Joint meeting

The 7th International Symposium on Neurocardiology

NEUROCARD 2015

The 6th International Symposium on Noninvasive Electrocardiology

SCIENTIFIC PROGRAM & BOOK OF ABSTRACTS

Editors:
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Organized by:

Serbian Neurocardiological Society, SNCS

Serbian Autonomic Society, SAS

Under auspices:

International Society for Holter and Noninvasive Electrocardiology (ISHNE)

Meeting endorsed by:

International College of nutrition
International College of Cardiology
Russian Society for Holter Monitoring and Noninvasive Electrophysiology
Russian Society of Cardiologists
Polish Society for Noninasive Electrocardiology
Ukraine Neurocardiological Society
University of Medicine and Pharmacy Targu Mures, Romania
Spitalul Clinic Judetean Timisoara
Society of Heart Brain Medicine
Neurophysiological Society of Serbia and Montenegro
Serbian Association for Arteriosclerosis, Thrombosis and Vascular Biology Researsh under auspicies of International Arteriosclerosis Society, IAS
Cardiology Society of Serbia, CCS

Under Patronage

Clinical Hospital Center Bezanijska Kosa
Republic of Serbia Ministry of Health
Republic of Serbia Ministry of Science and Tehnological Development
Medical School, Belgrade University
Serbian Medical Society

Dear colleagues,

It is our great pleasure to welcome you to our Joint meeting of the 7th International Symposium on Neurocardiology, (Neurocard 2015) and the 6th International Symposium on Noninvasive Electrocardiology. The meeting will be held in Belgrade on October 16th - 17th 2015 and organized by Serbian Neurocardiological Society and Serbian Autonomic Society, and auspices of International Society for Holter and Noninvasive Electrocardiology (ISHNE).

The previous NEUROCARD meetings and Joint Meeting on Noninvasive Electrocardiology, included participation of scientists from whole world, Europe and region and organized under the auspices of several international organizations. In order to improve scientific collaboration between experts from similar disciplines we decided to organize joint meeting of Neurocard 2015 and Symposium on Noninvasive Electrocardiology with hope that this formula will be successful.

We hope that NEUROCARD will become a good platform for international scientific cooperation as well as good opportunity to develop friendship in the nice environment and pleasant atmosphere.

The progression of heart disease is associated with changes in the neurohumoral mechanisms that control cardiac function.

Neurocardiology deals with the degree to which this neurohumoral remodeling occurs, even before overt signs of cardiac disease become manifest. With our cumulative understanding of these interdependent processes, new avenues for time-appropriate, targeted methods of treating heart diseases can be developed.

The Symposium will bring together medical researchers and specialists focused on the autonomic cardiovascular regulation in different fields such as cardiology, neurology, physiology, molecular biology, genetic, pharamacology, nephrology, endocrinology, psychology, engineering, nano medicine and other disciplines.

The purpose of the meeting is to endorse research in neurocardiology and related fields, especially noninvasive electrocardiology to improve prognosis and the outcome of cardiovascular disease and facilitate the dissemination of the state-of-the art.

Outstanding experts, members of the Scientific Advisory Board will assure scientific excellence.

On behalf of the Organizing Committee,
Looking forward to welcoming you,

Branislav Milovanovic
Professor of Internal Medicine and Cardiology
Chairman of the meeting
President of Serbian Neurocardiological Society

LOCAL ORGANIZING COMITEE MEMBERS OF THE BOARD

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Mirjana Krotin
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Malgorzata Kupressa	(Lodz, Poland)

TOPICS

Basic Neurocardiology
Electrocardiology and Telemedicine
Syncope, Orthostatic intolerance
Geneticall aspects in Neurocardiology
Biosignal processing and Artificial Intelligence
Myocardial dysfunction: cardiac-neural interactions
Cardiac sudden death: risk stratification
Cardiac arrhythmias and autonomic nervous system
Methabolic autonomic neuropathies
Oncocardiology
Autoimmune diseases: neuro-cardiological manifestations
Central mechanisms and heart
Blood pressure and neural mechanisms
Cardiac autonomic dysfunction and neurological diseases
Psychology and autonomic nervous system
Personalized medicine
Nano technology: new approach in medicine
Transcranial magnet stimulation
Sleep apnea
Nutrition, physical activity and brain- heart connection

Badge	All participants and exhibitors are kindly requested to wear their badges during the days of Symposium.
Official language	The official language of the Symposium is English.
Time schedule	Invited lecturers 25 minutes Oral presentations 15 minutes
Poster presentations	Poster presentations will be exhibited in form of ePoster during coffee breaks
Coffee breaks	Coffee breaks will be served at the exhibition area
Lunches	Lunch will be served at exhibition area
Exhibition	The Exhibition will be located in front of the Symposium Hall (Amfiteatar Hall) and around the Registration area. The working hours of the exhibition are the same as the Symposium working hours.
Opening ceremony	National Library of Serbia, Belgrade, Serbia
Gala dinner	Restaurant at Hotel Park, Belgrade, Serbia

SCIENTIFIC PROGRAM

NEUROCARD 2015 – FINAL PROGRAM

16th –17th October 2015, National Library, Belgrade, Serbia

October 16th

08:00-09:00 Registration

09:00-09:30 Opening Ceremony

Branislav Milovanovic
President of Serbian Neurocardiological Society, Chairmen of the Meeting

Sanja Pavlovic
President of Serbian Autonomic Society

Nina Japundzic-Zigon
President of Serbian working group of basic Neurocardiology

Academician Nebojsa Lalic
Dean of the Faculty of Medicine, University of Belgrade

Leonid Makarov
Member of ISHNE board, President of Rohmine
(Moscow,Russia)

Malgorzata Kupressa
Member of ISHNE board
(Lodz, Poland)

Thomas Klingenheben
Member of ISHNE board
(Bonn, Germany)

Harald M. Stauss
The University of Iowa
(Iowa, USA)

Viktor Moga
Member of ISHNE board
(Timisoara,Romania)

Bassim Irheim Muhammad,
Dean College of Pharmacy, University of Al Qadisiyah
(Al Qadisiyah, Iraq)

Ludovit Gaspar
(Bratislava, Slovak Republic)

Jan Galuszka
(Olomouc, Czech Republic)

09:30-10:30 Basic Neurocardiology I
Chairs: Harald Stauss (Iowa, USA), Nina Japundzic-Zigon (Belgrade, Serbia), Bassim I Mohammad (Al Qadisiyah, Iraq)

09:30-10:00Effects of Afferent vs. Efferent Vagal Nerve Stimulation on Glucose Regulation in Rats
Harald M. Stauss
(Iowa City,USA)

10:00-10:15 Cardiotoxicity in rats treated with doxorubicne nanoparticles
Marko Vasić, Olivera Šarenac, Maja Lozić, Elaine Ho Yan, Chung Lip Yong, Kiew Lik Voon, David Murphy and Nina Japundžić-Žigon
(Belgrade,Serbia)

10:15-10:30 Could determination of BCL-2 and caspase-3 activity indicate plaque evolution in ischemic heart disease patients?
T. Ristic, B.V. Djordjevic; M. Deljanin-Ilic; P. Vlahovic., V. Cosic
(Nis, Serbia)

10:30-11:15 Genetical Aspects in Neurocardiology
Chairs: Aleksandra Stankovic (Belgrade, Serbia), Maja Zivkovic (Belgrade, Serbia),

10:30-10:45 Gene polymorphisms related to cardiac autonomic response to particulate air pollution and oxidative stress
Stankovic A. and Zivkovic M.
(Belgrade,Serbia)

10:45-11:00The eNOS rs1799983 gene polymorphism (Glu298Asp) in association with cardiovascularprofiles in patients with vasovagal syncope
Ivan Zivotić, Tamara Djurić, Maja Zivkovic, Tijana Bojić, Branislav Milovanović, Dragan Alavantić and Aleksandra Stanković
(Belgrade,Serbia)

11:00-11:15 Effects of glutathione S-transferase T1 and M1 deletions on electrocardiographic and heart rate variability parameters in patients with vasovagal syncope
Maja Živković, Ivan Životić, Maja Boskovic, Branislav Milovanović, Tijana Bojic, Dragan Alavantic, Aleksandra Stanković
(Belgrade,Serbia)

11:15-11:30 Coffee break

11:30-12:30 Cardiometabolic risk, prevention and epidemiology
Chairs: Oscar Franco (Roterdam, Netherland), Rajiv Chowdhury (Cambridge, UK)

11:30-12:00Past, present and future of cardiovascular disease prevention
Oscar Franco
(Roterdam, Netherland)

12:00-12:30Saturated Fatty acids and cardiometabolic risk – a fresh look at the available evidence
Dr Rajiv Chowdhury
(Cambridge, UK)

12:30-13:30 **Bimed, Medtronic**

Symposium
New frontiers in extended cardiac rhythm monitoring
Chairs: Goran Milasinovic (Belgrade, Serbia), Bozidar Ferek Petric (Zagreb, Croatia)

12:30-13:00Extended cardiac rhythm monitoring for syncope of unknown reason
Goran Milasinovic
(Belgrade,Serbia)

13:30-13:30 Extended cardiac rhythm monitoring for atrial fibrilation
Bozidar Ferek Petric
(Zagreb, Croatia)

13:30-14:15 The New Challenges: Nano technology in Medicine
Chairs: Djuro Koruga (Belgrade, Serbia), Dejan Rakovic (Belgrade, Serbia)

13:30-13:55 Psycho-cardiology: Does blood on nano level possess quantum entanglement?
Koruga, D., Bandić,J., Mihajlović, S., Ilanković, N., Ilanković, A., Koruga,I., Matija, L.
(Belgrade, Serbia)

13:55-14:15 Investigation of hypertension drugs by Raman spectroscopy
B. Hadžić, N. Romčević, B. Milovanović
(Belgrade,Serbia)

14:15-15:00 Lunch

15:00-16:30 Cardiac sudden death:risk stratification
Chairs: Branislav Milovanovic (Belgrade, Serbia), Thomas Klingenheben (Bonn, Germany)

15:00-15:30 Autonomic nervous system, Repolarization, and Imaging: Integrative approach to sudden death risk stratification
Thomas Klingenheben
(Bonn, Germany)

15:30-15:50 Cardiac autonomic patterns and risk stratification by patients with myocardial infarction
Milovanovic Branislav, Elez Jelena, Pejovic Bojan, Zdravkovic Marija, Mutavdzin Slavica, Paunovic Jovana, Gligorijevic Tatjana, Arsic Marina
(Belgrade, Serbia)

15:50-16:10 Duirnal variation on myocardial contraction
Krasimira Hristova
(Sofia, Bulgaria)

16:10-16:30 Physiological heart rate pacing for preventing not only neurocardiogenic syncope
Michal Chudzik, Jerzy K Wranicz
(Lodz, Poland)

16:30-17:40 Methabolic Autonomic Neuropathies
Chairs: Ljudmila Stojanovic (Belgrade, Serbia), Zorica Rasic Milutinovic (Belgrade, Serbia)
Gordana Pekovic Perunicic (Belgrade, Serbia)

16:30-16:50 Antiphospholipid Syndrome as Risk Factor for the Neurological and Cardiac Involvement
Stojanovich Ljudmila, Djokovic Aleksandra, Banicevic Slavica, Zdravkovic Marija, Radovanovic Slavica, Bisenic Vesna
(Belgrade, Serbia)

16:50-17:10 Premature atherosclerosis and the antiphospholipid antibody category in patients with antiphospholipid sindrome-is there a relationship?
Djokovic A, Stojanovich L, Todic B, Bisenic V, Hinic S, Zdravkovic M, Milovanovic B
(Belgrade, Serbia)

17:10-17:25 Cardiac autonomic neuropathy in hemodialysis patients
Gordana Pekovic, Zorica Rasic-Milutinovic, Biljana Pencic, Snezana Gajic,Natasa Filipovic
(Belgrade, Serbia)

17:25-17:40 Effects of hemodialysis on heart rate variability and insulin resistance in end-stage renal disease patients
Zorica Rasic-Milutinovic, Gordana Perunicic-Pekovic, Biljana Pencic, Natasa Filipovic, Snezana Gajic
(Belgrade, Serbia)

17:40-18:30 Blood pressure-neural mechanisms
Chairs: Ludovit Gaspar (Bratislava, Slovakia), Biljana Pencic (Belgrade,Serbia)

17:40-18:00 Ambulatory blood pressure monitoring (ABPM) – comprehensive assessment of blood pressure parameters
Ludovit Gaspar, Andrej Dukat, Peter Gavornik, Iveta Gasparova, Andrea Komornikova
(Bratislava, Slovak Republic)

18:00-18:15Heart rate variability in patients with diastolic dysfunction
Pencic Biljana
(Belgrade, Serbia)

18:15-18:30Assessment of autonomic function in patients with hypertension
Slavica Mutavdzin, Branislav Milovanovic, Tatjana Gligorijevic, Jovana Paunovic, Marina Arsic
(Belgrade, Serbia)

20:00 Gala dinner, Restaurant Hotel Park

October 17th

09:00-09:15 Basic Neurocardiology II
Chairs: Harald Stauss(Iowa,USA), Bassim I Mohammad (Al Qadisiyah, Iraq),
Nina Zigon Japundzic (Belgrade, Serbia)

09:00-09:20Chronic Vagal Nerve Stimulation as a Potential New Treatment for the Metabolic Syndrome?
Harald M. Stauss
(Iowa City,USA)

09:20-09:40Cardioprotection Against Myocardial Ischemia-Reperfusion Injury: Effect Of Selenium And N-Acetylcysteine
Bassim I. Mohammad , Fhadil G. Al-Amran, Mahdi S. AL-Hilo
(Al Qadisiyah, Iraq)

09:40-09:55Pregnancy differentially affects neurogenic cardiovascular control in normontensive and spontaneously hypertensive rats
Mirjana Jovanović, Tatjana Tasić1, Maja Lozić1, Alexander Trbovich, David Murphy and Nina Japundžić-Žigon
(Belgrade,Serbia)

09:55-10:10 The comparative analysis of Tp-e and natriuretic peptides (ANP, BNP) concentration in plasma as risk marker of electrical instability in children with different myocardial hypertrophy
Linyaeva V.V., Leonteva I.V.
(Moscow, Russia)

10:10-11:30 Evaluation of sudden heart death risk in athlets
Chairs:Leonid Makarov (Moscow, Russia), Larysa Balikova (Saransk, Russia),
Marija Zdravkovic (Belgrade, Serbia)

10:10-10:40Peculiarity of the syncope in the young elite athletes
Leonid Makarov, Vera Komoliatova, Irina Kiseleva
(Moscow,Russia)

10:40-11:00Myocardium repolarization dynamics during phisical exercise test in young athletes and untrained adolescents
Larisa Balykova
(Saransk,Russia)

11:00-11:15Features of regulation of circulation during dehydration the athlete
Pavlov V., Odzhonikidze Z., Badtieva V., Poljanskij N., Deev V., Nikolaev V., Ivanova J.
(Moscow, Russia)

11:15-11:30The early ECG changes in preadolescent elite footballers
M. Zdravkovic, B. Milovanovic, S. Hinic, S. Dimkovic, M. Krotin, A. Djokovic, D. Lisulov-Popovic, S. Panic, J. Saric, V. Bisenic, T. Jakimov1, J. Gavrilovic T. Acimovic, S. Klasnja, V. Mudrenovic
(Belgrade,Serbia)

11:30-12:00 Coffee break

12:00-13.30 Syncope and Autonomic Nervous System
Chairs: Branislav Milovanovic (Belgrade, Serbia), Viktor Moga (Timossoara, Romania)

12:00-12:20 Sympatho-vagal interactions of autonomic nervous system activity in patients with syncope
Branislav Milovanovic
(Belgrade,Serbia)

12:20-12:40 Chaos and Entropy Analysis during Head-up Tilt test in Neurally mediated Syncope
Victor-Dan Moga, Tudor Ciocarlie, Ioana Cotet, Flavian Parge, Florin Vidu, Mariana Moga, Rodica Avram
(Timisoara, Romania)

12:40-13:00 Imbalance of autonomic nervous system in cases of TLOC caused by channelopathies
Jan Galuszka, Karel Vykoupil, Ivana Buriánková, Miloš Táborský
(Olomouc, Czech Republic)

14:00-13:15 Entropy Analysis of RR and QT Interval Measurements during Head-up Tilt test in Healthy Subjects
Ioana Cotet, Victor-Dan Moga, Jahraus Sabine, Elena Cristina Marin, Andreea Florea, Angela Laura Szekely, Flavian Parge, Florin Vidu, Mariana Moga, Rodica Avram
(Timisoara, Romania)

13:15-13:30 A novel approach in assesment of baroreflex sensitivity in syncope patients
Tatjana Gligorijevic, Slavica Mutavdzin, Vlado Djadjic, Sinisa Miljkovic, Jovana Paunovic, Marina Arsic, Marija Zdravkovic, Branislav Milovanovic
(Belgrade,Serbia)

13:30-14:30 Autonomic nervous system and Heart rate variability
Chairs: Michal Chudzik, (Lodz, Poland), Krassimira Hristova (Sofia, Bulgaria)

13:30-13:45 Heart rate variability computed on the basis of 24-hour ECG for cardiac autonomic neuropathy detection
I. Kurcalte, I.Tonne, R.Erts, O.Kalejs, I.Popova, A.Kalinin, A.Lejnieks
(Riga, Latvia)

13:45-14:00 Does meteosensitivity influence on heart rate variability in medical students?
Trtiakov Vitalii, Venevtseva Yulia, Melnikov Aleksandr
(Tula, Russia)

14:00-14:15 10-year trends in autonomic state in young healthy adults: 2006-2015
Venevtseva Yulia, Eliseev Dmitrii, Tretiakov Vitalii, Kazidaeva Elena
(Tula, Russia)

14:15-14:30 Reproducibility of 24 hour heart rate variability time-domain measures in children
Bjelakovic Bojko, Ilic Dragana, Lukic Stevo, Stankovic Zoran, Dimitrijevic Lidija, Saranac Ljiljana, Bjelakovic Ljiljana
(Nis,Serbia)

14:30-15:15Lunch, Poster Session

15:15-16:15 Cardiac Autonomic Dysfunction and Neurological Diseases
Chairs: Sanja Pavlovic (Belgrade, Serbia), Nikola Vojvodic (Belgrade, Serbia)

15:15-15:35 Epileptic asystole: Is it a model for sudden unexpected death in epilepsy?
Nikola Vojvodic, Ana Mihailovic, Ivana Petrovic, Aleksandar Ristic, Dragan Simic, Dragoslav Sokic
(Belgrade,Serbia)

15:35-15:55 Sudden neurogenic death in neurodegenerative diseases
Sanja Pavlovic, Branislav Milovanovic
(Belgrade,Serbia)

15:55-16:15 The presence of dysautonomia in different subgroups of myasthenia gravis patients
Ana Nikolić, Stojan Perić, Tanja Nišić, Srdjan Popović, Miroljub Ilić, Vidosava Rakočević Stojanović, Dragana Lavrnić
(Belgrade,Serbia)

16:15- 17:40 Sleep apnea and breathing disorders
Chairs: Malgorzata Kupresa (Lodz,Poland),Biljana Pencic(Belgrade,Serbia)

16:15-16:40 Sleep – disordered breathing as the cardiologic risk factor
Małgorzata Kurpesa
(Łodź, Poland)

16:40-16:55 The morning hypertension –a target to treat in patients with sleep apnea-hypopnea syndrome.
Milanov S, Vuckovic-Filipovic J, Davidovic G, Cekerevac I, Iric-Cupic V, Simovic S, Vuleta M, Miloradovic V
(Kragujevac,Serbia)

16:55-17:10 Predictors of adverse outcome in males with obstructive sleep apnea-hypopnea syndrome and arterial hypertension
Borodin N.V., Kostenko I.I., Lyshova O.V.Voronezh State Medical University named after N.N. Burdenko
(Voronezh, Russia)

17:10-17:25 The estimated apnea hypopnea index derived from Holter ECG accurately shows the association with frequent PVCs
Tesic D, Somer D, Vukoja-Kojicic M, Kopitovic I
(Sremska Kamenica,Serbia)

17:25-17:40 The relationship between severity of the obstructive sleep apnea and subclinical left ventricular systolic and diastolic dysfunctions in newly diagnosed patients with obstructive sleep apnea
M. Zdravkovic, B. Milovanovic, S. Hinic, S. Dimkovic, M. Krotin, A. Djokovic, D. Lisulov-Popovic, S. Panic, J. Saric, V. Bisenic, T. Jakimov, J. Gavrilovic, T. Acimovic, S. Klasnja, V. Mudrenovic
(Belgrade,Serbia)

17:40 -18.25 Biosignal Processing and Artificial Intelligence
Chairs: Dragana Bajic, (Belgrade, Serbia), Viktor Moga (Timossoara, Romania)

17:40-17:55: **CEVAS - A role of Centre of Excellence in cardiovascular data analysis**
Dragana Bajić, Ivana Kovačić
(Belgrade, Serbia)

17:55-18:10 A cross-approximate entropy of independent signals with known distribution with application to real data
Tamara Škorić, Dragana Bajić
(Belgrade, Serbia)

18:10-18:25 Application of artificial intelligence and heart rate variability spectrum in classificationof sympatho-vagal dis/balance
Z. Matić, Z. Ševarac, T. Gligorijević, B. Milovanović
(Belgrade, Serbia)

18:25-18:35 Fast ICA for extraction of fetal ECG
Antonina Aleksić, Nadica Miljković, Mirjana B. Popović
(Belgrade, Serbia)

18:35-18:45 Clossing of meeting

POSTERS

1**. ECG in rat with experimental pulmonary hypertension**
I. Roshchevskaya, O. Suslonova, S. Smirnova.
(Syktyvkar, Russia)

2. **Amplitude –temporal parameters of the cardioelectric field in rat with experimental pulmonary hypertension**
O. Suslonova, S. Smirnova, I. Roshchevskaya
(Syktyvkar, Russia)

3. **Daily treadmill running maintains the synthesis of catecholamines on the basal level anddecreases oxidative stress in the right and left heart auricles of chronically stressed rats"**
Ljubice Gavrilović, Vesne Stojiljković, Sladjane Dronjak, Nataše Popović, Snežane Pejić, Ane Todorović, Ivana Pavlovića i Snežane B. Pajović
(Belgrade, Serbia)

4. **Electrocardiography examination in 456 healthy medical students: influence of gender and ethnicity**
Venevtseva Yulia, Starostina Yulia
(Tula,Russia)

5. **Incidence of carotid artery stenosis in persons with heart diseases**
Đajić V, Vujković Z, Miljković S, Račić D
(Banja Luka, Bosnia and Herzegovina)

6. **Correlations between sleep quality and blood pressure, heart rate and heart rate variability in young men with natural history of arterial hypertension**
Nikolai Tcarev, Yulia Venevtseva, Aleksandr Melnikov, Elena Kazidaeva
(Tula, Russia)

7. **Adverse effects of energy drinks among young adults and athletes - case report**
Gavrilovic J, Mudrenovic V, Bisenic V, Hinic S, Zdravkovic M, Milovanovic B
(Belgrade, Serbia)

