1.67, p=0.004).



Conclusion: Longitudinal global strain measured by CMR-FT as a new technique was correlated with reverse remodeling as LVMI regression and was predictive of this outcome. As a simple and practical method, FT is promising to assess strain and predict reverse remodeling in severe AS, especially in patients with suboptimal TTE image quality.

P1418 | BEDSIDE
Native T1 mapping abnormalities in patients with aortic stenosis. Relationship with clinical features and strain changes assessed by tissue tracking

A.M.G. Almeida, G. Lima Silva, I. Goncalves, R. Placido, L.B. Rosario, C. David, A.R. Francisco, P.C. Ferreira, F.J. Pinto. *Hospital Lisbon North, Hospital Santa Maria, Lisbon, Portugal*

In patients with aortic stenosis, myocardial fibrosis underlines the progression to LV dysfunction, which impacts prognosis and clinical decision. Diffuse fibrosis may be assessed currently by CMR using T1 mapping, Additionally, deformation abnormalities of LV myocardium may precede changes in LV ejection fraction and influence the prognosis. We aimed to assess the presence of diffuse fibrosis by