8. **Atrial fibrilation and stroke–results of a six year study conducted by the clinic of neurology in Banja Luka**
Siniša Miljković
(Banjaluka, Bosnia and Herzegovina)

9. **Implantable cardioverter defibrillators in prevention of sudden heart death in ischemic heart disease and coronary artery bypass graft surgery**
Nataša Kovačević-Kostić, Goran Milašinović, Radmila Karan, Miloš Velinović, Mile Vraneš
(Belgrade,Serbia)

10. **A rare presentation of myocarditis in young patient : clinical conundrum**
M. Glisic, I. Milinkovic, P. M. Seferovic
(Belgrade, Serbia)

11. **Autonomic nervous system is affected in children with atopic dermatitis**
Loseva T.A., Rudneva N.S., Tsarev N.N.
(Tula, Russia)

12. **Acute inflammatory response after Scaffold stent implantation and impact of Trimetazidine**
Najah R. Hadi, Khalid I. Amber, Bashaer M. Muhammad-Baqir
(Kufa, Iraq)

13 .**Is there any corelation between severity of the obstructive sleep apnea and endothelial dysfunction?**
M. Zdravkovic, B. Milovanovic, S. Hinic, S. Dimkovic, M. Krotin, A. Djokovic, D. Lisulov-Popovic, S. Panic, J. Saric, V. Bisenic, T. Jakimov, J. Gavrilovic1, T. Acimovic, S. Klasnja, V. Mudrenovic
(Belgrade,Serbia)

14. **Conduction disturbances as predictors of adverse cardiovascular events for 30 days in patients with acute coronary syndrome undergoing percutaneous coronary intervention**
T. Jakimov, A. Djokovic, M. Zdravkovic, B. Milovanovic, S. Hinic, S. Dimkovic, G. Antic,I. Mrdovic
(Belgrade, Serbia)

15.**Treating hypertension using the basic principles of Traditional Chinese Medicine**
Ana Žikić, Zoran Matić, Branislav Milovanović
(Beijing, China, Belgrade, Serbia)

16. **Acute myocardial infarction with chronic myeloid leukemia – a case repost**
Zoran Marjanovic, Milena Kotorcevic, Milos Glisic
(Smederevska Palanka, Serbia)

17. **Adverse drug reaction to Ticagrelor – a stumbling stone of dual antiplatelet therapy – case report**
Mudrenovic V, Gavrilovic J, Kasnja S, Djuran P, Jovic D, Korica-Tresnjak J, Ninkovic N, Bisenic V, Hinic S, Zdravkovic M, Krotin M, Milovanovic B
(Belgrade, Serbia)

18. **Adverse drug reactions as the cause of hospitalization – case report**
Mudrenovic V, Gavrilovic J, Stojkovic N, Djuran P, Jovic D, Korica-Tresnjak J, Ninkovic N, Saric J, Bisenic V, Hinic S, Zdravkovic M, Milovanovic B
(Belgrade, Serbia)

19. **Multidisclipinary approach in patients with obstructive sleep apnea and obesety hypoventilation syndrome**
Vojislav Radosavljevic, Vera Gardijan, Teodora Ilic
(Belgrade, Serbia)

20. **Is there connection between obstructive sleep apnea syndrome and glycated hemoglobin?**
Vesna Đurić, Ana Stojanović
(Belgrade, Serbia)

21. **Early signs of impaired systolic and diastolic function of the right chambers in patients with OSA**
M.Zdravković, M.Krotin, D.Lisulov, R.Pokrajac, S.Hinic, J.Saric, B.Milovanovic
(Belgrade, Serbia)

22. **Masked hypertension in patients with obstructive sleep apnea – OSA**
M.Zdravkovic, M.Krotin, D.Lisulov, R.Pokrajac, J.Saric, S.Hinic, B.Milovanovic
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BOOK OF ABSTRACTS

ORAL PRESENTATIONS

O1 Effects of Afferent vs. Efferent Vagal Nerve Stimulation on Glucose Regulation in Rats

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Vagal nerve stimulation (VNS) causes weight loss in obese patients and parasympathetic activation of the liver reduces hepatic glucose release. Thus, VNS may be highly effective in treating obese type II diabetic patients. We tested the hypothesis that VNS reduces blood glucose concentration [Glu] potentially by increasing insulin and decreasing glucagon plasma concentrations.

Blood pressure (BP), heart rate (HR), and [Glu] (HD-XG, DSI) were continuously monitored in anesthetizedrats (1.5% isoflurane in O_2). Stimulation electrodes were placed around the right cervical vagus nerve. After establishing constant baseline conditions, continuous VNS (5 Hz, 3 V, 1 ms) was initiated and maintained for two hours. Then the stimulator was turned off, the vagus nerve severed either proximal (for efferent VNS) or distal (for afferent VNS) to the electrodes, and new baseline conditions were reestablished. Then efferent or afferent VNS was initiated for another two hours.Blood samples for determination of insulin and glucagon plasma concentrations were drawn at baseline conditions and at 30 min and 120 min into the VNS.

Combined afferent and efferent VNS (intact nerve, n=9) temporarily reduced HR anddid not significantly affect mean BP. Contrary to our hypothesis, *[Glu] increasedpersistently*from 138±8 mg/dLat baseline to 251±35 mg/dL at 30 min and to 287±40 mg/dL at 120 min of VNS.While *insulin plasma levels did not change*significantly, *glucagon plasma levels persistently increased* from 111±7 pg/mL at baseline to 194±27 pg/mL at 30 min and 180±36 pg/mL at 120 min of VNS.

Afferent VNS (nerve cut distally from the electrode, n=7) did not significantly change BP or HR. As with the intact nerve preparation, afferent VNS*persistently increased [Glu]* from 137±30 mg/dL at baseline to 190±38 mg/dL at 30 min and 224±48 mg/dL at 120 min of VNS. This response was associated with trends for a *persistent increase in plasma glucagon* (147±23 pg/mL at baseline, 179±23 at 30 min and 164±35 at 120 min of VNS) and a *temporary decrease in plasma insulin* (0.83±0.20 pg/mL at baseline, 0.65±0.12 pg/mL at 30 min and 0.85±0.14 pg/mL at 120 min of VNS) concentrations.

Efferent VNS (nerve cut proximally from the electrode, n=8) did not significantly change BP or HR. In contrast to the intact nerve preparation or afferent VNS that both persistently increased [Glu], *efferent VNS only temporarily increased [Glu]* from 164±32 mg/dL at baseline to 201±38 mg/dL at 30 min of VNS. After 120 min of VNS, [Glu] hadreturned to values that were slightly below baseline (156±27 mg/dL). This response was associated with an*increase in plasma insulin concentration*(0.96±0.33 pg/mL at baseline vs. 1.38±0.37 pg/mL at 30 min and 1.43±0.38 pg/mL at 120 min of VNS) and a *temporary increase in plasma glucagon concentration* (158±16 pg/mL at baseline vs. 211±30 pg/mL at 30 min and 176±29 pg/mL at 120 min of VNS).

In conclusion, VNS (with intact nerve) increases [Glu] via afferent pathways activating central nervous system-mediated glucagon release. Future studies are warranted to test if VNS using parameters selectively recruiting efferent nerve fibers may potentially lower [Glu] in type II diabetic subjects by increasing insulin plasma levels.

O2 CARDIOTOXICITY IN RATS TREATED WITH DOXORUBICINE NANOPARTICLES

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BACKGROUND: The clinical use of a highly effective antineoplastic agent doxorubicin is limited by late and irreversible life threatening cardiotoxicity. Recently engineered doxorubicin conjugated nanoparticles improved therapeutic index and tolerability.
OBJECTIVES: To investigate cardiotoxicity induced by doxorubicin nanoparticles conjugated with N-(2-Hydroxypropyl) methacrylamide (HMPA).
METHOD: Twenty two male Wistar rats equipped with radiothelemetric device (TA11PA-C40) were randomized in four experimental groups: 1) HPMA group of rats (n = 5) treated with N-(2-Hydroxypropyl) methacrylamide (5 mg/kg in 0,5 ml, i.v.); 2) SALINE group of rats (n = 5) treated with 0,9% NaCl (0,5 ml, i.v.); 3) HPMA-DOX group of rats (n = 5) treated with N-(2-Hydroxypropyl) methacrylamide conjugated with doxorubicin (5 mg/kg in 0,5 ml, i.v.) and 4) DOX group of rats (n = 7) treated with doxorubicin (5 mg/kg in 0,5 ml, i.v.). Body weight (BW), blood pressure (BP), heart rate (HR), HR short term variability (HRV), left ventricular ejection fraction (EFLV) and left ventricular end-diastolic volume (EDV) were monitored for 140 days. Kaplan-Meier curves of survial were calculated for all groups. At the end of the experiment, rats were euthanized and the harvested hearts were used for pathohistology.
RESULTS: In HPMA and SALINE group, BW of rats increased over time and median survival was 140 days. BP, HR and HRV were comparable in both groups. However, EDV was increased in 3 HPMA treated rats in respect to SALINE treated rats. There were no pathohistological signs of cardiotoxicity in both HPMA and SALINE group of rats. In HPMA-DOX rats BW increased over time and median survival was 140 days. BP, HR and HRV of these rats were comparable to controls while EDV was increased and EFLV was decreased in 3 rats. Pathohistology revealed fibrosis in 3 rats. DOX rats exhibited significant decline in body weight and low median survival (16 days). In all DOX rats BP and HR were normal while EDV was increased and EFLV and HRV were decreased. Pathohistological examination uncovered typical signs of cardiotoxicity in all DOX rats including severe fibrosis, vacuolization, necrosis and inflitration.
CONCLUSION: Our results indicate that HPMA-DOX treated rats have better survival and lower cardiotoxicity than DOX-treated rats. These findings are in agreement with previous reports on doxorubicin survival in rats. Increase in EDV and decrease of EFLV in DOX group indicate left ventricular dilatation associated with heart failure, in all rats treated with doxorubicin, and, only in 3 rats treated with HPMA-DOX. HRV was depressed only in DOX rats, and that is an expected finding since reduction of HRV has been reported to predict poor survival.

O3 COULD DETERMINATION OF BCL-2 AND CASPASE-3 ACTIVITY INDICATE PLAQUE EVOLUTION IN ISCHEMIC HEART DISEASE PATIENTS?

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Background. Apoptotic cell death may play a critical role in a variety of cardiovascular diseases, especially in those developing on the basis of atherosclerosis. The goal of this study was to compare the activity of caspase-3 and values of Bcl-2 protein in sera in patients with various forms of ischemic heart disease, and to correlate these markers with inflammatory and lipid parameters.

Methods. We studied 30 patients with chronic stable angina pectoris (SAP), 27 with unstable angina pectoris (USAP), 39 with acute ST-elevation myocardial infarction (STEMI) and 27 age-matched healthy volunteers (Control group). Caspase-3 activity was determined by a colorimetric commercially available method while serum Bcl-2 concentrations were determined using commercially available immunoassays (ELISA).

Results. Caspase-3 was significantly higher only in the USAP group (0.122±0.062 μmol/mg protein, $p<0.05$) in comparison with the control group (0.092±0.022 μmol/mg protein). Concentrations of Bcl-2 were significantly higher in patients with SAP (0.310±0.075ng/mL) and USAP (0.329±0.102ng/mL) compared to healthy (0.250±0.069ng/mL, $p<0.01$) and the STEMI (0.266±0.041ng/mL, $p<0.01$) groups. ROC curve analysis showed that Bcl-2 had the best characteristicsin patients with SAP andUSAP and represents the best indicator of atherosclerotic plaque activity. However, Bcl-2 could not be a marker of patients' stratification because there was no significant difference betweenareas of Bcl-2 curves of thesetwopatient groups. These resultssuggest that simultaneous determination of caspase-3 activityand Bcl-2 can indicate plaqueevolutionfrom stable to unstable one.

Conclusions. The studied markers of apoptosis present valuable parameters in evaluation of atherosclerotic plaque acivity and a new targets for drug therapy.

O4 Gene polymorphisms related to cardiac autonomic response to particulateair pollution and oxidativestress

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Genetic susceptibility is likely to play a role in response to air pollution. There are numeros studies which have examined gene–environment interactions in relation to the autonomic nervous system (ANS) and cardiovascular health effects of air pollutants. Changes in heart rate variability (HRV) may reflect changes in cardiac autonomic function and risk of sudden cardiac death. Particulate-related changes in autonomic nervous system activity, suggesting sympathetic activation or vagal suppression after particulate air pollution exposure, have been observed in both experimental animal studies (1, 2) and human studies (3-7). A number of studies in a recent meta-analysis support an inverse association between PM exposure and heart rate variability (8). Exposure to the highest concentration of PM induced changes in markers of HRV variability (increased root of the mean of squared differences of adjacent RR intervals (RMSSD), low frequency (LF), high frequency (HF, and decreased LF/HF), and attenuated myocardial micro-RNA (RNA that suppress translation by targeting messenger RNA) expression (2). The effects of PM2.5 on subjects with hypertension were larger than on the subjects without hypertension (9). PM-induced decreases in ANS control of heart rate and increase of the risk of arrhythmia and acute cardiovascular events, may be more pronounced in older people (3). Recent study suggest that oxidative stress and systemic inflammation could be modifiers of cardiac autonomic responses to particulate air pollution (10). Air pollution effects on reduced SDNN are stronger in subjects with elevated systemic inflammation (11).

A number of anti-oxidant related genes have been identified and several studies have examined the degree to which polymorphisms in these genes may modify responses to PM.Polymorphisms in genes coding for glutathione S-transferase enzymes (GSTM1, GSTP1, GSTT1) were examined most often but variants in genes for heme oxygenase-1 (HMOX-1), hemocromatosis (HFE), NAD(P) H dehydrogenase [quinine] 1 (NQO1), and catalase (CAT) were also examined. Several studies have reported that individuals carrying the null allele for GSTM1, an enzyme that plays a key role in the cellular defense against oxidants, are more responsive to PM (12-15). An association was reported between PM concentration and decreased HRV in individuals with the null GSTM1 allele (15). Borderline significant effect for GSTT1polymorphism in association with PM2.5 exposure with increased plasma homocysteinemia was found (16). Also polymorphisms in genes related to lipid or cholesterol metabolisms could modify the effects of the exposure to PM2.5 on HRV. The apolipoprotein E (APOE, G113C), lipoprotein lipase (LPL, 291S, D9N) and vascular endothelial growth factor (VEGF, G634C) significantly modified effects of PM2.5 on HRV(17). Molecules involved in immunoresponses are attractive as potential modulators of cardiovascular pathology following PM exposure. Toll-like receptors (TLRs), a group of receptors abundantly expressed on leukocytes, have emerged as crucial first-responders linking innate and adaptive immunity after environmental challenge. Higher TLR2 methylation may confer susceptibility to adverse cardiac autonomic effects of PM2.5 exposure in older individuals (18). Higher flavonoid intake may attenuate these effects, possibly by decreasing TLR2 methylation (18). PM-induced cardiac dysfunction is mediated by multiple mechanisms.

In general, stronger inverse associations were observed between PM2.5 and HRV among subjects with genetic polymorphisms that impaired oxidant defence. The anti-oxidant supplementation was found to reduce inverse associations between PM2.5 and both time and frequency-domain measures of HRV (19).

Gene-environment interactions studies can help explore the mechanisms and the potential pathway in the association between air pollution and a cardiovascular outcome. Here we review studies that explore the impact of polymorphisms in anti-oxidant related genes or anti-oxidant supplementation on PM2.5-induced cardiorespiratory outcomes in an effort

to summarize existing evidence related to oxidative stress defence and cardiac autonomic response and the health effects of PM2.5.

References:

1.Rhoden, et al. PM-induced cardiac oxidative stress and dysfunction are mediated by autonomic stimulation. Biochim. Biophys.Acta.2005;1725, 305–313.

2.Farraj et al., ST Depression, Arrhythmia, Vagal Dominance, and Reduced Cardiac Micro-RNA in Particulate-Exposed Rats. Am J Respir Cell Mol Biol 2011;44:185–196.

3.Liao, et al. Association of higher levels of ambient criteria pollutants with impaired cardiac autonomic control. Am. J. Epidemiol. 2004;159:768–777.

4.Pope, et al. Ambient particulate air pollution, heart rate variability, and blood markers of inflammation in a panel of elderly subjects. Environmental health perspectives. 2004; 112:339–345.

5.Park SK et al. Effects of air pollution on heart rate variability: The VA normative aging study. Environmental health perspectives. 2005; 113:304–309.

6. Samet, et al. Concentrated ambient ultrafine particle exposure induces cardiac Changes in young healthy volunteers. Am. J. Respir. Crit. Care Med. 2009;179, 1034–1042.

7.Devlin et al. Controlled Exposure of Humans with Metabolic Syndrome to Concentrated Ultrafine Ambient Particulate Matter Causes Cardiovascular Effects. Tox Sci 2014;140:61–72.

8.Pieters, et al. An epidemiological appraisal of the association between heart rate variability and particulate air pollution: A meta-analysis. Heart2012, 98, 1127–1135.

9. Xu, et al. Relationship between Ambient Fine Particles and Ventricular Repolarization Changes and Heart Rate Variability of Elderly People with Heart Disease in Beijing, China. Biomed Environ Sci. 2013;26:629-637.

10.Lee, et al. Oxidative stress and systemic inflammation as modifiers of cardiac autonomic responses to particulate air pollution. Int J Cardiol. 2014;176:166-70.

11.Luttmann-Gibson, et al. Systemic inflammation, heart rate variability and air pollution in a cohort of senior adults. Occupational and environmental medicine. 2010;67:625–630.

12.Chahine, et al. Particulate air pollution, oxidative stress genes, and heart rate variability in an elderly cohort. Environmental health perspectives. 2007;115:1617–1622.

13.Madrigano, et al. Air pollution, obesity, genes and cellular adhesion molecules. Occup Environ Med 2010; 67:312–317.

14. Schneider, et al. Endothelial dysfunction: Associations with exposure to ambient fine particles in diabetic individuals. Environ. Health Perspect. 2008;116:1666–1674.

15. Schwartz, et al. Glutathione-S-Transferase M1, obesity, statins, and autonomic effects of particles. Am J Respir Crit Care Med 2005, 172:1529–1533.

16.Ren et al. Air pollution and homocysteine: More evidence that oxidative stress-related genes modify effects of particulate air pollution. Epidemiology. 2010; 21:198–206.

17.Ren et al. Lipid and endothelial related genes, ambient particulate matter, and heart rate variability --the VA Normative Aging Study. J Epidemiol Community Health. 2010; 64: 49–56.

18.Zhong et al. Cardiac Autonomic Dysfunction: Particulate Air Pollution Effects Are Modulated by Epigenetic Immunoregulation of Toll-like Receptor 2 and Dietary Flavonoid Intake. J Am Heart Assoc. 2015;4:e001423.

19.Romieu, et al. Omega-3 fatty acid prevents heart rate variability reductions associated with particulate matter. Am J Respir Crit Care Med 2005, 172:1534–1540.

O5 The eNOS rs1799983 gene polymorphism (Glu298Asp) in association with cardiovascular profiles in patients with vasovagal syncope

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Background: The NO modulates cardiac function through its regulation of hemodynamics and coronary reserve, but it also affects cardiac muscle function directly. In the heart, endothelial nitric oxide synthase (eNOS, encoded by the NOS3 gene) modulate cardiac contraction. Moderate overexpression of NOS3 restore the sympathovagal balance and protect the heart against arrhythmia. Syncope, defined as a sudden and reversible loss of consciousness, could be based on different putative underlying pathophysiological mechanisms such as neurogenic or cardiogenic (with arrhythmias).There is evidence through family studies that some forms of syncope may have a genetic component. Previous studies have demonstrated an association between eNOS polymorphisms and arrhythmia. The aim of the study was to analyze possible association of NOS3 rs1799983 (Glu298Asp) polymorphism with frequency domain and time domain indexes of HRV and BPV in patients with vasovagal syncope (VVS) from Serbia.
Methods: The 63 patients with VVS (age (mean±SD)=31.9±11.8 years, 81% females and 19% males) where included in the study. All patients underwent 24-h Holter ambulatory electrocardiographic (ECG) monitoring and analysed for HRV parameters (Task Force® Monitor) prospectively, before and after therapy. Genotyping was conducted by PCR-RFLP method. Statistical analysis were performed using SPSS software (SPSS 20.0).

Results: According to dominant model of inheritance for the NOS3 rare, T allele(GG vs. GT + TT), we have found significant association of T allele carriers with higher values of VLF (p=0.049), LF (p = 0.013) and HF (p=0.021). After the therapy, the pattern and direction of NOS3 T allele association remained significant for LF (p=0.024) and HF(p=0.037) values.There was no significant association with blood pressure parameters.

Conclusions: Results suggest a significant association of NOS3 genetic variant with HRV parameters among patients with VVS from Serbia. Further validation studies on a larger patient group are needed.

O6 Effects of glutathione S-transferase T1 and M1 deletions on electrocardiographicand heart rate variabilityparameters in patients with vasovagal syncope

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Background: Glutathione (GSH) conjugating enzymes, glutathione S-transferases (GSTs), are present in different subcellular compartments including cytosol, mitochondria, endoplasmic reticulum, nucleus and plasma membrane. Altered GST expression has been implicated in cardiac and neurological diseases. Vasovagal syncope (VVS) is the most frequent type of syncope affecting about 25% of the population at least once during life. Sympathetic nervous system can control cardiovascular function and its failure could result in syncope. Depletion of the intracellular antioxidant GSH extended to the level of the whole heart could result in heterogeneous reactive oxygen species (ROS) production, and inhibition of oxidative phosphorylation could slow the heart rate and shortening of the action potential duration. Decreased functionality of antioxidant enzymes may pose a greater risk of toxic insult caused by chronic oxidative stress. Two detoxification enzymes GST isoforms Mu1 (GSTM1) and Theta1 (GSTT1) have role in antioxidant defense. Genetic polymorphisms of GST enzymes are gene deletions yielding no transcription or translation of the respective enzymes. The aim of the study was to investigate the association of GTSs polymorphisms with frequency domain and time domain indexes of HRV and BPV in Serbian patients with VVS.
Methods: The 70 patients with VVS of mean age 32.9±12.4 years (mean±SD, 80% females and 20% males) where tested for association of GST T1 and GST M1 deletion genetic variants with frequency domain and time domain parameters of HRV. All patients underwent 24-h holter ambulatory electrocardiographic (ECG) monitoring and analyzed for HRV parameters (Task Force® Monitor) prospectively, before and after therapy. Genotyping was done by PCR. Statistical analysis was performed using SPSS software (SPSS 20.0).
Results and Conclusion: The GSTT1 deletion variant showed no significant association with any of the tested HRV parameters in either of two performed measurements. We have found trend toward association of GSTM1 deletion variant with significantly lower values of maxQTc (p=0.066) and SDNN (p=0.053). After the second measurement, the significant association was found for the Max Qt (p=0.01), Max QTc (0.004) and SDNN (p=0.03). Deletion genetic variant carriers had significantly lower values of tested parameters. These results show possible influence of oxidative stress on HRV, and suggest the need for further genetic association studies on larger patient groups.

O7Past, present and future of cardiovascular disease prevention

Prof. Dr. Oscar H. Franco, MD, PhD, FESC, FFPH

Despite great advances in treatment of cardiovascular disease and improvements in survival after cardiovascular events, cardiovascular disease remains the number one cause of mortality and morbidity worldwide. During this talk, I will cover some of the historical factors that have constituted great advances in cardiovascular disease prevention. Furthermore, I would go through some of the current debates in cardiovascular disease prevention. Finally I will discuss what potentially constitute a new era in cardiovascular prevention. Since 2003 society could be witnessing the rise of a new era in the prevention and treatment of cardiovascular disease: the Polyera. This new era started when a promising concept – the Polypill – was introduced by Wald et al. in the BMJ. The Polypill is a theoretical combination of six pharmacological compounds (a statin, three different antihypertensives, aspirin,and folic acid) that in combination could reduce cardiovascular disease by more than 80%. Although the Polypill could theoretically be a highly effective intervention, it is not yet available in the market and its effectiveness and costs remain unlear. In the population at large, cheap prizes may come at prohibitive costs. With frail elderly and population prevalences of co-morbidity far higher than in drug trials, rare adverse effects may be frequent. In December 2004, a more natural, safer, and probably tastier alternative to the Polypill – the Polymeal – was introduced. Contrary to the Polypill, the Polymeal combined 6 different foods (fruits and vegetables, almonds, chocolate, wine, fi sh, and garlic) that taken together in a regular basis could cut cardiovascular disease risk by over 75 % . Products from the polyera in true populations might hide unexpected interactions. Hype or hope, for the polyera to be established, further evidence will need to establish benefits, harms, and costs. Could this be the future of cardiovascular disease prevention?

O8 Saturated Fatty acids and cardiometabolic risk – a fresh look at the available evidence

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Current dietary recommendations encourage reducing the intake of total saturatedfatty acids (SFAs) to preventcardiometabolic diseases; however, recent findings have questioned the role of total SFAs. Several recent systematic reviews and meta-analyses, based on prospective observational studies that examined dietary total SFA intake in relationship with subsequent risk of cardiometabolic outcomes (i.e.coronary heart disease, stroke and type-2 diabetes), found no significant overall association. However, in the observational studies of fatty acidbiomarkers,where individual SFA subtypes in blood phospholipids were measured, there seems to be a substantial heterogeneity inthe risk associations within the totalSFA family. For example, in thesebiomarker studies,specific odd-chain SFAs appear to have an inverse association with cardiometabolic risk, whereas by contrast, even-chain SFAsare associated positively. Additionally, available randomised secondary prevention trials (where totalSFAconsumption was replaced with omega-6 polyunsaturated fatty acid intake) are generally small, insufficiently prolonged, vary widely in quality and rigor, and report weak inverse or no significant effects on clinical cardiometabolic outcomes. Furthermore, in metabolic ward studies with intermediate outcomes, in overall, supplementing with diet high in SFA contentreducedcirculating low-density lipoprotein cholesterol concentration importantly, however, also tended to increase circulating high-density lipoprotein cholesterol,triglycerides and lipoprotein(a) levels, and had no significant effect on insulin resistance. In summary, the value of broad grouping of nutrients such as total SFA and their effects on intermediate factorsor clinical outcomes may be limited owing to the potential diversity of specific SFA subtypes in terms of their wide-ranging food sources and discrepant clinical consequences. Further research, therefore, is required to reliablyclarify:(1) the roles of individual SFA subtypes, in isolation and in combination,on cardiometabolic risk,particularly in free-living general populations; and (2) potential cardiopreventive or cardiopromotive effects of their principal food sources,when compared with other appropriatefood alternatives (such as specific forms of carbohydrates).

O9 Psycho-cardiology: Does blood on nano level possess quantum entanglement?

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***Background*:** In scientific literature and clinical reports connections between a heart condition (blood properties) and emotional and mental states are well documented (1).It is well known that psychosocial risk factors may lead to activation of mechanisms responsible for somatic dysfunction of cardiovascular system. In this perspective, psychological and cardiac issues are not seen separately and there is a belief that a multidisciplinary approach (psycho-cardiology) is necessary for the wellbeing of the patient.

***Motivation*:**Our initial motivation for blood investigation was its diamagnetic/paramagnetic state, because O_2itself is paramagnetic, as well as Fe^{2+}. However, when joined together in hemoglobinthan complex O_2/Fe^{2+} is diamagnetic. By measuring magnetic properties of blood we may obtain information about oxygen/iron state, which has influence on molecular code of cooperativity in hemoglobin, which is responsible for pathogenesis of disorders, such as cardiovascular disease nephropathy and retinopathy, and some common disease such as diabetes mellitus (2,3). It is known thatglycatedhemoglobin(HbA_{1c}) is used as a physiological measure of stress, sinceit has high correlation with some other psychological stress indicators (4).

***Material and methods*:** Our study comprised of 12 volunteers, seven male and five female. Sample of 5 ml of blood was taken from each; 3.0 ml for biochemical analysis and 2.0 ml for experiment.Sample with3.0 ml of blood was stored in standard test tube and transported to biochemical laboratory, while 2.0 ml blood sample was immediately stored in speciallydesignedplastic container for medical use and transported to laboratory for magnetic measurement. Measurements were done using JR-6 spinner magnetometer (AGICO, Czech Republic; measurement range from 3pT to 15.7 mT, with ±3pT accuracy). After initial sample measurements, sample containerswere storedin a separate isolatedroom,under control conditions, and with N-S defined directions.Every day, at the same time, and in order of samples as the initial measurement was done, measurementswere repeated for next 20 days.

***Results*:**Biochemical analysis of blood for ten volunteers was in normal range; while for two volunteersit was outside of normal range (their organoleptic medical examinations were done). Average value of the first magnetic measurements of blood forten volunteers was 0.185 nT, while for two volunteers with irregular readings was 9.43 nT and 12.07nT.Afterfifteen days, blood magnetic values for two volunteersoriginally with normal results, jumped from average of 0.185 nT to 9.50 nT and 10.20 nT, respectively. Two volunteers were immediately called, and it was established that both were under very high emotional stress.

***Conclusions*:**This initial study indicates that quantum engagement is one of the more promising phenomena which may be used to explain experimental psycho-craniologicalresults of increasing magnetic values of blood. More theoretical and experimental research has to be done before final conclusions are reached.

1. Koch,H., Psychocardiology: the specrum of stress in the genesis of heart disease : a point of view, *Reseaerch Reports in Clinical Cardiology*, 4: 153-159, 2013.
2. Holt,R.I.G., Cockkram,C.S., Flyvbjerg,A., Goldstein, Textbook of Diabetes, Wiley-Blackwell, Chichester, UK, 2010.
3. Ackers,G.K., Doyle, M.L., Myers,D., Daugherty, M.A., Molecular Code for Coopravity in Hemoglobin, *Science*, 255:54-62, 1992.
4. Schuck,P. GlycatedHemoglobin as a Physiological measure of Stress and its Relations to Some Psychological Stress Indicators, *Behav Med*., 24: 89–94, 1998.

O10 Investigation of hypertension drugs by Raman spectroscopy

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Abstract. Raman spectroscopy has been method of choice for many investigation in solid state physics and chemistry as rapid, sensitive and non-destructive tool. It is based on analysis of inelastic scattered light. Recently Raman spectroscopy has attracted significant attention due to its large possibility of application in medicine, biomedical issues, clinical implementation, food industry and pharmacy, because he permit obtain information about sample quality, study local atomic arraignment, chemical composition, dopant incorporation, molecular structure, molecular interactions in cells and tissues and others [1]. All this advantages of Raman spectroscopy introduce it in nanomedicine and pharmacy as powerful tool to study drugs as well as cells and tissues affected by disease [1] for example determination of concentration of commercially available medicines, identification and quantification of active ingredients [2], blood analysis, monitoring the effects of therapies and using the feedback to individualize drug or radiation treatment, rapid identification of pathogenic microorganisms [1]. The aim of this work is to study influence of information on industrially produced hypertension drugs such as carvedilol, losartan, perindopril, moksonidin, amlodipin, fosinopril and digoksin. In order to detect possible changes on nano level, samples have been investigated by micro-Raman spectroscopy on 532 nm laser line in spectral range from 100 to 3100 cm^{-1}. Significant changes in Raman spectra of all samples are noticed. Influence of information on samples are visible in change of spectral and peak intensity.

[1] L.-P. Choo-Smith, H.G.M. Edwards, H.P. Endtz, J.M. Kros, F. Heule, H. Barr, J.S. Robinson JR, H.A. Bruining, G.J. Puppels, Biopolymers (Biospectroscopy) 67 (2002) 1
[2] L. Silveira Jr., L. Marmo Moreira, V.G.B. Conceição, H.L. Casalechi, I.S. Muñoz, F. Fernandes da Silva, M.A.S.R. Silva, R. Aparecido de Souza, M.T.T. Pacheco, Spectroscopy 23 (2009) 217

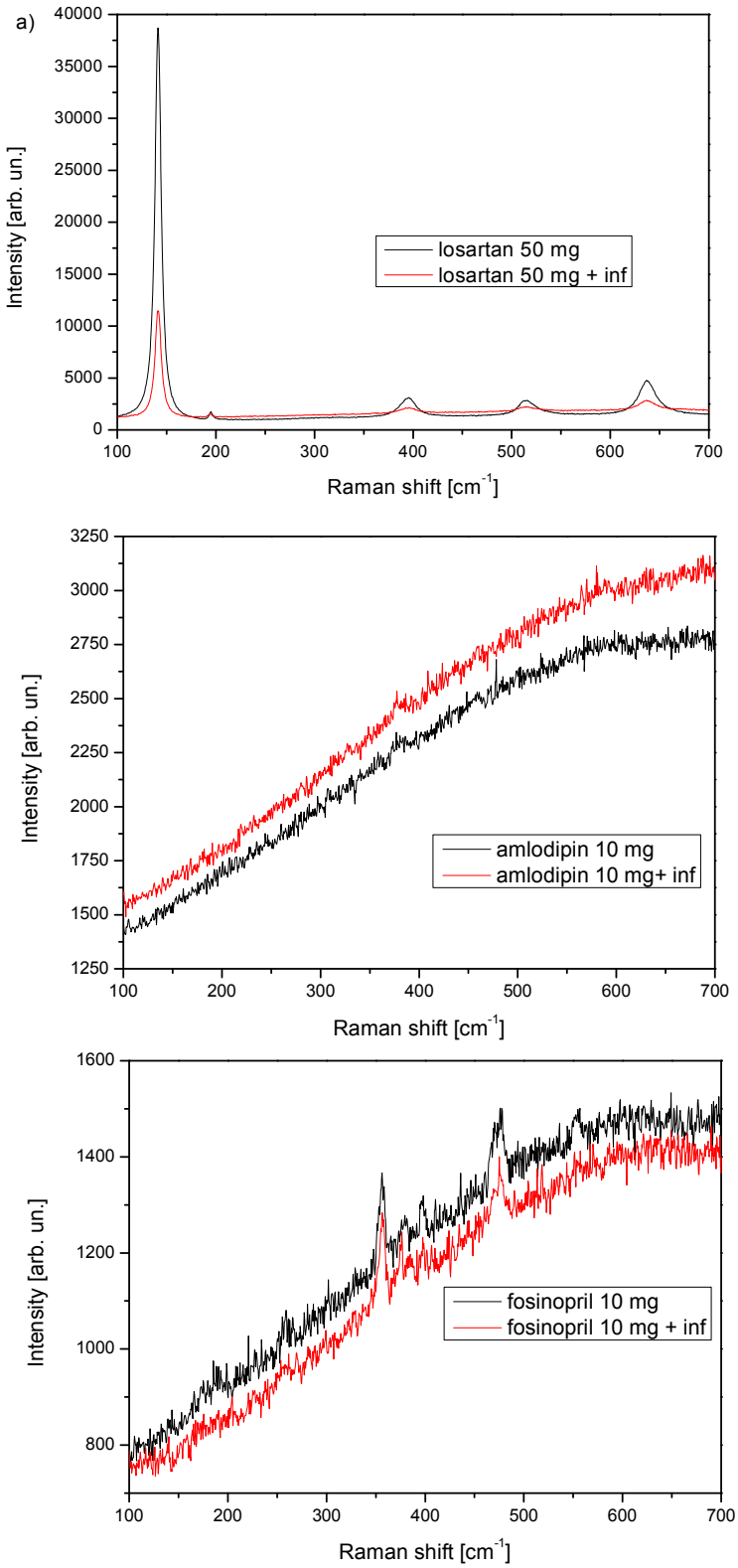

Fig. Raman spectras of a)losartan, b) amlodipin and c) fosinopril in spectral range from 100-700 cm^{-1}

O11 Autonomic Nervous System, Repolarization, and Cardiac Imaging: Integrative approach to Sudden Death Risk Stratification

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Arrhythmia risk stratification (RS) with regard to primary prevention of sudden arrhythmic death remains a clinical challenge. In the past, RF based on single ECG alone has been shown to have no significant positive predictive value. New markers of autonomic nervous system activity, such as heart rate turbulence and deceleration capacity of heart rate, however, seem to be of more predictive value, particularly in patients with better preserved left ventricular function. The same holds true for T wave alternans (TWA) as a marker of repolarization and arrhythmogenic substrate. Since it is now possible to characterize the extent of the arrhythmogenic substrate using MRI techniques, cardiac imaging has been introduced as a new mainstay of arrhythmic RS. In various cardiac disorders such as nonischemic DCM, hypertrophic cardiomyopathy or in post MI patients, substrate quantification in combination with one electrocardiographic risk marker may increase specificity with regard to identifying patients at arrhythmogenic risk.
For example, in a study of Sakamoto et al the relation between TWA and amount of late gadolinium enhancement (LGE) on cardiac MRI was assessed in 42 patients with hypertrophic cardiomyopathy. They found that the magnitude of localized LGE was correlated to the maximual amplitude of TWA and both were significantly higher in patients with ventricular tachyarrhythmia events.
The present review summarizes available data on new approaches of sudden death RS with special focus of combining cardiac imaging with new ECG-based arrhythmia risk markers.

O12 Cardiac autonomic patterns and risk stratification by patients with myocardial infarction

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It is very known fact that autonomic nervous system is geneticaly determinated especialy related to heart rate and blood pressure. According to Framingham study parameters of heart rate variability are also constant especially spectral components Low (LF%) corresponding with sympathetic activity and High frequency (HF%) with vagal activity. In order to detect some types of autonomic patterns we analysed 2450 patients after myocardial infarction and follow up (survival time 36, range 0-138 months). End-point of the study was total mortality.

All patients were tested in Neurocardiological unit using Task Force system (Graz, Austria) commercial software with real time analysis of spectral parameters TP (Total power), VLF (Very low frequency), LF (Low frequency) and HF (High frequency). All parameters were analysed third week after onset of myocardial infarction. We detected four types of autonomic patterns: Strong Sympathetic group (predominance of Sy, low TP), Moderate Sympathetic group (predominance of Sy, high TP), Moderate Parasympathetic group (predominance of Psy, low TP), Strong Parasympathetic group (predominance of Psy, high TP).

The analyse of survival showed that third group corresponds with predominance of vagal activity and low total power was univariate risk predictor. This result was opposite to accepted scientific conclusions from many studies that sympathetic hyperactivity is the strongest risk predictor. We included in multivariate analysis set of parameters: Ejection fraction lower than 30%, positive late potentials and vagal groups with normal and decreased total power. The multivariate risk predictors were both parasympathetic groups with high statistical significance (Vagal group with normal TP, p-0.009 and Vagal group with decreased TP , p-0.034).

These results showed need for further steps in risk stratification using new approaches which will include analysis of some autonomic patterns associated with high mortality.

013 Diurnal variations in myocardial deformation on the left ventricle

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Time-of-day–dependent synchronization of organisms with their environment is mediated by circadian clocks.This cell autonomous mechanism has been identified within all cardiovascular-relevant cell types, including cardiomyocytes. Subjects:The aim of the study is the analyze this circadian pattern in the left ventricle (LV) contractility,using myocardial deformation imaging by 2D speckle tracking echocardiography. Material and Methods: In the study were enrolled 11 clinically healthy volunteers (mean age 38y ±9.8), including 4 men (mean age 35y ±10.6) and 7 women (mean age 41y ±8.7). All the images were obtained at a frame rate of 60 to 70 frames/s. Echocardiography was performed in all volunteers within 24 hours at 6.00 a.m. 12.00 a.m., 6.00 p.m. and 12.00 p.m. and analyzed offline in order to extract the global and segmental strain values and twist/ untwist rate of the LV. Strain and twist /untwist measurements were performed offline with dedicated automated software. Results: The highest value for GLS, GCS ,GRS, LVT and LVUR are around 6.00 am and the lowest value are around 6.00 pm. Considering results from all 6 walls as independent replications, a statistically significant very similar results are obtained when the analysis is carried out on the average values (based on basal, middle, and apex)as seen. The least negative values occur, on average, around 06:00 p.m., circadian rhythm is found for both regional circumferential strain ($P<0.001$) and for radial strain ($P=0.002$) and longitudinal too as rotational parameters. Conclusions: This is the first study to assess global physiological consequences of the circadian clock specifically within the myocardial deformation.We provide evidence that the cardiomyocyte circadian clock influences not only heart rate and the responsiveness of the heart to increased workload, but and circadian pattern of regional dysfunction and deformation, which is important for global ventricular function.

	06:00	12:00	18:00	24:00
GL Strain (%)	-23.22±3.19	-22.99±2.3	-22.76±3.19*	-22.95±2.86
GC Strain (%)	-20.93±4.91	-20.78±5.45	-18.42±6.73*	-20.53±4.45
GRStrain(%)	40.99±11.26	41.06±14.12	37.04±12.34*	39.31±12.28
Twist (˚)	10.77±3.01	10.12±4.73	9.13±4.43*	10.72±6.2
Untwist rate (˚/s)	-84.37±32.76	-71.29±34.19	-64.02±32.54*	-78.28±46.01

O14 Physiological heart rate pacing for preventing not only neurocardiogenic syncope

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Neurocardiogenic syncope NCS is a term that encompasses trigger-mediated, situational, vasovagal, and other forms of dysautonomic syncope. Standard pacing in an attempt to prevent these episodes in classic vasovagal syncope have therefore met limited success, as increasing a patient's heart rate may provide no immediate correction to the preceding drop in blood pressure which contributes to the syncopal response. With the development of closed loop stimulation, the detection of the vasovagal response is established earlier in its progression and the corrective action of increasing heart rate is activated to stabilize blood pressure and prevent syncope.

In patients with chronotropic incompetence correct cardiac output is not possible to provide according to hemodynamic heart request. In 30-70% patients with implanted pacemaker we can expect CI.

In patients with systolic heart failure (HF) CI is common (30-50%). Additionally, CI occurs in >70 % of patients with advanced systolic HF irrespective of beta-blocker use and is an independent predictor of mortality, cardiac transplantation or ventricular assist device placement

The CLS system is the special sensor in pacemaker (PM) that can provide to emotional stress. This CLS provides also a more physiological response to all signals coming from the heart which should lead to correct heart rate increasing. Due to special algorithm PM get information about heart contractility and myocardial wall motion. By measuring changes in the heart's contractile state, CLS automatically adjusts to changes in a patient's lifestyle, activity and drug regimens. That is why, in these two issues CLS seems very promising for three group of patient in which correct, physiological heart rate is crucial: NS, heart failure patients and chronotropic incompetence (CI).

HF patients must rely to a greater extent on increases in HR to augment cardiac output to compensate for their inadequate stroke volume during physical exertion. In heart failure patients with severe CI rate adaptive pacing with CRT provides a benefit on exercise capacity. The use of rate-adaptive pacing only increases heart rate (HR) during exercise, but not the resting rate, and the increase in 24h-HR due to rate adaptive pacing is minimal. Exercise training and rate-adaptive pacing have been shown to improve chronotropic response and exercise capacity in HF.

CLS was developed as an algorithm for physiological rate modulation in patients suffering from neorocardiogenic syncope, chronotropic incompetence and improve hemodynamic in heart failure patients. This algorithm seems very promising in reduction symptoms and improving hemodynamic status in those patients.

O15 Antiphospholipid Syndrome as Risk Factor for the Neurological and Cardiac Involvement

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Introduction: Antiphospholipid syndrome (APS) is a systemic autoimmune disease associated with arterial and venous thrombotic events and recurrent fetal loss. Cardiac and neurological manifestations in APS primarily include accelerated atherosclerosis leading to neuro-cardiovascular disease. Neuro-Cardiovascular risk is even higher in secondary APS in lupus patients. Several traditional and disease-related, autoimmune-inflammatory risk factors are involved in APS-associated atherosclerosis and its clinical manifestations.However, the importance of specific antiphospholipid antibodies (aPL) as a risk factor for neuro-cardiovascular riskin APS patients remains controversial.
Methods: We investigated 558 patients: 330 pts with PAPS followed up for an average of 44.00±12.97y., and 148 pts with secondary APS (SAPS) in scope of SLE (47.74±14.84y). Antiphospholipid antibody (aPL) analysis included detection of aCL (IgG/IgM), ß$_2$GPI (IgG/IgM). Data considering acute myocardial infarction (IM), unstable angina (UA), coronary artery bypass grafting (CABG) or percutaneus coronary artery angioplasty (PTCA, TIA, and stroke. Carotid ultrasound was performed and the intima-media wall thickness (IMT) and presence of plaque was investigated in all patients and controls. The diagnosis of neurovascular diseases has been established by neurologist. Traditional vascular risk factors and APS-disease and treatment related factors were also analyzed.
Results: Presence of aCL IgG was more common (p=0.001) in SAPS, and LA in PAPS patients (p=0.002). More than one type of antibodies (category I) was present in 64.5%. Age was a significant risk factor for MI: 56.6 and 43.6 years, respectively (p=0.0001). Highly statistically significant difference was revealed considering presence of aβ_2GPI antibodies and carotid arteries plaque presence (p= 0.020), in pts with PAPS and aβ_2GPI (0.049), as well PAPS pts with smoking (p=0.008). PAPS and SLE patients did not differ among themselves with regard to the occurrence of MI (p = 0,102) ,and UAP (p = 0.123) unstable angina pectoris (UAP), but presence more than 2 aPL was a significant risk factor for UA (p=0.017). After adjustment for age, current cigarette smoking, diabetes, hypertension and hyperlipidemia, the relative odds for stroke in PAPS patients with ß2GPI IgG positivity was 3.87 (95% confidence interval 1.00 to 3.60, p=0.049, bootstrapped for 1000 samples) whereas in SAPS patients was 5.25 (95% confidence interval 0.10 to 1.81, p=0.021, bootstrapped for 1000 samples).
Conclusion: The results from this study support the importance of PL as an independent risk factor for neurological and cardiac manifestations.Presence of aβ2GPI positivity brought higher atherosclerotic risk in our study group. Presence of more than one aPL in APS patients additionally accelerate atherosclerotic continuum. In this subgroup of APS patients more aggressive approach towards prevention and control of standard atherosclerotic risk factors is crucial.
Conflicts of interest: Authors declare no conflicts of interest.

ACKNOWLEDGEMENTS
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O16 PREMATURE ATHEROSCLEROSIS AND THE ANTIPHOSPHOLIPID ANTIBODY CATEGORY IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME – IS THERE A RELATIONSHIP?

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INTRODUCTION: Carotid intima-media thickness (cIMT) has been established as a distinguished marker of cardiovascular risk.Patients with antiphospholipid syndrome (APS) have been evaluated in the context of accelerated atherosclerosis in numerous studies, bringing this concept into the focus regarding proper treatment of this population of patients.nThe aim of this study was to evaluate relationship between category of antiphospholipid antibodies (aPL) and cIMT in APS patients.

MATERIALS: We analyzed 181 APS patients (101patients with primary and 80 with secondary APS – systemic lupus erythematosus (SEL)) 159female (87.8%) and 22male (12.2%), average age 48.7±13.1years. Patients were classified into **CategoryI**, (more than one aPL present in any combination), **CategoryIIa** onlylupus anticoagulans (LA)), **CategoryIIb** (only anticariolipin (aCL IgG/IgM) present) and **CategoryIIc** (only anti-β_2 glycoprotein-I antitela (anti-β_2GPI IgG/IgM) present). Measurement of cIMThas been performed on common carotid artery (CCA), its bifurcation (CCAbiff) and internal carotid artery (ICA) on both sides. We defined cIMT values 1.1mm and higher as plaque presence.

RESULTS: There was 65.7% pts in aPLCategoryI, 8.8% IIa, 19.3% IIband 6.6% IIc. 23.2% APS had all three aPLpresent.Prevalence of standard atherosclerotic risk factors was below 40%. There was 49.3% pts in CategoryI with carotid plaques present, compared to 4.0% pts in category IIa, 13.3% pts in CategoryIIb and 4.0% pts in IIc category 29.3% pts with all three aPLhad carotid plaqes (p=0.049). Average values of cIMT were significantly higher in patients with Category I comparing to other aPL categories for almost all segments of carotid trunk (CCAright, p=0.003, CCAleft, p=0.001, CCAbiffright, p=0.026, CCAbiffleft, p=0.162, ICAright, p=0.028, ICAleft, p=0.410).

CONCLUSION: Presence of more than one aPL in APS patients additionally accelerate atherosclerotic continuum. In this subgroup of APS patients more aggressive approach towards prevention and control of standard atherosclerotic risk factors is crucial.

Key words: antiphospholipid syndrome, antiphospholipid antibodies categories, carotid intima media thickness

O17 Cardiac autonomic neuropathy in hemodialysis patients

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Objective: To evaluate the presence and severity of cardiac autonomic neuropathy (CAN) in hemodialysis, by heart rate variability (HRV) measurements.

Introduction: In recent years, there has been increased interest about autonomic nervous system function in chronic uremia, especially in pathogenesis of complications such as sudden cardiac death.Identification of high-risk individuals, particularly those susceptible to cardiac death, is of clinical importance.

Materials and Methods: We investigated26 chronic uremic patients who were on regular chronic bicarbonate hemodialysis (age 18-67,) by a battery of six cardiovascular autonomic tests, and 24 Holter h ECG for analysis of time- and frequency-domain HRV.

Results: All long-term HRV measures of the patients were significantly reduced compared with those obtained from 25 age-matched healthy subjects.Abnormal response did not correlate with age, serum albumin, or parameter of chronic inflammation (hsCRP).

Conclusions: We confirm high incidence of CAN in uremic patients, even after introduced hemodialysis program.Importantly, we showed that this association was independent of potential confounders, as age, albumin and chronic inflammation.

Key words: cardiac autonomic neuropathy, hemodialysis, outcome

O18 Effects of hemodialysis on heart rate variability and insulin resistance in end-stage renal disease patients

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Objective: End-stage renal disease (ESRD) is associated with the presence of cardiac autonomic neuropathy (CAN), as well as the presence of insulin resistance (IR), strong risk factors for cardiovascular disease (CVD). We hypothesized that hemodialysis (HD) would improve CAN together with metabolic abnormalities, particularly in non high-risk patients.
Materials and Methods: The study was cross-ectional and investigated 24 chronic kidney disease patients (CKD), 12 pre-dialysis (group 1), and 12were on regular chronic bicarbonate hemodialysis no more than 12 months (group 2), by a battery of six cardiovascular autonomic tests and HRV analysed using 24 h ambulatoryHolter recordings of electrocardiogram (ECG). Besides the conventional laboratory parameters we investigated the presence of insulin resistance (IR), and left ventricular mass index(LVMI).The degree of IR was estimated by the Homeostasis Model Assessment (HOMA-IR).
Results: We found that all HRV indices were significantly higher, and HOMA-IR, phosphorus, iPTH, IL-6, and uric acid were significantly lower in group 2, compared with those obtained from group 1. In a multivariatelogistic regressionmodelHOMA-IR and uric acid were independent predictors of HRV indices, particularly in group 2.
Conclusion: It seems thatsympathovagal balance could be improved in association with IR improvement after the beginning of the treatment of uremic patients by chronic hemodialysis program.

O19 Ambulatory blood pressure monitoring (ABPM) – comprehensive assessmentof blood pressure parameters

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Introduction: Ambulatory blood pressure monitoring (ABPM) allows an insight into the values and variability of blood pressure over a defined period.
The aim of our study was to analyze the logs ABPM and to evaluate comprehensively the contribution of this method not only in terms of blood pressure control and diurnal index setting, but also from the prognostic aspect.
Patients and methods: We analyzed 206 ABPM records from patients admitted to theinternal department in the calendar year 2013. 15 entries (7.3%) could not be evaluated due to an insufficient number of measurements. 93 men (45%) and 113 women (55%) have been divided into 4 groups according to their age. In the age group 18 to 44 years were 31 subjects, aged 45 – 64 years were 78 subjects, aged 65 – 74 years were 52 persons and aged 75 years and more 45 persons. The results of ABPM permitted the identification of four different profiles based on changes in diurnal index: dippers, non-dippers, extreme dippers and risers. ABPM examinations were carried out on fully automatic devices with defined day and night phase measurements and correlated with the diary of activities and quality of sleep.
Results: In 88 subjects (42.7%) the average values of the ABPM for 24-hour monitoring were achieved. Dippers group consisted of 79 individuals (38.3%), in the group of non-dippers were also 79 individuals (38.3%), risers were 30 (14.6%) and extreme dippers were 3 (1.5%). By tracking the fate of persons under investigation, we found that until June 30, 2014 19 persons died (9.2%), of which 14 were from groups with a disturbed diurnal index (9 non-dippers and 5 risers).
Conclusions: Our results point to the fact, that in addition to the basic parameters of blood pressure used as an indicator of blood pressure control, the analyses of diurnal character failures has a importance in prognostic aspect. Identifying these patients may therefore be helpful in the management of arterial hypertension and comorbidities.

O20 HEART RATE VARIABILITY IN PATIENTS WITH DIASTOLIC DYSFUNCTION

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Numerous studies have revealed the influence of sympathovagal balance to cardiovascular morbidity and mortality. Data also suggest the strong link between risk factors and heart rate variability (HRV). Arterial hypertension, diabetes mellitus, obesity, metabolic syndrome contribute significantly to sympathovagal imbalance via complex pathophysiological condition. The role of neurohumoral mechanisms involved in deterioration of HRV was emphasized. Neurohumoral regulation leading to diastolic dysfunction is also associated with changes in myocardial structure. Exactly the upregulated renin-angiotensin system related to autonomic dysfunction is involved in the development of impaired myocardial relaxation. It was also demonstrated that increased myocardial stiffness occurred usually in patients with myocardial hypertrophy.

More investigators reported impaired HRV especially low frequency while others suggested the importance of low/high frequency related to arterial hypertension and diastolic dysfunction New data have shown even the link between the altered HRV and early myocardial deformation in hypertensive patients

Studies dealing with glucometabolic abnormalities demonstrated the relationship between parasympathetic dysfunction and insulin resistance, obesity or increased glucose production.According to some investigators cardiovascular autonomic neuropathy in diabetic patients with impaired myocardial relaxation may be detected by decrease in time-domain parameters. Reduction in all of the frequency domain components was shown among the patients with advanced neuropathy. It was also found that even subjects with higher risk for diabetes mellitus presented impaired HR;. their day time low frequency was reported as an independent predictor of damaged autonomic system.

Although the majority of data underline the association between sympathivagal imbalance and arterial hypertension, diabetes, obesity, metabolic syndrome some of them are conficting. Some new techniques and advanced data analysis might be necessary to provide important information about the complex pathophysiological mechanisms involved in affected HRV and early myocardial structural changes in patients with the most frequent cardiovascular risk factors.

O21 ASSESSMENT OF AUTONOMIC FUNCTION IN PATIENTS WITH HYPERTENSION

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Introduction: Cardiovascular reflex tests and spectral analysis of heart rate variability can be used to assess parasympathetic and sympathetic modulation of the autonomic nervous system (ANS). Previous studies have found either reduced or unchanged heart rate variability in hypertension.
The aim: Assessment ofautonomic nervous system function in patients with prehypertension and first stage of hypertension.
Materials and methods: The investigation was performed on 155 patients (81 males), aged 32 to 79 years (50.86±10.88), with hypertension. The control group was presented by 155 healthy volunteers matched in age and gender with the examinees. Study protocol included the evaluation of autonomic function and hemodynamic status (according to the comprehensive tree steps protocol performed in our Neurocardiology Laboratory, Clinical Hospital Center "Bežanijska Kosa"), 24 hour ambulatory ECG monitoring with long term heart rate variability (HRV) analysis and 24 hour ambulatory blood pressure monitoring.
Results: Pathological results of cardiovascular reflex test were more common among patients with hypertension compared to the control group: Severe autonomic dysfunction was detected in 27.1% of patients and only in 2.8% of controls. All time- and frequency-domain parameters were significantly decreased in comparison with control group. Only LF/HF ratio was higher in the hypertension group, indicating that sympathetic nervous system dominates the parasympathetic.Mean value of baroreflex sensitivity parameters were lower in hypertension group also with statistical significance.
Conclusions:Low HF component of heart rate variability may mark diminished modulation of vagal activity, while decreased LF component of heart rate variability in our hypertensive subjects may reflect decreased sympathetic excitation owing to baroreceptor loading. The present study shows that there is distortion of both components of ANS in patients with prehypertension and mild hypertension, but prospective studies are needed to find out whether reduced heart rate variability identifies hypertensive subjects with increased risk of cardiac mortality.

Key words: Autonomic nervous system, hypertension, cardiovascular reflex test, heart rate variability.

O22 Chronic Vagal Nerve Stimulation as a Potential New Treatment for the Metabolic Syndrome?

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Three important components of the metabolic syndrome are abdominal obesity, insulin resistance and/or glucose intolerance and elevated blood pressure. In this presentation experimental data will be discussed demonstrating that chronic cervical vagal nerve stimulation (VNS) reduces body weight through changes in caloric intake, feeding efficiency and metabolic rate andthat VNS has the potential to lower blood glucose concentration if efferent nerve fibers are stimulated selectively. Furthermore, preliminary data of an ongoing study will be presented that is designed to test the hypothesis that chronic cervical vagal nerve stimulation prevents hypertension-induced cardiovascular end-organ damage. If this hypothesis can be confirmed, chronic vagal nerve stimulation may potentially be useful as a novel treatment strategy for patients with metabolic syndrome.

O23 Pregnancy differentially affects neurogenic cardiovascular control in normontensive and spontaneously hypertensive rats

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BACKGROUND: It is well established that during pregnancy period female body succumbs to significant adaptive changes in order to provide positive foetal outcome. It is also known that pregnancy-induced adjustments of circulatory system may affect the health of females with preexisting hypertension. Nevertheless, the understanding of neurogenic cardiovascular control throughout normotensive and hypertensive pregnancies seems to be vague and deserves thorough approach.

OBJECTIVES: To investigate the effects of pregnancy-induced bodily changes on autonomic cardiovascular control in normotensive and spontaneously hypertensive rats.

METHOD: All experiments were performed in conscious female Wistar (WR) and spontaneously hypertensive rats (SHR), equipped with radio telemetry device. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were derived from the arterial pulse wave as maximum, minimum and inverse inter-beat interval. Spectral analysis of BP and HR was performed on 7 minute-long recordings in total (0-3Hz), very low frequency (VLF: 0-0,2 Hz), low frequency (LF: 0,2-0,8 Hz) and high frequency (HF:0,8-3 Hz) range. Spontaneous baro-receptor reflex sensitivity (sBRS) was evaluated using the sequence method.

RESULTS: Significant reduction in SBP accompanied by an increase in HR was observed during pregnancy in both rat strains without evident changes in sBRS. By the end of pregnancy, total SBP variability notably changed in both rat strains, albeit in different manner-while it increased in WR, total SBP variability decreased in SHR. In non-pregnant state there was a significant difference in VLF and LF bands between strains, which could not be observed by the mid- and late- pregnancy.

CONCLUSION: Our results show for the first time differences in autonomic control of cardiovascular system during normotensive and hypertensive pregnancies. As expected, accentuated activity of renin-angiotensin system along with increased sympathetic drive during hypertension was noticed in non-pregnant SHRs. This phenomena, seen as increased VLF and LF SBP bands, could not be noticed in pregnant SHR dams, probably due to prevailance of mechanisms inducing vasodilation. Normalization of SBP and BP variability in SHRs reveal potential adaptational mechanisms which can be beneficial for maternal health during pregnancy in hypertensive state.

O24 The comparative analysis of Tp-e and natriuretic peptides (ANP, BNP) concentration in plasma as risk marker of electrical instabilityin children with different myocardial hypertrophy

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Background: Myocardial hypertrophy is electrical instability predictor of risk of life-threatening arrhythmias and SCD. Transmural dispersion of repolarization (TDR) used to determine the ventricular arrhythmias risk. Most clearly the dynamics of TDR manifested in treadmill test. ANP and BNP are biochemical markers of myocardial remodeling. This study determined the ventricular arrhythmias risk in patients with different myocardial hypertrophy.
Patients and Methods: For 93 teenagers with left ventricular hypertrophy included 63 junior athletes with physiological hypertrophy ("Athletes"), 30 children with myocardial hypertrophy in arterial hypertension ("Hypertension"), and 30 healthy children (control group). All children conducted treadmill test with Tp-e interval manual evaluation at rest, on peak exercise, on the 1st and 3rd minutes of the recovery phase. Laboratory method for assessing myocardial remodeling conducted theanalysis of concentration of atrial and brain natriuretic peptides in plasma (ANP, BNP).
Results: The values of Tp-e in "Athletes" group at the 3rd stage of load (<0.001) and the 3rd minute of recovery phase (<0.05) were significantly higher than the control group. Tp-e in "Hypertension" group in the 3rd stage of the load was significantly higher than the control group too (<0.001). The level of ANP concentration in "Athletes" group significantly higher than the control group (<0.001) and it confirms the ANP role as myocardial remodeling marker. In "Hypertension" group ANP comparable with the control group value (>0.05) and it indicates the low information content ANP oninitial stage of remodeling. The BNP concentration level in "Athletes" group significantly lower than the control group (<0.05), it confirms the nature of the physiological cardiac hypertrophy in athletes. In the "Hypertension" group BNP significantly higher than the control group (<0.05), it confirms the great informative value of this indicator of remodeling.
Conclusion: In athletes with physiological and favorable nature myocardial hypertrophy the criteria for myocardial electrical instability is lack. BNP deviation and the growing of electrical instability as increased Tp-e values in children with arterial hypertension myocardial hypertrophy confirmed pathological hypertrophy in these patients.

O25 Peculiarity of the syncope in the young elite athletes

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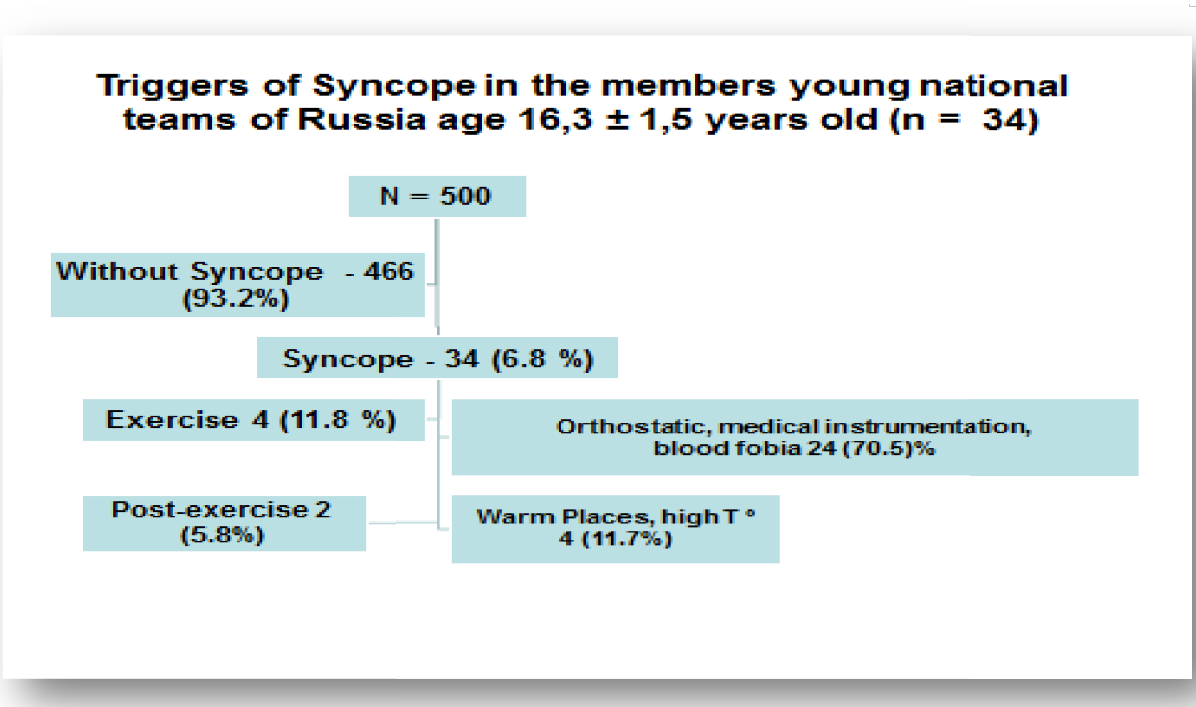
Aims of this study was evaluation rate and nature of Syncope (S) in young elite athletes. Methods and results: Were evaluated a cohort of 500 young elite athletes, members of national young teams of Russia (43 males, 130 females) 16,3±1,5 years old. S in the history was reported in 34 athletes (6,8%) 28 females, 6 men in 53 cases, with median rate 2,9 (1-3) cases. Control group were 40 athletes of the same age and gender proportion without S.



S were induced orthostatic stress in 24 from 40 (70,5%) athletes, manipulations, instrumentation and blood fobia in 4 (11,7%), rapid of head or body position changes in 10% and other triggers were revealed in 45% cases. 19 athletes demonstrated more than one trigger for syncopal episodes. Passive, active and post- exercise orthostatic tests had detected vassodepressive type S (VASIS III) in 15 athletes 6 (%), cardioinhibitor variant (VASIS II) in 4 and VASIS III in 5 cases.Cardiac investigations during ECG, Holter monitoring, stress-test not revealed congenital heart diseases, cardiomyopathy or conditions with risk of lifethreathening arrhythmias. Interval QTc on rest the ECG (MAC 5500, GE, USA) and microvolt T wave alternance during exercise test (Cardiosoft, GE, USA) were nonsignificantly higher in athletes with S (414±26 vs 406,6±23 ms and 37,1±15 vs 32,9±38 uV accordingly, $p > 0,05$). For athletes with S were proposed standard prevention therapy. All athletes were followed for 1.2±1 years, no recurrent syncope or adverse events was noted during follow-up.Conclusions: In young competitive athletes, syncope can occur until 12% cases, predominantly in young women. As a rule syncope in athletes have neurally-mediated nature and low recurrence rate. Exercise-related syncopesis infrequent and is not associated with an adverse outcome in subjects without cardiovascular abnormalities. But in all cases S in athletes need to exclude diseases with risk lifethreatening cardiac arrhythmias because athletes with S have more often signs of electrical nonstability of the heart.

O26 Myocardium repolarization dynamics during physical exercise test in young athletes and untrained adolescents

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Introduction. QT interval prolongation on a resting electrocardiogram (ECG) is a big problem for young athletes, whichrequires in-depth examination to rule out the primary long QT syndrome (LQTS) and may be a reason of medical disqualification. Now, there are a lot of evidences concerning stress test importance for diagnostics of this syndrome, because myocardium repolarizationrespond differently to stress in different LQTS variants. But up till now the norm values of myocardium repolarization indices during exercise stress in young athletes have not yet been established.
Aim of study: to determine physiological limits of myocardial repolarization response to exercise test and to develop simple efficient technology for noninvasive diagnostics of electrical myocardial instability in young athletes.
Methods: 100 young athletes (11-16 yrs old) - sport school attendants and 100 untrained healthy children of a similar age and gender were enrolled in our study. All the children underwent complex examination, including exercise bicycle test by Bruse protocol with synchronic ECG recording.Intervals RR and QT were measured manually. Corrected QT interval was calculated by Bazett and Fridericia formulas (QTc, FQTc). Dispersions of absolute and corrected QT interval (dQT, dFQT, dQTc, dFQTc) as well as δQT (QT variability as a difference between maximal and minimal QTc during the exercise test) were calculated
Results. Potentially dangerous ECG changes - inverted T–waves, long QTc and short QTc were not revealed in any of the athletes. Non significant QTc prolongation (440-460 ms) and shortening were recorded in 2 athletes. In our study mean QTc in the athletes at rest was compared to that in untrained, but absolute QT at rest and at the 1 stage of exercise was higher in the athletes, due to bradycardia and myocardial hypertrophy.. Gradual, smooth QT interval shortening in both groups were recorded, which correlated with gradual intensification of exercise. But at peak load QT in the athletes was considerably lower than in untrained due to hyperadaptation of repolarization processes to the heart rate grows. During recovery period QT duration in athletes returned to the original values more promptly than in untrained.Dynamics of QTc in the young athletes during exercise–test was similar to that in healthy untrained adolescents.QTc interval in both groups increased ad maximum during low-intensity load despite the heart rate growth, but did not exceed 450-460 ms for boys and girls respectively. Minimal QTc values in both groups were recorded at peak load. But the athletes showed a more marked QTc shortening (less than 390 ms) compared to untrained (so-called “QTc hyperadaptation”). During the recovery period QTc returned to the original level in most of the athletes similar to the control group. As established by doctor I.A.Gorbunova, QTc prolongation in athletes exceeding 450 ms in early recovery period suggests myocardium pathology and requires additional examination to rule out LQTS. 17 children in our group had no adequate QTc shortening at peak load or early recovery period, in 3 out of them rhythm disturbances during test were recorded. Thorough medical examination showed myocarditis in 1 athlete, congenital and acquired LQTS in 2 athletes, signs of myocardial athletic remodeling, medication damage or/and overtraining - in 14. Dynamics of the QTc interval, estimated by different formulas was similar in both groups, but Bazett QTc values were higher than the Fridericia ones. We have determined the norm values of an absolute and corrected (by Bazett and Fridericia formulas) QT interval in young athletes during exercise test. Dispersions of absolute and corrected QTinterval during moderate exercise (50-100Wt) in athletes exceeded the corresponding indices in untrained children, while at peak load they were considerably lower. Like in a control group QT dispersion in athletes increased significantly during early recovery, up to the highest value in the test (did not exceeded 35-40ms). Another significant sign of electrical instability of the myocardium is δQT. In our study permissible QT variability in athletes was 50-60ms. More significant QT variability was noted in 21% of athletes, 11 of whom had cardiac remodeling an overtraining syndrome, 3 - structural cardiovascular diseases and 1 probably LQTS.

Conclusions: In young athletes, as well as in the untrained maximal QTc (by Bazett) have been recorded at the initial stages (not exceeding 460 ms) and minimal - at the peak of exercise. QTc prolongation over 390 ms at peak load and over 450 ms at min 4 of recovery, as well as QTc variability more than 50 ms during exercise test in young athletes can be considered as a signs of cardiac pathology. They require an extensive medical examination to rule out primary and secondary LQT. Maximal QT and QTc interval dispersions have been recorded at the initial stage of exercise and during recovery, they did not exceed 35 and 40 ms, respectively. Assessment of myocardial repolarization dynamics during exercise in young athletes can be a significant diagnostic method for revealing LQTS and some conditions associated with sudden cardiac death.

O27 Features of regulation of circulation during dehydration the athlete

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It is known that there are sports with long duration physical activities that cause a large loss of body fluids within a relatively short period of time. The high qualification athlete, his ability to tolerate aerobic exercise by higher temperature and humidity of the environment, the more expressed this process. For this reason, many athletes many athletes admitted to a mobile medical center with symptoms of dehydration and centralization of blood circulation.

Objective: to study the peculiarities of regulation of the cardiovascular system in athletes, with the most expressed symptoms of dehydration.

Materials and methods: the analysis was applied to 16 male athletes, participants of the marathon world Championships in athletics in Moscow 2013 admitted to a mobile medical center with symptoms of dehydration

Results. Patients mobile medical center were in an amount of 23.2% of all participants of the marathon (the race was attended by 69 athletes from 39 countries, of which finished 51 marathoner). 8 athletes (50%) out of the race to the finish. 12 athletes (66,7%) was observed spasms of the muscles of the legs, which is characteristic for continuous competition in a hot humid climate (air temperature during the race exceeded 30° C, humidity – 85%). Attract attention physiological characteristics admitted to a medical center athletes - were expressed signs of circulatory centralization characteristic of hypovolemic shock - the average body temperature of patients was equal to 31,2 ± 1,5 ° C, the skin was cold and dry (despite the heat environment and previous sweating).

The average body mass of the athletes was equal 56,4±5.9 kg with an average body length of 172±7,2 cm.

Attracted attention, however, not characteristic of shock hemodynamic changes - the vast majority of athletes tended to bradycardia - average heart rate (HR) was 62 ± 6,8 beats per minute and blood pressure - systolic - 105.1 ± 10,2 mmHg diastolic - 68,2 ± 7,1 mmHg.

Here it should be noted that for hypovolemic shock characterized by tachycardia and hypotension.

However, athletes in the state hypohydration not observed tachycardia and hypotension is a normal characteristic of endurance athletes.

Discussion. It is known that the best marathon runners-men run the distance at an average speed of about 20 km/h as shown for more than 42 km distance, and losing to 4-5% of the fluid that the body weight is 56 kg is approximately 2.5 liter blood .Blood loss for a normal person, not involved in sports, during this time, accompanied by characteristic changes in hemodynamic shock, and is deadly. Thus, we can distinguish the differences and similarities of these conditions

Common features of dehydration marathoner and shock due to blood loss:

- Rapid loss of large amounts of fluid (within 2-3 hours)
- Typical symptoms
- Signs of impaired microcirculation
- Signs of centralization of a circulation
- The effect of treatment (rehydration, compensation of electrolytes, etc.)

Differences dehydration marathoner and shock due to blood loss:

- Occurs without morphological integrity of organs and systems
- Not accompanied by a loss of blood cells and clotting factors
- Accompanied by hemoconcentration (not the hemodilution), hypoglycaemia, and dyselectrolytemia
- Normally, is familiar to athletes, it goes against the background of fatigue and permit oral necessary components
- Clinical value of assessment of blood pressure and heart rate remains uncertain

Conclusions.

1. The clinical symptoms of centralization of blood flow during dehydration in athletesis similar to the classic hypovolemic shock, however, with the features associated with the physiology of the athlete.
2. The blood pressure and heart rate in athletes (as opposed to classical hypovolemic shock) cannot be the criteria of severity of hypovolemia

O28 The early ECG changes in preadolescent elite footballers

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Objective: To assess the early ECG changes induced by physical training in preadolescent professional footballers.
Methodology: Ninety-four highly trained male footballers (mean aged 12.85 ± 0.84) competing in our Football League (at least 7 training hours/week) and 47 age-matched healthy male controls were enrolled in the study. They were screened by ECG and echocardiography at a tertiary referral cardio centre. The control group had sedentary life style (less than 2 training hours/week). Characteristic ECG intervals and ECG voltage were compared and reference range was given for preadolescent footballers.
Results: Highly significant differences between preadolescent athletes and sedentary controls were registered in all ECG parameters: P wave voltage ($p<0.001$), S wave (V1 or V2 lead) voltage ($p<0.001$), R wave (V5 and V6 lead) voltage ($p<0.001$), ECD sum of the S1,2+V5,6 ($p<0.001$), T wave voltage ($p<0.001$), QRS complex duration ($p<0.001$), T wave duration ($p<0.001$), QTc interval duration ($p<0.001$) and R/T ratio ($p<0.001$). No differences were registered in PQ interval duration between these two groups ($p>0.05$). QTc interval duration in athletes had not very strong, but indeed positive correlation to left atrium dilatation, LV end-systolic and end-diastolic dimensions, LVMI, LVM / BSA1.5 and LVM / h2.7 indexes. There was no correlation between QTc interval duration and LVM as well as LV wall thickness.
Conclusions: ECG changes are present in the early stage of athlete's heart remodeling. QTc prolongation could be the early ECG marker of physiological LV remodeling in young preadolescent footballers.

O29 Chaos and Entropy Analysis during Head-up Tilt test in Neurally mediated Syncope

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Syncope is a temporary loss of consciousness and posture, described as fainting, usually related to temporary insufficient blood flow to the brain, which has high medical, social, and economic relevance. Vasovagal syncope is a common clinical event, the pathogenic mechanisms of which are still poorly understood. The orthostatic stress causes many hemodynamic changes in cardiovascular system. The exact mechanisms responsible for loss of consciousness associated with profound hypotension and/or bradycardia, and mediated by vagal excess and sympathetic withdrawal, remain uncertain. Nonlinear analysis may quantify abnormalities in RR intervals series based on fractal analysis (chaos theory). A subject open to debate is to compare heart rate variability (HRV) parameters and the chaos theory analysis methods for the assessment of the clinical status and the outcome in neurally mediated syncope.The aim of our study was to perform the head-up tilt test in patients who described pre-syncope symptoms or had a syncope history and to assess the role of the autonomic tone and the dynamic changes of heart rate. Approximate entropy (ApEn) was applied to quantify the regularity and complexity of time series, as well as unpredictability of fluctuations in time series.***A group of 21 patients with mean age 57.5 years (13 men, 8 women) have performed a*** 90° head-up tilt test. ***The assessment was performed using standardized protocols for neurally mediated syncope.***All subjects were placed supine on an electronic tilt table and were attached to an ECG recorder, Cardiax V 3.50.4 ECG system by IMED Co Ltd, Hungary, and a blood pressure cuff. A Sphygmocor system was used for continuous blood pressure measurements.Compared to the heart rate variability parameters, the nonlinear dynamics parameters, mainly the entropy parameters have a different behavior related to the postural changes.

O30 Imbalance of autonomic nervous system in cases of TLOC caused by channelopathies

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Introduction: Cardiac arrhythmias belongs among possible cause of transient lost of consciousness (TLOC) with lifethreatening potential, especially in association with inherited abnormalities involving ion channels.
Aim: Case demonstration of two young people without structural heart disease with history of TLOC. Men 23 years with history of exercise associated syncope. Girl 17 years with history of occasional lost of consiousness especially in early morning with impossibility to awake her up.
Methods: Standard ecg, heart rate variability assessment during supine-standing supine test and exercise testing were provided in both cases. Morover Holter monitoring - loop recorder in case of case of TLOC during rest time.
Results: Men with exercise induced TLOC: normal rest ecg, Brugada-like pattern on exercise ecg, HRV 5 minute supine: Total power 5636 ms^2, LF 1937 ms^2, HF 1312 ms^2, LF/HF 1,4772. Standing LF/HF 14,1362!
Girl with rest TLOC: normal rest ecg, exercise test with multiple ventricle ectopies, Holter loop-recorder dynamic changes of QT interval up to QTc 600 ms and sustained ventricle tachycardia Torsade de pointes with spontaneous termination in early morning. HRV during supine-standing-supine test: Total power 2771 ms^2, LF 198 ms^2, HF 2556 ms^2, LF/HF 0,0779.
Conclusion: We demonstrate two types of so called channelopathies. Typical ecg patterns were not permanent finding. That is why the diagnose could be overloooked. We observed conspicuous shift in LF/HF caused by orthostatic chalenge in the case of Brugada syndrom. We can suppose further augmentation of sympathovagal imbalance in association with catecholamins released due to exercise with possible impact on ecg morphology. In case of long QT we recorded enormously dominant vagal acivity in supine position (vigilant). According to literature sympatovagal changes during sleep causes QT interval prolongation. It correlated with occurrence of Torsade de pointes in our case during sleeping time when heart rate decreased.

O31 Entropy Analysis of RR and QT Interval Measurementsduring Head-up Tilt test in Healthy Subjects

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Neurally mediated syncope represents one of the most frequent condition for admission and hospitalization worldwide. The QT interval of body surface ECG represents a global measure of ventricular electrical activity. The main objective of this study was to investigate the relationship of entropy parameters with other time series parameters in healthy subjects to highlight the role of the autonomic tone mechanisms in neurally mediated syncope.The main feature of this method is the lack of studies characterizing heart rate, blood pressure or electrocardiographic (ECG) responses in healthy subjects during head-up tilt test compared to the most frequently affected population.Measurements of entropy , like approximate entropy (ApEn) and sample entropy (SamEn) , mean values and standard deviations (meanNN, SDNN) of RR time series and spectral analysis parameters have been measured in resting conditions and during head-up tilt test. Automatically measurements of the QT and QTc intervals have been performed in resting condition and after tilting at 90^0. Our results proved that the mean RR interval has shortened during head-up tilt (p: 0.07) but in mean time the entropy parameters significantly changed after tilting (p: 0.0001). A strong negative correlation was observed after tilting between QTc (ms) and entropy parameters (r: - 0.6).Our study proves that entropy-based measures provide useful indicators of pathological changesin cardiac activity and be suitable for the early detection of autonomic dysfunction.

O32A NOVEL APPROACH IN ASSESMENT OF BAROREFLEX SENSITIVITY IN SYNCOPE PATIENTS

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ABSTRACT
Spontaneous baroreflex sensitivity (BRS), heart rate variability (HRV) and blood pressure variability (BPV) are established tools for the assessment of arterial baroreflex and cardiac autonomic activity. Arterial barorefex function is commonly assessed through a number of laboratory tests based on quantifcation of the reflex responses in heart rate or blood pressure to external stimuli applied to the cardiovascular system. Spontaneous baroreflex sensitivity during selective autonomic nervous system testing can provide valuable information and insight in type of autonomic dysfunction in vasovagal syncope patients. The present results suggest that the initial cardiovascular response accompanied by baroreflex sensitivity is associated with modified sympathetic response and inability of adjustment to provocation. It is possible that stressors inducing acute increases in vasoconstriction and blood pressure might nevertheless trigger compensatory baroreflex-mediated bradycardia and vasodilation in susceptible individuals as vasovagal syncope patients. The present results suggest that the initial cardiovascular response accompanied by baroreflex sensitivity is associated with modified sympathetic response and inability of adjustment to provocation. The precise impact and behavior of baroreflex sensitivity in syncope patients needs to be further investigated, according to its importance it will attract attention of researchers.

INTRODUCTION

The arterial baroreflex adapts variation of blood pressure and prevents pressure from rising or fallingexcessively. Arterial baroreceptors provide a tonic inhibitory influence on sympathetic tone, thus controlling peripheral vasoconstriction and cardiac output. Spontaneous baroreflex sensitivity (BRS), heart rate variability (HRV) and blood pressure variability (BPV) are established tools for the assessment of arterial baroreflex and cardiac autonomic activity [1]. The physiology of syncope is diphasic. The presyncopal first phase starts with generalized sympathetic activity, one manifestation of which is a sudden vascular constriction. The second, syncopal phase, involves a pronounced increase in vagal activity, which leads to reduction in vascular resistance in skeletal muscles, heart rate deceleration, and a consequent reduction in blood pressure. Since the presyncopal phase tends to elicit sudden increases in heart rate, vasoconstriction and hence blood pressure, the syncopal phase may result from pressor-induced stimulation of baroreflex activity and subsequent bradycardia andvasodilation [2]. The first step of the diagnostic evaluation of every patient suspected of presenting with syncope begins with an "initial evaluation" as described in the Guidelines of the European Society of Cardiology [3]; this step consists of careful history taking, physical examination including orthostatic blood pressure measurement and electrocardiogram (ECG). However, after "initial evaluation" in approximately 50% of cases the diagnosis of vasovagal syncope could not be provided and additional clinical evaluation is needed [4] . The aim of this article is to review the role of some of these additional diagnostic tests. Arterial barorefex function is commonly assessed through a number of laboratory tests based on quantifcation of the reflex responses in heart rate or blood pressure to external stimuli applied to the cardiovascular system. Spontaneous baroreflex sensitivity during selective autonomic nervous system testing can provide valuable information and insight in type of autonomic dysfunction in vasovagal syncope patients. Since it is a noninvasive technology that provides a lot of valuable information in a short time and reduces the costs of hospital treatment distinguishes this diagnostic method compared to other additional clinical examination.

METHODS

The 306 individuals, 195 vasovagal syncope patients (age 35.90 ± 14.36) with lifetime history of vasovagal syncope and 111 healthy controls (37.14 ± 11.24) both genders were enrolled in the study. Exclusion criteria for syncope patients were known coronary artery disease, atrial fibrillation, secondary arterial hypertension, renal failure (serum creatinine > 1.2 mg/dL), autoimmune disease, or use of such drugs as neuroleptics, antidepressants, lithium, antiarrhythmics or cimetidine. Patients with well controlled arterial hypertension and diabetes mellitus with good metabolic control were enrolled. All patients were tested during supine position at least 5 minutes before performing the tests of autonomic function. Testing of baroreflex sensitivity was performed on Task Force Monitor (CNSystem, Graz, Austria). The selective autnomomic nervous system testing results were correlated with baseline recording and between groups. All experimental protocols were approved by the. The Task Force Monitor (CNSystems, Graz, Austria), was used to monitor beat-to-beat heart rate (HR) by ECG and beat-to-beat blood pressure by the vascular unloading technique [5], which was corrected automatically to the oscillometric blood pressure measured on the contralateral arm. Baroreceptor reflex sensitivity (BRS) is automatically assessed using the sequence technique according to Parati [6]. For selective autonomic nervous system testing it was used battery of cardiovascular reflex tests according to Ewing's [7].Scientific Ethical Committee of Clinical Hospital Center Bezanijska Kosa number, license number 1039/3 within the project, the Ministry of Education, Science and Technological Development Republic of Serbia TP32040, which gave the accordance for the study. All participants gave written informed consent in accordance with the declaration of Helsinki.

RESULTS

Comaparison vasovagal syncope group with healthy controls clearly demonstrates the difference between groups. All subjects were normotensive during testing (Table 1). In syncope group there is slightly abatement in slope mean values during all selective autonomic nervous system testing in baseline recordings and during performing tests. Interesting, in syncope group there is no statistical significance in baseline recordings and during hand grip test comparing to healthy controls (17.24 ± 9.86 vs. 15.53 ± 8.49, P = 0.037) which indicates potential sympathetic damage in syncope patients. In syncope group of patients during mental stress test (16.02 ± 12.88 vs. 13.04 ± 8.25, P = 0.001) there is drop in values of slope mean comparing to controls which also suggests sympathetic dysfunction. High statistical significance (13.74 ± 7.50 vs. 16.47 ± 10.22, P = 0.001) appears in vasovagal syncope groupe, as well in healthy controls (15.01 ± 7.00 vs. 19.09 ± 9.21, P = 0.001) which indicates normal reponce during deep breathing test and preserved parasympathetic response (Table 2). Interesting and statistical significant difference between groups seems to appear in cold pressure (14.21 ± 9.40 vs. 15.98 ± 7.68, P = 0.035) and hand grip test (13.35 ± 8.54 vs. 15.53 ± 8.49, P = 0.038), which indicates pathological sympathetic response. Comparison between groups did not show statistical significance in any other tests from battery (Table 3). Also in correlation between LFnuRRI, HFnuRRI and LF/HF-RRI with Slope Mean during all test it is clearly that there is powerful negative correlation between LFnu-RRI and Slope Mean, as well as, between LF/HF-RRI and Slope Mean (Table 4).

DISSCUSION

The present results suggest that the initial cardiovascular response accompanied by baroreflex sensitivity is associated with modified sympathetic response and inability of adjustment to provocation. It is possible that stressors inducing acute increases in vasoconstriction and blood pressure might nevertheless trigger compensatory baroreflex-mediated bradycardia and vasodilation in susceptible individuals as vasovagal syncope patients. In the other hand, sympathetic dysfunction allows the Vagal nerve to take the lead and disables the recovery of blood pressure leading the subject to faint. The genetic predisposition some of the subjects to experience vasovagal reactions may be due to changed baroreflex sensitivity in situations which elicit many conditions [8, 9]. Also, the interesting to note is that parameter as Slope Mean in combination with components of heart rate variability reveals the type of autonomic nervous system patterns. Spontaneous baroreflex sensitivity is a valuable specific risk marker which can be used for evaluation of cardiovascular risk in some patients experiencing syncope cardiovascular etiology. Depressed baroreflex sensitivity (< 3 ms/mmHg) is a strong risk factor for cardiac death especially in patients below age 65 years old [10]. Simple battery of selective tests gives important insight in autonomic nervous system condition, type and level of the damage. It is possible that syncope patients experience dysfunction in both parts, sympathetic and parasympathetic part of autonomic nervous system, but one, sympathetic is affected more frequently.

CONCLUSION

Sponataneus baroreflex sensitivity is very important parameter for evaluation of vasovagal syncope which became easily accessible by the guidance of novel signal processing technology which overcome problems during history. The precise impact and behavior of baroreflex sensitivity in syncope patients needs to be further investigated. The importance and regenerative potential of this adoptive mechanism has been confirmed in previous investigations and is worth for further commitment of researchers.

REFERENCES

1. Maurizio Acampa, Francesca Guideri, Giovanna Marotta, Rossana Tassi, Paolo D'Andrea. Autonomic activity and baroreflex sensitivity in patients submitted to carotid stenting. Neuroscience Letters 491 (2011) 221–226.
2. Perry S. J. Adler, Christopher France and Blaine Ditto. Baroreflex sensitivity at rest and during stress in individuals with a history of vasovagal syncope. Joumol of Psychosomaric Reurorch. Vol. 35, No. 415, pp. 591-597. 1991.
3. Moya A, Sutton R, Ammirati F, Blanc JJ, Brignole M, Dahm JB, et al. Guidelines for the diagnosis and management of syncope (version 2009): the Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC). Eur Heart J. 2009;30:2631-2671.
4. Jean-Jacques Blanc. Clinical Laboratory Testing: What Is the Role of Tilt-Table Testing, Active Standing Test, Carotid Massage, Electrophysiological Testing and ATP Test in the Syncope Evaluation? Progress in Cardiovascular Diseases 55 (2013) 418-424.
5. Parati, G., Ongaro, G., Bilo, G., Glavina, F., Castiglioni, P., Di Rienzo, M. et al. Non-invasive beat-to-beat blood pressure monitoring: new developments. Blod Press Monit. 8(1):31-36 (2003).
6. Parati, G., Di Rienzo, M., Mancia, G. How to measure baroreflex sensitivity: from the cardiovascular laboratory to daily life. J Hypertens. 18:7-19 (2000).
7. Ewing DJ, Martyn CN, Young RJ, Clarke BF. The value of cardiovascular autonomic function tests: 10 years experience in diabetes. Diabetes Care 1985; 8: 491-498.
8. Atala MM, Goulart A, Guerra GM, Mostarda C, Rodrigues B. Arg16Gly and Gln27Glu β2 adrenergic polymorphisms influence cardiac autonomic modulation and baroreflex sensitivity in healthy young Brazilians. Am J Transl Res. 2015 Jan 15;7(1):153-61.
9. Rodrigues FL, Silva LE, Hott SC, Bomfim GF, da Silva CA. Toll-like receptor 9 plays a key role in the autonomic cardiac and baroreflex control of arterial pressure. Am J Physiol Regul Integr Comp Physiol. 2015. 15;308(8):R714-23.
10. La Rovere MT. Baroreflex sensitivity as a new marker for risk stratification. Z Kardiol. 2000;89 Suppl

Table 1. Baseline recording of blood pressure and heart Rate on Task Force Monitor in vasovagal syncope patients and healthy controls.

	Syncope (N = 195)	**Controls (N = 111)**
sBP (mmHg)	114.57 ± 13.10	116.01 ± 13.28
dBP (mmHg)	77.67 ± 10.15	77.17 ± 10.27
mBP (mmHg)	89.15 ± 10.53	88.55 ± 12.09
HR (bpm)	74.28 ± 14.54	72.30 ± 9.95

sBP, systolic blood pressure; dBP, diastolic blood pressure; mBP, mean blood pressure; HR, heart rate.
Data represent mean ± SD values.

Table 2. Selective autonomic nervous system battery of tests performed on Task Force Monitor during baseline recording and tests in vasovagal syncope and healthy controls group.

Battery of tests		**Syncope** Slope Mean	**P value**	**Controls** Slope Mean	**P value**
HGT	Before	18.22 ± 13.71	NS	17.24 ± 9.86	P = 0.037
	After	13.35 ± 5.54		15.53 ± 8.49	
CP	Before	13.72 ± 8.70	NS	15.69 ± 8.02	NS
	After	14.21 ± 9.40		15.98 ± 7.68	
DBT	Before	13.74 ± 7.50	P = 0.001	15.01 ± 7.00	P = 0.001
	After	16.47 ± 10.22		19.09 ± 9.21	
MST	Before	16.02 ± 12.88	P = 0.011	16.23 ± 7.44	NS
	After	13.04 ± 8.25		16.75 ± 9.41	
HT	Before	16.72 ± 8.05	P = 0.001	15.59 ± 7.40	P = 0.001
	After	10.50 ± 5.04		9.32 ± 6.93	
HVT	Before	14.62 ± 8.68	P = 0.015	16.07 ± 1.81	NS
	After	14.03 ± 12.66		18.27 ± 11.22	

HGT, hand grip test; CP, cold pressure test; DBT, deep breathing test; MST, mental stress test; HT, head up tilt test; HVT, hyperventilation test; Slope Mean in ms/mmHg; NS, without statistical significance. Data represent mean ± SD values.

Table 3. Selective autonomic nervous system battery of tests performed on Task Force Monitor during tests in vasovagal syncope healthy controls group.

Battery of tests	Syncope	Controls	P value
	Slope Mean (ms/mmHg)		
HGT	13.35 ± 8.54	15.53 ± 8.49	P = 0.038
CP	14.21 ± 9.40	15.98 ± 7.68	P = 0.035
DBT	16.47 ± 10.22	19.09 ± 9.21	NS
MST	13.04 ± 8.24	16.75 ± 9.41	NS
HT	10.50 ± 5.04	9.32 ± 6.93	NS

HGT, hand grip test; CP, cold pressure test; DBT, deep breathing test; MST, mental stress test; HT, head up tilt test; NS, without statistical significance. Data represent mean ± SD values.

Table 4. Correlation between LFnuRRI, HFnuRRI and LF/HF-RRI with Slope Mean performed on Task Force Monitor during tests in vasovagal syncope patients.

Slope Mean (ms/mmHg)	LFnuRRI	P value	HFnuRRI	P value	LF/HF-RRI	P value
HGT	r = -0.398	p = 0.001	r = 0.398	p = 0.001	r = -0.413	p = 0.001
CP	r = -0.477	p = 0.001	r = 0.477	p = 0.001	r = -0.495	p = 0.001
DBT	r = -0.216	p = 0.056	r = 0.217	p = 0.055	r = -0.210	p = 0.063
MST	r = -0.214	p = 0.065	r = 0.214	p = 0.065	r = -0.283	p = 0.014
HT	r = -0.462	p = 0.013	r = 0.462	p = 0.013	r = -0.536	p = 0.003
HVT	r = -0.453	p = 0.001	r = 0.462	p = 0.001	r = -0.468	p = 0.001

HGT, hand grip test; CP, cold pressure test; DBT, deep breathing test; MST, mental stress test; HT, head up tilt test; HVT, hyperventilation test; LFnu-RRI, percent of normalized Low Frequency interval component; HFnu-RRI, percent of normalized High Frequency interval component; LF/HF-RRI, LF/HF ratio of heart rate variability.

O33 HEART RATE VARIABILITY COMPUTED ON THE BASIS OF 24-HOUR ECG FOR CARDIAC AUTONOMIC NEUROPATHY DETECTION

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Introduction: Cardiac autonomic neuropathy (CAN) is a very common and often underestimated long-term complication of diabetes mellitus (DM). The prevalence of CAN varies between 1%-90% in patients with type 1 DM (T1DM) and 20%-73% in patients with T2DM [1] and depends on the criteria used to identify CAN and the population studied [2]. CAN has been detected at time of diagnosis of diabetes in patients with T2DM irrespective of age, suggesting that CAN presentation is not limited by age or duration of diabetes and can occur before DM is evident clinically [1]. According to the Subcommittee of the Toronto Consensus Panel statement following the 8th international symposium on diabetic neuropathy in 2010, the criteria for diagnosis and staging of CAN are as follows: (1) A single abnormal cardiac autonomic reflex tests (CART) result suffices for the diagnosis of possible or early CAN; (2) The presence of two or three abnormal test among the seven autonomic cardiovascular indices (5 CARTs, time-domain and frequency-domain HRV tests) are required for the diagnosis of definite or confirmed CAN; and (3) The presence of orthostatic hypotension in addition to the above criteria signifies the presence of severe of advanced CAN [1].During its sub-clinical phase, heart rate variability (HRV) that is influenced by the balance between parasympathetic and sympathetic tones can help in detecting CAN before the disease is symptomatic [1]. A decrease of HRV is earliest clinical indicator of CAN. Although arecent data has demonstrated that short-term ECG recordings can provide reliable information for CAN detection [2], previous recomendations wroteHRV computed from 24-hour Holter records were more sensitive than simple bedside tests (Valsalva maneuver, orthostatic test, and deep breathing) for detecting diabetic autonomic neuropathy[4].

Aim of study: to compare twenty-four hours HRV parameters in patients with T2DM and without DM and with cardiovascular autonomic reflex tests (CARTs) in DM patients.

Materials and methods: In groups of 49 T2DM patients and 38 age and gender matched controls HRV indexes computed from Holter records (5 Time domain, 4 Frequency Domain, 2 circadian indexes [4], [6]) were compared between DM and control groups and with 2 bedside CARTs (deep paced breathing, lying-to-standing tests[6]) in DM patients. All patients were admitted to Riga East Clinical University Hospital for different mostly cardiovascular indications and exposed to HM because of complaints on unexplained palpitations, fatigue, dizziness or syncope for possible arrhythmia detection.No patient had decompensated heart, kidney, endocrine or other disease which can have an impact onHRV,no heart rhythm influencing medicines were used 24 hours before and during HRV tests.

Results: Only 31 (63,3%) DM patient had one or both positive CARTs (CARTpos), whereas 48 (98%) patients had changed one and more 24-hour HRV parameter, the sum of changed 24-hour HRVindexes was higher in CARTpos patients compared with CARTneg(5[5] vs 3[2] , $p<.01$) and in T2DM patients compared with controls (4[4.5] vs 1[2], $p<.001$). ROC curve showed fair diagnostic effectiveness of HM based HRV for CAN detection (AUC=.761 (.625;.897) with cut-off point of 4 positive 24-hours HRV tests (sensitivity 77%, specificity 67%, $p<.01$).

Conclusions: 1. HRV should be analysed for evaluation of autonomic cardiovascular tone in every DM patient undergoing long-term ECG recording. 2. Inclusion of 24-hours HRV in DM patient evaluation could improve CAN detection at early subclinical stages. 3. 24-hour HRV can be discussed for CAN detection in DM patients with negative bedside CARTs.

References:

1. Gerasimos Dimitropoulos, Abd A Tahrani and Martin J Stevens. Cardiac autonomic neuropathy in patients with diabetes mellitus. World J Diabetes2014 February 15; 5(1): 17-39
2. Rodica Pop-Busul. Cardiac Autonomic Neuropathy in Diabetes. Diabetes care, volume 33 number 2, February 2010.
3. Solomon Tesfate et al. Diabetic Neuropathies: Update on Definition, Diagnostic Criteria, Estimation of Severity, and Treatment. Diabetes care 33:2285-2293,2010.
4. Marek Malik. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task force of the European Society of Cardiology the North American Society of Pacing and Electrophysiology. Circulation. 1996;93:1043-1065
5. Комолятова и др. "Национальные российские рекомендации по применению методики холтеровского мониторирования в клинической практике", Москва, 2013
6. Manfred Haslbeck, Dieter Luft, Bernhard Neundorfer, Hilmar Stracke, Dan Ziegler. Diagnosis, Therapy and Follow-up of Diabetic Neuropathy. Medline (OVID): 1998 – 2004-01, 2004-02.

O34 Does meteosensitivity influence on heart rate variability in medical students?

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Human activity is realized in conditions of environment. Geophysical disturbances causing meteopathological reactions in persons with reduced reserves of adaptation make a significant contribution to the forming of many pathological processes, mainly in the cardiovascular and nervous systems.

We aimed to investigate the relation between meteosensivility and autonomic nervous system obtained by heart rate variability (HRV) in 123 VI-year medical students (41males and 83 females) aged 23-26 yrs in spring 2015. Short-term HRV was assessed by 5 min. ECG recording in sitting and standing position (NeuroSoft, Ivanovo, Russia) with analysis in time and frequency domains.

Participants were asked to answer about meteosensitivity according 10 point scale.

Students were proposed to evaluate the influence of meteorological parameters (air temperature, air pressure, strong winds, precipitation, solar radiation intensity, etc.) and describe the symptoms of health impairment. One student may have more than one complain.

Results. The data of questionnaire have showed that weather factors influence on the health status of 72.0% of females and 56.1% of males. The most prevalent complain in females was headache (86.7%) and decreased working capacity (28.3%), in males - headache (65.2%), fatigue (29.1%) and sleepiness (29.1%). Females with headaches had increased heart rate (HR, 87.2+/1.86 bpm vs 80.7+/2.3 bpm in those without complains; $p<0.05$) and tendency to reduced HF% power (23.2+/-1.9 vs 29.7+/2.7%). The similar autonomic pattern had those with decreased working capacity. Females with daytime sleepiness had normal HR but elevated LF% due to increased sympathetic tone, those with vertigo – normal HR and diminished stress-index according to R.M.Baevskiy both in sitting and standing position. The elevated response to standing demonstrated females with headaches, decreased working capacity and fatigue.

No differences were found in sitting position in the male group while in ortostasis males with weather sensitively and fatigue had diminished autonomic response.

In conclusion, there was mild sympathetic predominance and HF% decline with hyperreactivity to ortotest in medical VI-year female students having meteosensitivity displayed headaches and diminished working capacity, whereas males with fatigue due to meteofactors demonstrated diminished postural changes. Thus, HRV is a measure of autonomic nervous system activity, which reflects an individual's ability to adapt to physiological and environmental changes.

O35 10-year trends in autonomic state in young healthy adults: 2006-2015

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Changes in modern adolescents' priority (electronic devices, Internet use includes computer games, sedentary lifestyle) may negative influence on functional status of organism. Low resting heart rate variability (HRV) has been linked to several mental health conditions; including depression, anxiety, and alcohol dependence. Insufficient data exist on population-based trends in autonomic nervous system state in young healthy adults.

The aim of this study was to determine trends in HRV over 10 consecutive years in population of last (VI) year medical students examined in spring semester during 2006-2015. All 5-min. ECG-recordings in sitting position in the morning (9-11) were made by single technician in one device (NeuroSoft, Ivanovo, Russia). Widely used HRV parameters were calculated in time and frequency domains.

The total number of participants was 783 (244 males and 539 females). There was significant trend to decreasing mean RR interval duration, increasing resting heart rate in both genders and decreasing SDNN, especially in females. Total power (TP) tended to increase in males and decrease – in females. It is interesting to note, that TP increase in males has been due predominantly to VLF power augmentation while other bands have not changed.

In females TP has diminished due to decreasing in LF and HF bands. Probably, this fact may reflect the tension (cost) of adaptation to environmental and social factors providing with different physiological mechanisms operate in neuro-endocrine system in males and females.

Sympatho-vagal balance has increased both in males (2.55 in 2007, 3.16 in 2015) and females (1.89 in 2007, 2.29 in 2015). The relative power of VLF band has increased and relative power of HF – declined in both genders.

Obtained pattern has been confirmed with detailed analysis of autonomic state in students having poor academic performance. Males often demonstrated increase in relative power of VLF band >48% accompanied with moderate TP increase, while females - decline (<1200 ms2) in TP and in spectral power in all bands with exact sympathetic predominance.

Thus, in this unique temporal series of studies spanning 10 years, sympatho-vagal balance in VI-year medical students has shifted toward sympathetic predominance both in males and females. The adaptation to environmental and social factors in males and females provide by different physiological pathways.

O36 Reproducibility of 24 hour heart rate variability time-domain measures in children

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Background. Over the last decades time domain heart rate variability (HRV) analysis has been explored in a different pediatric clinical settingsto obtain information on the simpathovagal balance. However, the consistency over time of time domain HRV measures in children is not well-known.
Methods. We investigated the reproducibility of 24 hour HRV time-domain measures (1 day apart), from 33 healthy children (8.5±5,6 years, 54,5 % girls).
The parameters analyzed included: standard deviation of all the adjacent NN intervals (SDNN), standard deviation of the averages of NN intervals in all five-minute segments (SDANN), square root of the mean of the sum of the squares of the differences between adjacent NN intervals (RMSSD).
Reproducibility between two 24-hour ECG recordings was evaluated by intraclass correlation coefficients (ICCs), standard error of measurement (SEM), coefficients of variation (CVs) and Bland–Altman plots.
Results. Of analyzed time-domain parameters SDNN and RMSSD showed best reproducibility with highest ICC (0,983; 0,972), lowest CVs (5,2%, 9,92 %) and best level of agreement between two recordings as assessed by Bland-Altman plots.
Conclusions. According to our results, time domain HRV measures obtained from 24-hour ambulatory recordings are consistent and reproducible over time and hence are suitable for detecting real differences of autonomic tone in children both for classification and prediction purposes.

KEYWORDS: heart rate variability; children; reproducibility

O37 Epileptic asystole: Is it a model for sudden unexpected death in epilepsy?

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Patients with epilepsy have a mortality rate 2-3 times higher than in the general population. Approximately 8-17% of deaths in patients with epilepsy are the phenomenon of sudden unexplained death (SUDEP). SUDEP is defined as the sudden, unexpected death in patients with epilepsy, which is not due to trauma or drowning and for which posmortem tests do not indicate a structural or toxicological cause of death. The incidence of fatal complications of epilepsy is about 9 cases per year in 1000 patients with refractory epilepsy.

In lot of papers published so far different risk factors for SUDEP have been listed. All can be classified into three groups: **i**) demographic factors (male sex and the average age 28-35 yr.); **ii**) factors related to epilepsy (GTC seizures, onset at a younger age, long duration of epilepsy, high seizure frequency) and **iii**) factors related to treatment (poor compliance, a large number AE drugs, frequent changes of the medication regime).

Unfortunately, a pathophysiological mechanism underlying SUDEP is not known. The assumption is that different mechanisms, either independently or in various combinations, can lead to death in patients with epilepsy. As in 30-80% of cases of SUDEP witnesses stated that the death was preceded by an GTC seizure, it is assumed that death was caused by inducing a central mechanism that leads to cardiac bradyarrhythmias and central sleep apnea.

Ictal bradyarrhythmia and ictal asystole as its extreme manifestation, are seen in less then 0.5% of patients with focal seizuresHowever, the interest for ictal bardycardia and asystole is the result of their potential connection with SUDEP and also possibility to affect seizure semiology. Besides, important issue is whether those patients need cardiac pacemakers in order to decrease seizure severity as well as the risk of sudden death.

Key words: refractory epilepsy, sudden death, ictal asystole

O38 SUDDEN NEUROGENIC DEATH IN NEURODEGENERATIVE DISEASES

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The role of the central nervous system in the precipitation of sudden death (SD) has been recognized for a few decades. Mechanisms of sudden cerebrogenic death have been well established in stroke, epilepsy and head injury. Experimental evidence and clinical observations indicate a crucial role of central autonomic structures, especially the amygdala and insular regions in acute cardiovascular events leading to SD. However, mechanisms of SD in neurodegenerative diseases are less clear and, in addition to cardiovascular events, include central respiratory failure as well. .

The purpose of this review is to present mechanisms of neurogenic SD in patients with neurodegenerative diseases. Patients with Parkinson's disease (PD) have many non-motor symptoms including marked autonomic dysfunction. Retrospective autopsy studies have shown that a non-negligible number of patients with PD die suddenly without a clear cause. There is cardio-selective sympathetic denervation in PD due to loss of catecholaminergic neurons in basal ganglia and cardiac plexus. The uptake of I-123- MIBG in the heart of PD patients is selectively and significantly reduced early in the disease, unlike in any other neurodegenerative disease or in healty controls. This suggests cardiac sympathetic dysfynction or denervation and is associated with an increased risk of QTc interval prolongation. The leading cause of death in patients with multisystem atrophy (MSA) is SD. Depletion of sympathetic preganglionic neurons in the spinal iintermediolateral cell column and medullary catheholaminergic and serotonergic neurons is partly responsible for autonomic failure in MSA and is more pronounced in patients who succumbed to SD. Loss of serotonergic neurons could be responsible for SD in MSA patients, since medullar serotonergic neurons project to many autonomic nuclei in the medulla oblongata and spinal cord, which then influence the sympathetic outflow as well as respiratory and cardiovascular regulation**.** In addition, breathing disturbances due to loss ofNK1 neurons in the ventrolateral brainstem, including the pre-Botzinger complex could also cause SD in PD and MSA**.** Patients with amyotrophic lateral sclerosis (ALS) are also prone to SD. In our series of 55 patients, 22 (40%) died during the three-year follow-up period. Nine patients (16.36%) died suddenly. Cox regression analysis showed that pathologic stand-up test, reduced SDNN index and presence of bursts of PST were independent predictors of death. This suggests that autonomic dysfunction is implicated in SD in ALS patients.

In conclusion, SD is not rare in neurodegenerative diseases. Early recognition of risk factors for SD could help prevent this outcome and possibly increase quality of life of these patients.

O39 The presence of dysautonomia in different subgroups \ of myasthenia gravis patients

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Objectives: To analyze the presence of autonomic dysfunction in different subgroups of myasthenia gravis (MG) patients.
Methods: Standard cardiovascular reflex tests according to Ewing, spectral and time-domain analysis of heart rate variability (HRV) at rest were assessed in 27 patients with thymoma associated acetylcholine receptor (AChR) positive MG, 25 AChR positive MG patients without thymoma and 23 patients with muscle specific tyrosine kinase (MuSK) MG. All patients were compared to the healthy controls, matched for sex and age.
Results: In the group of AChR positive MG patients with thymoma, hand grip ($p<0.05$), orthostasis ($p<0.05$), breathing test ($p<0.05$) and Valsalva maneuver ($p<0.01$) were more often pathological than in the controls. Analysis of the spectral domain of HRV showed increased low frequency ($p<0.05$) and decreased high frequency component ($p<0.05$). Time domain parameters of HRV and baroreflex sensitivity (BRS) at rest were significantly reduced ($p<0.01$). In the patients with AChR MG without thymoma, Valsalva maneuver test was more often pathological ($p<0.05$) and higher rate of supraventricular extrasystoles ($p<0.01$) was registered than in the healthy controls. In the patients with MuSK positive MG, hand grip and Valsalva maneuver tests were more often pathological than in the controls ($p<0.05$). Low frequency component of the spectral domain of HRV ($p<0.05$), and the frequency of cardiac arrhythmia were increased. BRS at rest was significantly lower in patients compared to the controls ($p<0.01$).
Conclusion: We determined the presence of autonomic failure in all subgroups of MG patients. Since autonomic dysfunction can lead to cardiac arrhythmias and even sudden death, it is of major importance to be aware of this association and to properly diagnose and treat these patients.

Key words: myasthenia gravis, autonomic nervous system, thymoma, MuSK

O40 Sleep – disordered breathing as the cardiologic risk factor

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There are two major types of sleep disordered breathing (SDB): obstructive sleep apnea (OSA) and central sleep apnea (CSA) which may manifest in periodic (Cheyne-Stokes) respiratory pattern.Apnea is defined as cessation of air flow for 10 or more seconds. Hypopnea is usually understood as reduced air flow (>50%) or impairment of respiratory movements of chest and abdomen with oxygen blood saturation decreased by at least 4% and/or arousal.In order to assess the severity of SDB, apnea-hypopnea index (AHI) is calculated. Its value represents a number of apnea and hypopnea episodes during an hour of sleep. Criteria for syndrome of SBD are met when either AHI exceeds 10-15/hour or AHI is >5 but is associated with symptomes. Two other indices used for assessment of SDB severity are: RDI (respiratory disturbance index) and ODI (oxygen desaturation index).The gold standard for apnea detection and assessment is polysomnography.Apnea is often underdiagnosed because of the scarcity of polysomnography. New, available method obtains electrocardiographic estimated apnea/hypopnea index eAHI on the basis of Holter ECG monitoring. Recently, SDB and especially OSA became a subject of interest for cardiologists. It was documented that the presence of OSA is connected with the initiation or progression of several cardiovascular pathologies. Patients with OSA are more likely to have arterial hypertension, ventricular and supraventricular arrhythmias, coronary artery disease, cerebrovascular disease and heart failure. The presence of OSA may be responsible for the unfavourable changes in the clinical course of cardiovascular disease. In patients with SDB arterial hypertension is often resistant for the conventional treatment. Sudden cardiac death occurs in the presence of SDB more often during the night than in the early morning. Potential mechanisms linking OSA to cardiovascular pathologies include a number of humoral, neural, vascular, and inflammatory abnormalities.In patients with SDB physiological variability patterns of sympathetic nervous system activity dependent on sleep phases is disturbed by recurring episodes of apnea. Apneas cause hypoxia and hypercapnia and these stimulate chemoreceptors to activate sympathetic nervous system, including nerves in the walls of blood vessels. In OSA at the end of each apnea episode sympathetic activation reaches maximum level and blood pressure even in normotensive individuals may rise as high as to 250/110 mmHg. Recurrent hypoxemic stress seems to increase endothelin secretion and induces vasoconstriction. Catecholamines levels are elevated. Impairment of autonomic regulation extend to daytime, which is reflected by greater variations in blood pressure levels but diminished heart rate variability. Taking into account the knowledge about the negative consequences of OSA for cardiovascular system this phenomenon should be included to the cardiologic risk factors and should be assimilate into cardiovascular diagnostic and therapeutic paradigms.

O41 MORNING HYPERTENSION – A TARGET TO TREAT IN PATIENTS WITH SLEEP APNEA-HYPOPNEA SYNDROME

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There are two types of morning hypertension – nocturnal hypertensive morning hypertension and morning surge hypertension, both often associated with sleep apnea-hypopnea syndrome. The morning surge in blood pressure is influenced by the sympathetic nerve system. Aim was to determine which type of morning hypertension is more common in patients with sleep apnea-hypopnea syndrome.

Research included 100 patients who underwent polygraphic examination in UCC Kragujevac. According to apnea-hypopnea index (AHI) all patients were divided into 4 equal groups, 25 patients in each group (AHI <5; 5-15; 15-30 and >30). Diagnosis of hypertension was made, and diurnal and nocturnal blood pressure profile was assessed using ABPM. In addition, spectral analysis of heart rate variability was used for non-invasive testing of autonomic function. The analysis was performed using a fast Fourier transform of the autoregression method integrated into 24h ECG Holter monitoring. All datawere statisticallyanalyzed in theSPSS for Windows.

Study population consisted of 69% of male and 31% of female patients with mean age of 55.05±11.16 years. Prior hypertension was present in 76% of patients (χ^2=27.04;p=0.000) in total group, with 68% on antihypertensive therapy (χ^2=12.96;p=0.000). Non-dipping of SBP during 24h recording was present in 37% of study population (x2=16.40;p=0.007) and for DBP in 31% of patients in total group. Morning surge of blood pressure >10mmHg was present in 79% of patients (χ^2=33.64;p=0.000), with even more than 50% having rise >20mmHg. Mean morning surge was 24.25±19.37mmHg. LF/HF ratio was >2.0 in 70% of patients confirming that autonomic balance is shifted towards sympathetic activity (χ^2=12.96;p=0.000).

Non-dipping blood pressure profile was present in these patients causing the presence of nocturnal hypertensive mornig hypertension, but morning surge hypertension was more prevalent, probably due to sympathetic overactivity. Regardless of the type morning hypertension represents a major challenge in clinical practice, especially in sleep apnea-hypopnea syndrome.

O42 PREDICTORS OF ADVERSE OUTCOME IN MALES WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME AND ARTERIAL HYPERTENSION

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Background. Obstructive sleep apnea-hypopnea syndrome (OSAS) and arterial hypertension (AH) are the most common problems, especially in males. OSAS is associated with non-fatal and fatal cardiovascular events. The researchers focus on the study and designing of predictors of adverse outcome for risk stratification of patients with OSAS. Number of studies was revealed that the apnea-hypopnea index (AHI) ≥20 per hour; minimum and mean oxygen saturation (SpO_2) ≤78 % and ≤93 %, respectively; JT and QT intervals prolongation and it's dispersion (QTd) ≥60 ms on the electrocardiogram (ECG) are predictors of adverse outcome.
Keywords: obstructive sleep apnea-hypopnea syndrome, arterial hypertension in males, QT and JT intervals prolongation, QT and JT dispersion, adverse outcome.
Objectives. To determine the occurrence of predictors of adverse outcome (minimum and mean SpO_2 ≤78 % and ≤93 %, respectively; JT and QT intervals prolongation; increased QTd ≥60 ms) in males with OSAS and newly diagnosed AH. To identify the relationship between severity of OSAS and investigated predictors of adverse outcome.
Material and methods. Between September 2013 and May 2015, the study was conducted at the therapeutic and rehabilitation in-patient departments. One hundred and thirty-four males were included in the cross-sectional study according to the criteria. The mean age (mean±SD) in the population was 40.5 ± 7.0 years (from 22 to 59 years), mean body mass index (BMI) was 34.5 ± 4.7 kg/m^2 (from 24.7 to 50.5 kg/m^2). The inclusion criteria were age from 20 to 60 years, newly diagnosed AH (office blood pressure or BP ≥140 and/or 90 mm Hg) at the annual physical exam, complaints on snoring and daytime sleepiness. The exclusion criteria were diagnosed cardiovascular and lung diseases in history, atrial fibrillation and bundle branch block, abnormality of thyroid function, diabetes mellitus and use of antiarrhythmic agents and antibiotics. After routine physical and biochemical investigations, all subjects underwent a 24-hour multifunctional monitoring ('Kardiotekhnika 07', Incart, St. Petersburg, Russia). This monitoring includes simultaneous registration of 12-lead ECG, 2-lead rheopneumogram and actogram (with ECG electrodes), BP measurement (Korotkoff's acoustic tones and oscillometric method), in addition, oximetry by portable pulse oximeter and oronasal airflow by cannula during sleep ($S_3C_1O_1P_2E_4R_2$).
ECG data were examined during 'sleep-wakefulness' cycle. The 'sleep-wakefulness' cycle was individual to each patient. Periods of wakefulness (activity) and sleep (bedtime) were allocated on the recording with allowance to the heart rate, the breathing pattern on the rheopneumogram and activity on the actogram. QT and JT intervals duration were analyzed automatically to the 8-lead ECG (II, III, V_1-V_6). Corrected QT and JT intervals (QTc and JTc, respectively) were calculated automatically using Bazett's formula. QTc interval prolongation was considered as ≥450 ms. QT and JT dispersion (JTd) were defined as the difference between the maximum and minimum values of the QT and JT intervals, respectively. Increased QTd was considered as ≥60 ms.
Apnea and hypopnea were defined as a reduction in of oronasal airflow and respiratory effort amplitude of ≥90 % and ≥50 % for 10 seconds, respectively. AHI was calculated automatically as the total number of apneas plus hypopneas per hour of sleep. Oxygen desaturation was defined as a reduction in oxygen saturation of at least 3.5 % for 10 seconds of sleep. Hypoxemia index (HI) was calculated automatically as the total number of desaturation episodes per hour of sleep.
Twenty-four-hour BP monitoring was measured every 15 minutes during the daytime (7:00 a.m. to 11:00 p.m.) and every 30 minutes during the nighttime (11:00 p.m. to 7:00 a.m.) using the cuff of appropriate size on the left arm. The normal daytime and nighttime BP was considered to be <135/85 and <120/70 mm Hg, respectively.
Statistical analysis data were performed using Statgraphics Plus 5.0. Variables with normal and abnormal of the distribution were expressed as mean ± SD and as median; lower quartile – upper quartile, respectively. The intergroup differences were evaluated by a Mann-Whitney W test and for the percentage by Z test. The relationship between the studied parameters was assessed by a Pearson correlation coefficient. A value of $p<0.05$ was considered a statistically significant.

Results. According to data of 24-hour multifunctional monitoring, 134 males were divided, 34 to the non-OSAS group (AHI <5 per hour) and 100 to the OSAS group (AHI ≥5 per hour). The intergroup differences in age and duration of the 'sleep-wakefulness' cycle were absent. However, patients in the OSAS group had greater BMI compared to the non-OSAS group (35.0 ± 4.8 vs. 33.1 ± 4.3 kg/m^2, p<0.05).

In the OSAS group AHI ≥20 per hour of sleep was observed in 45 (45 %) patients (AHI from 21 to 97 per hour). Patients with minimum and mean SpO_2 ≤78 % and ≤93 %, respectively, were greater in the OSAS group than in the non-OSAS group (35 vs. 3 % and 73 vs. 44 %, respectively). There were differences between the OSAS and the non-OSAS groups in minimum SpO_2 (78.9 ± 9.4 vs. 86.7 ± 4.5 %), mean SpO_2 (91.7 ± 2.8 vs. 93.4 ± 1.4 %) and HI (16.5; 6.0-42.0 vs. 1.0; 0-9.0 per hour), p<0.05 in all cases.

During 24-hour ECG monitoring sinus rhythm was registered in all patients. Average values of heart rate were significantly greater in the OSAS group than in the non-OSAS group during the 'sleep-wakefulness' cycle (79.8 ± 9.3 vs. 75.3 ± 9.6 per minute), the wakefulness (86.8 ± 9.7 vs. 81.9 ± 10.9 per minute) and the sleep (67.9 ± 8.2 vs. 62.9 ± 9.1 per minute), p<0.05 in all cases. There were no differences in the percentage of QTc prolongation in patients in the OSAS group than in the non-OSAS group (44 vs. 38 %). However, the average values of QTc and JTc were significantly greater in the OSAS group compared to the non-OSAS group during the 'sleep-wakefulness' cycle (417.4 ± 22.8 vs. 409.9 ± 17.4 ms and 312.6 ± 7.3 vs. 300.8 ± 19.8 ms), the daytime (419.1 ± 20.2 vs. 410.7±17.2 ms and 311.3 ± 17.1 vs. 300.1 ± 20.8 ms) and the nighttime (417.8 ± 21.1 vs. 409.3 ± 18.3 ms and 313.9 ± 17.9 vs. 305.0 ± 14.8 ms), p<0.05 in all cases. The differences in the percentage of maximum values of the increased QTd during the 'sleep-wakefulness' cycle were absent between the OSAS and the non-OSAS groups (39 vs. 35 %). Also there were no differences of maximum values of QTd and JTd between the OSAS group and the non-OSAS group during the 'sleep-wakefulness' cycle (52.3; 30.0-67.0 vs. 52.5; 38.0-71.0 ms and 53.0; 32.5-67.0 vs. 52.5; 39.0-66.0 ms), the daytime (42.5; 24.5-61.0 vs. 40.0; 30.0-53.0 ms and 45.0; 27.0-61.0 vs. 41.0; 31.0-52.0 ms) and the nighttime (47.0; 27.0-64.5 vs. 49.5; 37.0-63.0 ms and 49.5; 28.5-64.5 vs. 50.0; 37.0-62.0 ms).

According to data of 24-hour BP monitoring, differences of the average values of systolic BP between the OSAS and the non-OSAS groups were not installed both diurnal (142.7 ± 15.9 vs. 137.7 ± 10.3 mm Hg) and nocturnal (128.8 ± 18.9 vs. 122.7 ± 12.6 mm Hg). While, differences of the average values of diastolic BP were observed both diurnal (85.4 ± 10.6 vs. 81.1 ± 7.1 mm Hg) and nocturnal (73.4 ± 11.6 vs. 65.9 ± 9.2 mm Hg), p<0.05 in all cases.

Statistically significant positive linear correlation was revealed between the QTc and JTc intervals with AHI (wakefulness r = 0.32; r = 0.27; sleep r = 0.29; r = 0.22, respectively) and HI (wakefulness r = 0.30; r = 0.24; sleep r = 0.30; r = 0.20). Statistically significant negative linear correlation was revealed between the QTc and JTc intervals with mean SpO_2 during the wakefulness (r = –0.23; r = –0.25) and the sleep (r = –0.31; r = –0.23). Statistically significant positive linear correlation was revealed between the systolic and diastolic BP with AHI (wakefulness r = 0.22; r = 0.21; sleep r = 0.39; r = 0.41) and HI (wakefulness r =0.16; r = 0.19; sleep r = 0.33; r = 0.39), p<0.05 in all cases.

Conclusions. In males with OSAS and AH (n=100) high occurrence of AHI ≥20 per hour (45 %), minimum and mean SpO_2 ≤78 % and ≤93 % (35 and 73 %, respectively) as predictors of adverse outcome were revealed. Incidence of the increased QTd ≥60 ms was 39 %, however, was not differed from patients without OSAS. It is established that AHI, HI increase and SpO_2 decrease during sleep leads to raising of systolic and diastolic BP, myocardial repolarization delay in males with OSAS and AH.

O43 THE ESTIMATED APNEA HYPOPNEA INDEX DERIVED FROM HOLTER ECG ACCURATELY SHOWS THE ASSOCIATION WITH FREQUENT PVCs

-A case report-

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More than 10 cardiac deaths per 100,000 inhabitans annualy in the United States are associated with obstructive sleep apnea (OSA). There is still not enough data about the association of OSA and arrhytmias of ventricular origin. We present a patient, male, 34 years old, single, admitted to cardiology unit in November 2014 because of suspected sick sinus syndrome and frequent PVCs previously observed. During the last 5 years he gained in weight 30 kg, his BMI raised from 24.2 to 33.9, neck circumference was 48 cm and neck height 7 cm. Malampati score was IV. A year ago he started to snore intensely. Several months later his mother noticed frequent episodes of apnea during the night and tiredness and sleepiness during the day. 24h ECG Holter monitoring showed very frequent PVCs and estimated apnea hypopnea index was (AHI) 54. On polysomnography (PSG) AHI was 60.1, mean saturation index 89%, with minimum oxygen saturation of 74%. Blood glucose in morning 4.3 mmol/l. HbA1c 6.1 %, insulinemia 30.0 mIU/L; HOMA-IR 5.7 and HOMA-B 750. Metoprolol 50mg daily was introduced and some reduction of the number of extrasystoles seen, but only during the active period of the day. Patient didn't accept continuous positive airway pressure (CPAP) therapy. He stopped heavy smoking (40 cigarettes per day) and continued prescribed therapy. From March 2015 patient started to sleep without unplesant arousals. Control 24h Holter ECG in August 2015 showed only few (40/24h) PVCs and estimated AHI of 35.3. Body weight was unchanged. We conclude that Estimated AHI is a good parameter for both indicating PSG investigation and also the effect of therapy. In our patient there is still the place for introducing CPAP therapy, as well as insulin sensitising therapy (e.g. Metformin). All these therapies should aim to further reduce sympathetic hyperactivity.

O44 The relationship between severity of the obstructive sleep apnea and subclinical left ventricular systolic and diastolic dysfunctions in newly diagnosed patients with obstructive sleep apnea

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Background: The aim of the study was to evaluate the impact of the severity of obstructive sleep apnea (OSA)on subclinical left ventricular (LV) systolic and diastolic dysfunction in newly diagnosed obstructive sleep apnoea (OSA) and normal left ventricle ejection fraction.

Methods: According to the study eligible criteria 160 consecutive patients among overall number of 792 patients were prospectively enrolled in the study.Control group consisted of 78 asymptomatic age-matched healthy subjects who did not have any cardiovascular and respiratory symptoms. All patients had undergone overnight polysomnography and complete standard transthoracic and advanced tissue imaging echocardiogram have been also performed next morning. Statisctical adjustment according to hzpertensio and BMI were successfully done in order to evaluate impact of disease severity. According to the AHI all patinets were devided into teo groups: Group I - mild OSA and group II - moderate to severe OSA.

Results: Even 81 (51%) of the newly diagnosed OSA had severe stage of the disease. The E/A ratio and the peak E wave at mitral flow were significantly lower and the peak A wave at mitral flow was significantly higher in OSA patients in Group II compared with OSA patients from the Group I. Left ventricle isovolumetric relaxation time (IVRT) and mitral valve flow propagation (MVFP) were significantly longer in OSA patients from group II than in patients from Group I. Significant difference in S' amplitude of septal part of the mitral valve and E' wave both at the lateral and septal part of the mitral valve were noted in OSA patients from Group II compared to OSA patients from Group I.

Conclusion: Patients with mild stage of OSA have better parameters of the subclinical left ventricular dysfunction. OSA stage has a direct impact on the subclinical left ventricular systolic and diastolic dysfunction

O45 CEVAS - A role of Centre of Excellence in cardiovascular data analysis

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Background: Oscillations are the functional core of living creatures. If a living organism can be regarded as a network of sensors and actuators with a brain regarded as a CPU, it could be concluded that all the data - all information necessary for functioning - are transmitted using frequency modulated signals – i.e. using time varying oscillations. CEVAS is approved by the National Council for Scientific and Technological Development as the 7th Center of Excellence in Serbia, and the 2nd at University of Novi Sad. Its acronym means "Centre of Excellence for Vibro-Acoustic systems and biomedical Signal processing". Activities of CEVAS are predominantly devoted to the scientific research, organized within the three related fields: non-linear dynamics and oscillations, acoustics and speech technologies, and biomedical signal processing. The nexus between the three fields are signals and phenomena related with oscillatory movements, their generation, modelling, analysis, control and application. The theoretical expertise of the first field, coupled with the practical knowledge of the third field, can contribute a lot to the better understanding of the non-linear occurrences within the cardiovascular and related signals.

Objectives:CEVAS has proposed multiple aims: to maintain a high-quality scientific research; to improve international visibility of the Centre and its results and increase already existing international cooperation; to augment the interdisciplinary synergy at local and international level and jointly take part in multiple events. We are proud to announce that our fundamental and technical projects funded by Serbian Ministry were among the best within their respective fields. To be precise, the projects OI174028 **"**Multiscale methods and their applications in biomedicine**"** and TR32040 "Multivariable methods for analytical support to biomedical diagnostics" were ranked the second best in theoretical mechanics group, and the best in the electrical/computer engineering group.

Methods: CEVAS has organized seasonal seminars accompanied by Vivaldi's "Four Seasons". At each seminar an invited lecturer gives a presentation on relevant achievements. The inaugural presentation for CEVAS, when it got the papers of approval from the National Council, was on a mathematical concept of Copula that, quite conveniently, explains the synergy on two or more time series. This introductory talk at Neurocard about CEVAS, the new Center of excellence that devotes a great part of its research efforts to the non-linear dynamic processes within the living organisms, will be illustrated by a talk on copulas.

Results and conclusion: The concept of copula was tested using the two time series taken from the arterial blood pressure waveforms of healthy Wistar rats at baseline conditions, obtained by the courtesy of prof dr Nina Japundzic-Zigon and her team. The parallel time series analyzed by copulas were systolic blood pressure (SBP) and pulse interval (PI). The results reveal statistical dependence and independence where other mathematical methods show ambiguity.

O46 A cross-approximate entropy of independent signals with known distribution and its application to real data

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Background: Approximate entropy (*ApEn*) is one of the most exploited nonlinear techniques to quantify the complexity of a time series. Applications range from seismological and financial data to biomedical signals recorded from animals and human beings. The introductory *ApEn* contributions have already reached more than 4000 citations and its annual 1991-2012 quotation rate earned a graphical presentation in a scientific paper.

The role of *ApEn* as a supporting tool for biomedical data analysis has been approved by numerous pre-clinical and clinical studies. But in spite of vast and firmly established implementation, the activities on *ApEn* improvement have never ceased. The research efforts are split into the two lines. The first one is devoted to the variations of entropy estimation tools, like *SampEn*, *CApEn*, *FuzzyEn*, *MultiScaleEn*, *ApEn* based on wave mode, and also to the algorithms for speeding up he estimation process. The other research line is dedicated to the problem of parameter choice that influence the value of *ApEn* estimates and may induce biased and inconsistent results.

One of the very first variations of *ApEn* is *Cross-ApEn* (*XApEn*) that evaluates mutual complexity of two parallel signals. In view of successof *ApEn* as a toolapplied to the solitary time series, *XApEn* should have become an equivalent tool for measuring the synchronism of related physiological processes. However, *XApEn* has never reached the reputation and deployment of its predecessor.
Objectives:The aim of this paper is to introduce a method for improving the cross-entropy estimates based on analysis statistically independent random data with known distributions, and to test its application realistic environment, using the signals recorded both from healthy volunteers and from the laboratory animals.
Methods*:* The analysis is performed using artificial data with known probability density functions. Such data enable an exact evaluation of control parameters and test the *XApEn* procedure in a way that would be impossible with data recorded from subjects. The proposed guidelines are then checked using the data recorded from healthy volunteers (short time series) and male Wistar rats at baseline conditions (long time series).
Results and conclusion: This investigation resulted in a series of guidelines for parameter selection that ensure increased reliability for *XApEn* estimation. In particular, the formulae for thresholds r_{MAX} for which the *XApEn* reaches it maximal value are obtained for a range of template lengths m. Based on this results, the recommendation for threshold value r_{CON} that yields the consistent results is given.

O47 Application of artificial intelligence and heart rate variability spectrum in classification of sympatho-vagal dis/balance

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Abstract: In this research article automatic classification of increased, equlibrium or decreased status of sympathetic and parasympathetic autonomic nervous system (ANS) in regulation of heart rate is presented.

Introduction. In clinical observation analysis of cardiac autonomic function parameters are showing that there is relationships between regulation mechanisms of ANS and symptoms of diseases [1][2][3]. Increased/decreased predominance of sympathicus or parasympathicus is affecting health condition. In further, that information is helpful for prescription of adequate therapy [4][5][6]. It is stated that low frequency band LF_RRI and high frequency band HL_RRI of heart rate variability (HRV) spectrum in normalized units are generated from sympathicus and parasympathicus [7]. Ratio LF_RRI/HF_RRI can be used as one of the indicators of simpatho-vagal balance. Mean values of these parameters may be taken for determination of sympathicus/parasympaticus predominance by comparing parameters with their normal values given by [8]. This can be done manual, but it would be useful to make simple algorithm for automatic classification of simpato-vagal predominance. For that purpose artificial neural networks are one of the best solutions.

Method. Experiment of classification of simpatho-vagal dis/balance was conducted by means of different architectures of multilayer perceptron (MLP, a kind of artificial neural network). MLPs were created in Neuroph studio software [9] and thereafter they were trained and tested with numerical values of HRV spectrum parameters from 195 subjects divided in 4 diagnostic groups (hypertension, infarct, syncope with orthostatic hypotension and healthy subjects as a control group). This data were retaked from archive of Neurocardiological laboratory of KBC Bežanijska Kosa and all parameters of 195 subject were recorded in resting on Task Force Monitor (Cnsystems, Graz, Austria). We made 3 kind of classifiers by means of which 3 sorts of classification were carried out. The first classifier had 3 inputs (LF_RRI, HF_RRI, LF_RRI/HF_RRI) and 3 outputs (the simpathetic predominance, the parasympathetic predominance and the equlibrium state). The second classifier had 2 inputs (LF_RRI and PSD_RRI) and 4 outputs (the sympathetic predominance with high/low PSD_RRI, the parasympathetic predominance with high/low PSD_RRI). The third classifier had 2 imputs (LF_RRI and PSD_RRI) and 9 outputs (the simpathetic predominance with low/normal/high PSD_RRI, the equlibrium state with low/normal/high PSD_RRI and parasympathetic predominance with low/normal/high PSD_RRI). For each kind of classifier several configuration of MLPs were tested. The most important features for good classification results was number of neurons in hidden layer/s and amount of data for training; after that, parameters of training process (maximum mistake of network and learning rate) were significant. In first classification 40 % of data were used for training of MLPs and the rest 60 % were used for testing. In other two classification 60 % were used for traing and the rest 40 % were used for testing.

Results. In first classification enough optimal performance had MLP with 3 neurons in hidden layer. After training network had testing results accuracy of 100 %. In second classification from all classifiers, MLP with two hidden layers and 6 neurons in each hidden layer had satisfactory performances: after 1060 training process iterations network gave test accuracy of 96.15 %. In third classification MLP with 12 neurons in hidden layer acomplished optimal

results: traing process included 4 770 iterations and after testing network gave accuracy of 96.15 %. After this, statistical analize was performed. It is worth to mention that there was significantly more simpathetic predominance in group with hipertension and infarction comparing to control group; in other hand, parasimpatethic predominance was more present in group with syncope + OH then in control group.

Conclusion. The analisys and implementation of ANS predominance is still in the begining phase of research. Stastical comparations of ANS predominance in this research showed that it may have clinical significance. If further research give detailed confirmation of that, especially in field of therapy of deseases, fast and automaic classification will be very important. Artificial neural networks created in Neuroph studio software may be used as simple and efective solution with possibility of easy adjusting classification algorithm for any specific clinical trial and practical use. Also, if future research find precise functional relationship between atributes of diseases and dynamics of ANS predominance this way of classification would be suitable for automatic diagnosis. When these two aspects are combined in one unit it will be possible to develop an expert system which makes diagnostic based on state of ANS and basic symptoms, and gives recommendation of therapy in agreement with desired ANS responce.

References

[1] Mutavdzin S, Milovanović B, Filipović B, Zdravković M, Gligorijević T, Paunović J, Arsić M. Assestment of autonomic function with gastroesophageal reflux disease, The Book of Abstracts: The Sixth International Symposium on Neurocardiology, Neurocard 2014,Belgrade, 2014; 020: 54.

[2] Gligorijević T, Milovanović B, Mutavadzin S, Hajder J, Marković O, Filipović B, et al. Evaluation of cardiovascular autonomic dysfunction in patients with lymphoproliferative disease, The Book of Abstracts: The Sixth International Symposium on Neurocardiology, Neurocard 2014,Belgrade, 2014; 021: 55.

[3] Peković-Peruničić G, Rašić-Milutinović Z, Milovanović B, Penčić B, Bajić D. The role of heart rate variability parameters in chronic kidney disease, The Book of Abstracts: The Fifth International Symposium on Neurocardiology, Neurocard 2013, Belgrade, 2013;059: 113.

[4] Milovanović B, Radivojević V, Mutavadžin S, Simić M, Milićević N, Milovanović A. Genetic determination of cardiac autonomic function and individualized approach in treatment of hypertension, The Book of Abstracts : The Fourth International Symposium on Neurocardiology, Neurocard 2012, Belgrade, 2012; 07: 36.

[5] Milovanović B, Hadžić B, Jodanov D, Gligorijević T, Mutavadžin S, Romčević N, Rosić M.The Programmed Placebo Effect and modulation of autonomic activity in treatment of syncope: new challenge using nano-technology, The Book of Abstracts: The Sixth International Symposium on Neurocardiology, Neurocard 2014, Belgrade, 2014; 029:63.

[6] Bersenev Eyu, Selionov VA, Solopova IA. Continous monitoring of heart rate variability for neurorehabilitation of poststroke patients, The Book of Abstracts: The Fifth International Symposium on Neurocardiology, Neurocard 2013, Belgrade, 2013; 028: 67.

[7] Guidelines, Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of The European Society of Cardiology and The North American., Society of Pacing and Electrophysiology (Membership of the Task Force listed in the Appendix), European Heart Journal, 1996; 17: 354–381.

[8] Schwalm T., Modern tilt table testing and non-invasive monitoring, ABW Wissenschaftsverlag GmbH, Frankfurt, 2006;

[9] http://neuroph.sourceforge.net/;

O48 FastICA for extraction of fetal ECG

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Objective: The aim of this study was to extract fetal electrocardiogram (fECG) from a composite cECG of a mother recorded by surface electrodes using fast fixed point independent component analysis (fastICA).

Materials and methods: FastICA was applied on two Physionet data sets (1,2) with cECG. In the first data set, signals were acquired with two surface ECG leads positioned on thorax and three surface leads placed on abdomen from one woman in labor. The second data set contained recordings from 5 women in labor. Each of these recordings consisted of 4 signals acquired by surface ECG from abdomen and one signal recorded directly from the fetal head. For the analysis only signals from thorax and abdominal leads were used. FastICA (1) was performed with 2, 3, and 5 independent components (ICs) for the first data set. For the second data set, algorithm was performed with 2, 3, and 4 ICs, as the output variables. For the algorithm evaluation, heart rate (HR) of the ICs was calculated using Pan-Thompkins method (3) and compared to a maternal HR from thorax or the HR registered on a fetal head for the first and second data set, respectively.

Results: fECG was successfully extracted from the first data set only for case when two abdominal channels were used as inputs to the fastICA. From the second data set, fetal ECG was detected twice with 4 independent components, while three times with 3 independent components. Fetal ECG was not extracted when using 2 independent components for both data sets.

Conclusion: At least three ICs were needed for successful application of fastICA. This might be due to low signal to noise ratio for recording fetal ECG with surface electrodes. Our results suggest that higher number of abdominal ECG channels is required for successful fetal ECG extraction when implementing fastICA.

References:

1. http://www.masys.url.tw/AU/2015SP/BMSD-D/HW/HWfinal-Maternal_Fetal_ECG/ProjectDescription.htm, July 2015.

2. http://physionet.org/physiobank/database/adfecgdb/, July 2015.

3. Pan J. and Tompkins J. W., A real-time QRS detection algorithm, IEEE transactions on biomedical engineering, vol. BME-32, No. 3, March 1985

O49 Cardioprotection Against Myocardial Ischemia-Reperfusion Injury: Effect Of Selenium And N-Acetylcysteine

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Background: Myocardial ischemia–reperfusion injury represents a clinically relevant problem associated with thrombolysis, angioplasty and coronary bypass surgery. Injury of myocardium due to ischemia–reperfusion includes cardiac contractile dysfunction, arrhythmias as well as irreversible myocytes damage. These changes are considered to be the consequence oxidative stress, inflammation and apoptosis in the heart .

Objective: This study was undertaken to investigate the potential role of Selenium and N-acetylcysteinein amelioration of myocardial I/R injury induced by ligation of coronary artery in a rat model .

Material & method: A total of 36 adult male Sprague Dawely rats were randomized into 6 equal groups. Group (1) sham group: rat underwent the same anesthetic and surgical procedure as the control group except ligation of LAD coronary artery; Group (2) control group: rat subjected to regional ischemia for 30 minutes by ligation of LAD coronary artery and reperfusion for 2 hours; Group (3) control vehicle group: rat received normal saline as vehicle for the study agents orally and subjected to regional ischemia for 30 min by ligation of LAD coronary artery and reperfusion for 2 hours; Group (4) Selenium treated group: rat pretreated with oral Selenium 2 mg/kg every day for 5 days before and up to surgery (ligation of LAD coronary artery); Group (5) N-acetylcysteine treated group: rat pretreated with oral N-acetylcysteine (NAC) 500 mg/kg every day for 5 days before and up to surgery (ligation of LAD coronary artery); and Group (6) Low dose combination treated group: rat pretreated with Selenium (1mg/kg) and N-acetylcysteine 250 mg/kg every day for 5 days before and up to surgery (ligation of LAD coronary artery). At the end of experiment, TNF-α, IL-1β, IL-6, caspase-3, Bcl-2 were measured in the cardiac tissue. Plasma level of cardiac troponin I and histological changes were also assessed.

Results: Compared with the sham group, levels of (TNF-α, IL-1β, IL-6), caspase-3 and plasma level of cardiac troponin I increased in control group ($p<0.001$) while level of Bcl-2 decreased in control group ($p<0.001$). Histologically, all ratsin control group showed significant ($p<0.001$) cardiac injury. Selenium, N-acetylcysteine and low dose combinationsignificantly counteract the increase in myocardium levels of (TNF-α, IL-1β, IL-6), plasma cTnI & apoptosis by decreasing myocardial level of caspase-3 ($P<0.001$) and increasing myocardium level of Bcl-2 ($P<0.001$). Histological analysis revealed that Selenium, N-acetylcysteine and their low dose combination markedly reduced ($P < 0.001$) the severity of cardiac injury in the rat underwent LAD ligation procedure .

Conclusions: Results of the present study reveal that Selenium and N-acetylcysteine ameliorated myocardial I/R injury in rat via interfering with inflammatory reactions & apoptosis induced by I/R injury.

POSTER PRESENTATIONS

P1 ECG IN RAT WITH EXPERIMENTAL PULMONARY HYPERTENSION

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Pulmonary arterial hypertension leads to increased pulmonary vascular resistance and an increase in right ventricular afterload.Progressive increase of the pressure in the pulmonary artery leads to right ventricular hypertrophy and heart failure. The aim of this work was to analyze the change of electrocardiographic characteristics in rats with experimental pulmonary hypertension.

The experiments were carried out in female Wistar rats (n=17). Pulmonary hypertension was caused by a single subcutaneous injection of monocrotaline (60 mg/kg body wt). Before and four weeks after the injection of the drugECGs were recorded with an orthogonal three-lead system.The ECG in lead II was analyzed. Values given are means ± standard deviation.Validity was defined by the Wilcoxon criterion for two dependent samples.

It is shown that the thickness of the right ventricular wall significantly increased in monocrotaline treated rats. The maximal thickening was observed in the area of the pulmonary cone. In the monocrotaline treated rats, a decrease in the heart rate was showed.QRS_{II} duration, PQ_{II} and QT_{II}-intervals were prolonged. The amplitude of $P_{II,}$ $R_{II,}$ S_{II} and T peaks was significantly increased (tab.).

The development of pulmonary hypertension is marked by ECG changes associated with structural changes in the right ventricle.

Animals	PQ_{II} Time (s)	QRS_{II} Time (s)	QT_{II} Interval (s)	Amplitude P (mV)	Amplitude R (mV)	Amplitude S (mV)	Amplitude T (mV)	Heart rate (beats/min)
Control	0.044±0.002	0.019±0.013	0.068±0.015	0.099±0.106	0.705±0.022	-0.291±0.017	0.155±0.115	450±27
MCT-treated	0.052±0.008 *	0.022±0.002*	0.086±0.017*	0.139±0.047*	0.897±0.017*	-0.418±0.014*	0.244±0.064*	340±32*

Table. ECG parameters recorded from control and MCT-treated rats

* significantly different from control at $p \leq 0.05$.

The work is supported by the grant of RFBR ***№15-04-07580.***

P2 AMPLITUDE –TEMPORAL PARAMETERS OF THE CARDIOELECTRIC FIELD IN RAT WITH EXPERIMENTAL PULMONARY HYPERTENSION

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The aim of this work was to analyze the change of amplitude-temporal characteristics of body surface potential maps in rats with experimental pulmonary hypertension during ventricular depolarization and repolarization. The experiments were carried out in female Wistar rats. Pulmonary hypertension was caused by a single subcutaneous injection of monocrotaline (60 mg/kg body wt). Before and four weeks after an injection of the drug cardioelectrical potentials were recorded from 64 subcutaneous needle electrodes uniformly distributed around the animal chest. Values given are means ± standard deviation. In monocrotaline treated rats during depolarizationthe maximum amplitude of positive and negative extrema of cardiopotentials significantly increases, the positive extremum makes 1.39±0.37mV, the negative extremum - (-0.87±0.41mV) in comparison with a control group (1.05±0.38mV; -0.61±0.19mV), respectively. The time of achievement of positive and negative extrema of their maximum values doesn't significantly differ. In hypertensive rats, the positive extremum reaches its maximum value on 0.32±0.73 ms that corresponds to the moment of the *R*–peak in the ECG, the negative extremum – on the 4.57±0.62 ms after the *R*–peak, in the initial state - (0.57±0.40 ms; 4.11± 0.79 ms), respectively.In rats with experimentally induced pulmonary hypertension during the ventricular repolarization, the maximum amplitude of positive and negative extrema of cardiopotentials significantly increases, the positive extremum makes 0,37±0,07 mV, the negative extremum – (-0,25±0,08mV) in comparison with a control group (0,27±0,06 mV; -0,18±0,05mV), respectively.

Right ventricular hypertrophy of the heart in monocrotaline-induced rat models of pulmonary arterial hypertension results in changes of temporal and amplitude characteristics of the body surface cardioelectric potential distribution during ventricular depolarization and repolarization.

The work is supported by the grant RFBR №15-04-07580.

P3 Daily treadmill running maintains the synthesis of catecholamines on the basal leveland decreases oxidative stress in the right and left heart auricles of chronically stressed rats

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Chronic social isolation is a **psychosocialstress** which has effects on sympathoneural system and is associated with development of many disorders including cardiovascular diseases. It is known that exercise training acts as an important modulator of sympathoneural system.

This study examined the effects of daily exercise on gene expression of tyrosine hydroxylase (TH), dopamine-β-hydroxylase (DBH) and phenyl ethanolamine N-methyltransferase (PNMT), as well as on activity of monoamine oxidase (MAO A and MAO B) in both heart auricles of chronically psychosocially stressed rats. We also investigated gene expression of vesicular monoamine transporter 2 (VMAT2) in stellate ganglia, as well as the concentration of malondialdehyde (MDA) and activity of the antioxidant enzymes catalase (CAT) and glutathione peroxidase (GPx) in both *heart* auricles. We used model of chronic combined social isolation and treadmill running (CSITR). CSITR treatment was achieved by exposing the individually housed rats to the daily treadmill running for a period of 12 weeks.

Exposure of chronically stresed rats to daily exercise maintains protein levels of TH and DBH in basal level, which probably confirms absence of de novo noradrenaline synthesis in both auricles.CSITR increased protein levels of PNMT in the left heart auricle, which confirms conversion of noradrenaline to adrenaline. The increased activities of MAO A and MAO B in the left auricle probably indicate adrenaline degradation. The decreased gene expression of VMAT2 in the right and left stellate ganglia probably confirms absence of impact of sympathoneural system. Decreased concentrations of MDA in the left auricle, and unchanged concentrations of MDA in the right auricle, are followed by decreasedactivity of CAT and GPx in the left auricle, as well as by unchanged activity of CAT and GPx in the right auricle.

Daily exercise decreases impact of sympathoneural system on both auricles, maintains the synthesis of catecholamines on the basal level and decreases oxidative stress level in the heart auriclesof chronically stressed rats.

P4 Electrocardiography examination in 456 healthy medical students: influence of gender and ethnicity

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There is some evidence that ethnicity may play a role in the distribution of certain electrocardiographic patterns leading to life-threatening events.
The aim of the study was to investigate the prevalence of ECG features among healthy young adults.
12-lead ECG was recorded in 456 medical students of Tula State University aged 23-26 years during spring 2010-2015. Study population included 285 females (44 – foreign born) and 171 male (69 – foreign born). The vast majority of foreign students came from Central Asia (Tajikistan, Turkmenistan), Palestine, Sri Lanka, Central Africa and Ecuador. All ECG were reported by a single doctor.
The mean heart rate (HR) did not differ in the male's group and was 74.9+/-1.1 bpm in Russian males (RM) and 74.3+/-1.4 bpm in foreign males (FM), but HR in foreign females (FF) was lesser (72.8+/-1.8 bpm) than in Russian females (RF) - 75.9+/-0.7 bpm ($p<0.05$).
HR>80 bpm had 13.7+/3.4% of RM, 18.8+/-4.7% of FM, 15.8+/2.4% of RF and 6.8+/-3.8% of FF ($p<0.05$). Bradycardia <60 bpm was seen in 6.6+/-1.6% of RF, 13.6+/-5.2% of FF, 9.8+/-3.0 of RM and 7.2+/-3.1% of FM.
T-wave abnormalities (flat T-wave in AVF) were detected in 6.6+/-1.6% of RF, 9.1+/-4.4% of FF, 2.9+/-1.7% of RM and in 5.8+/2.8% of FM. No students demonstrated deep T-wave inversion suspected for hypertrophic cardiomyopathy.
Early repolarization pattern (ERP) was obtained in 6.6+/-1.6% of RF, 9.1+/-4.4% of FF, 6.9+/2.5% of RM and more often (18.8+/-4.7%) in FM ($p<0.05$). This fact support previous findings that ERP is more often detected in black individuals engaged in sport activity.
Incomplete RBBB (normal finding) was found in 19.1% of RF, 13.6% of FF, 22.5% of RM and 20.3% of FM.
Right atrial voltage enlargement that may reflect transient right ventricular diastolic dysfunctionin stress situation was obtained in 17.8% of RF, 11.4% of FF, 14.7% of RM and 13.0% of FM. Isolated QRS criteria for left ventricular hypertrophy were seen only in FF (2.3%) and RM (2.9%). CLC pattern was detected only in female groups (0.4% in RF and 2.3% in FF). 2 students (0.4%) had WPW pattern, 3 (0.66%) – Brugada-like pattern (includes 2 foreign students, 1.8% among foreign born).
Premature supraventricular and ventricular beats were seen rarely (0.4 and 0.8% in RF, 2.3 and 2.3% in FF, in 2.9 and 1.7%. in RM) and were lacking in FM. First degree AV-block had 1.7% of RF, 6.8% of FF; 2.9% of RM and 2.9% FM.
In conclusion, short ECG recordings revealed some features in regarding gender and ethnicity in healthy young adults: foreign born females had lower HR that Russian ones, whereas foreign born males more often – early repolarization pattern and tendency to Brugada-like pattern. No differences between Russian males and females were found. The data collection will be continued.

P5 Correlations between sleep quality and blood pressure, heart rate and heart rate variability in young men with natural history of arterial hypertension.

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OBJECTIVE: Sleep-disordered breathing (SDB) leading to complains on insomnia and daytime sleepiness is common in patients (pts) with arterial hypertension (AH). Nevertheless little is known about sleep habits in young men with mild essential AH.
We aimed to investigate the association between subjective sleep quality, daytime sleepiness, blood pressure (BP) dynamics, heart rate variability (HRV) and thoracoabdominal excursion irregularity in young men with mild AH.

METHODS: 24-h outpatient polyfunctional Holter monitoring was provided in 167 untreated young men(mean age – 19.3+/-0.2 yrs, body mass index (BMI) 26.5+/-0.4 kg/m2) during 2012-2015. Self-reported questionnaire to examine sleep quality and smoking status was completed in the same time.

RESULTS: Mean systolic blood pressure (SBP) was 142.0 mm Hg at day and 123.5 mm Hg at night; mean diastolic blood pressure (DBP) - 72.6 and 58.8 mm Hg, respectively; Nighttime decline was -12.6% for SBP and -19.1% for DBP. Mean apnea-hypopnea index (AHI) was 7.4 episodes/hour.
Questionnaire results showed that "good" sleep had 45.5% of young men, "satisfactory" - 50.3% and "poor" - 4.2%. Association of sleep quality and BMI was not found.
Young men reported "good" sleep had lower heart rate during day-time (83.3 bpm) than those with "satisfactory" (90.4 bpm, $p<0.01$) and "poor" sleep (93.6 bpm, $p <0.001$). Only DBP but not SBP has any differences between groups: DBP was lower at the day (70.6 mmHg) in men having good sleep than in the group with poor sleep (78.8 mm Hg: $p<0,05$). At night DBP was also higher in poor sleepers (62.1 vs. 57.1 mmHg respectively, $p<0.05$). Day power of all frequency HRV bands (VLF, LF and HF) significantly progressively decreased from good sleepers to poor ones.
Significant correlations were obtained between difficulty falling asleep, poor sleep quality and number of supraventricular premature beats ($r=0.29$, $p<0.05$; $r=0.69$, $p<0.001$). Young men having difficulties with falling asleep had higher heart rate at the day (93.6 bpm) than men without this problem (83.3 bpm). Pts with daytime sleepiness more frequently reported smoking (43.3% vs 21.7%) and snoring (83.3% vs 45.2%, $p<0.05$).

CONCLUSION: The increasing heart rate and DBP, lower total power spectrum of HRV (in all bands) and smoking status negatively influence on sleep quality in young men with mild AH. Lacking of correlations between breathing irregularity, BMI and sleep quality in young pts requires further study.

P6 Adverse effects of energy drinks among young adults and athletes - case report

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Introduction. The increasing use of energy drinks in young adults has contributed to a better comprehension of their effects on the body as well as the side effect. Studies have shown that consumption of larger quantities of energy drinks can cause many cardiovascular disorders as well as sudden cardiac death in previously healthy young individuals. The most stated cardiovascular disorders are different forms of cardiac arrhythmias. Adverse reactions and toxicity of energy drinks derives from high caffeine concentrationand its interactions with other substances, such as the guarana, ginseng and taurine.

Case report: A 30 year old football player presented himself with a cardiovascular event after an intake of large quantities of energy drinks. The conducted medical investigation showed primarily numerous electrocardiographic abnormalities in conduction and repolarization: RBBB, AV block first degree, second degree AV block - Wenckebach including several recorded episodes of an escape rhythm, QT prolongation and atype IIIBrugada sign. No rhythm disorders were recorded. Metabolic status were normal. The cardiovascular tests performed during hospitalisation excluded the existence of structural damage of the heart muscle as a mayor cause of these arrhythmias. Holter ECG, recorded three days after the last energy drink intake, showed a reduction in second degree AV block – Wenckebach episodes with a normalization of QT interval and QRS width. As concluded, the event was most probably the case of a non-hereditary channelopathy caused by a high volume energy drink consumption.

Conclusion: The variety of signs and symptoms of intoxication caused by high volume energy drink conspumption can make thediagnose seting process and patients treatment difficult. Therefore it´s very important to suspect at existence of this disorder, especially in young people and athletes. Thus the leading premise is to raise the consciousness of young people about the harmfulness and side effects regarding energy drinks intake.

Keywords: energy drinks, athletes, young adults , arrhythmias, sudden cardiac death.

P7 ATRIAL FIBRILLATION AND STROKE - RESULTS OF A SIX-YEAR STUDY CONDUCTED BY THE CLINIC OF NEUROLOGY IN BANJALUKA

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ABSTRACT:
Stroke is the second cause of death and the leading cause of disability among patients. One in every six strokes occurs in patients with atrial fibrillation. When transitory ischemic attacks and clinically hidden, "silent", strokes are also taken into account the rate of cerebral ischemia which follows non-valve atrial fibrillation exceeds seven percent per year.
This research was conducted as a prospective study in the period from 2009 to 2015 at the Clinic of Neurology, University Clinical Centre Banja Luka. It included 2049 patients who were treated for stroke at the Clinic of Neurology, University Clinical Centre of the Republic of Srpska. The aims of this research were to determine the connection between atrial fibrillation and stroke, the connection of atrial fibrillation after stroke with neurological and functional status, and to determine the effect of atrial fibrillation after stroke on the outcome of the disease.
Of the total number of patients, 25.62% had atrial fibrillation as a risk factor for stroke. In patients with stroke and atrial fibrillation,the total mortality was 42.86%, which is, in statistic terms, significantly greater than the total mortality which was 33.72%.
By analysing NIHSS, we could notice that it was 14.8% in patients with atrial fibrillation compared with 13.08% in those without atrial fibrillation and that it remained its deficiency even after patient's release (NIHSS was 7.5 on release compared with 5.86). Also, when we, on admission, analysed the Rankin score, we found that patients with atrial fibrillation had more difficult functional deficiency on Admission (Rankin score was 4.36 on admission compared with 3.87), and that deficiency remained on release too (Rankin score was 3.87 on release compared with 2.84)
In conclusion, it should be emphasised that fibrillation presents a significant risk factor for stroke and that patients with atrial fibrillation have worse prognosis both when it comes to the final outcome of the disease,that is**,** survivng and functional recovery of patients.

Key words: stroke, atrial fibrillation, incidence, prognosis

1. INTRODUCTION

STROKE

Stroke is one of the leading causes of morbidity and mortality in the world. It is the second cause of death and the first cause of disability of patients.

Definition

Acute stroke is defined as a focal or global disturbance of cerebral function which occurs suddenly as a result of the disturbance of cerebral circulation or of a condition when blood flow is not sufficient to meet metabolic needs of neurons for oxygen and glucose.

Classification

Depending on the mechanism of occurrence, acute stroke (AS) can be classified into two large groups:
– acute ischemic stroke (AIS) as a consequence of blood vessel's occlusion (thrombotic or embolic), which occurs more often and affects about 75-80% of patients, and
– acute hemorrhagic stroke, that is, an intracerebral or subarachnoid hemorrhage, which affects remaining 20-25% of patients.

Epidemiology

Acute stroke is the third cause of death in developed countries of the world, after cardiovascular and malignant diseases, and the second cause of death in the whole world. The incidence increases with age with specific mortality rate which doubles every ten years, after the age of 55. The *prevalence* of acute stroke ranges from about 600 affected per 100 000 citizens in developed countries to 900 in underdeveloped countries. *Mortality* varies from 63.5 to 273.4 deaths per 100 000 citizens a year.

Risk factors

Risk factors for acute ischemic stroke, which are, at the same time, also the risk factors for atherosclerosis, can be divided into those that can be and those that cannot be influenced. **Risk factors that cannot be influenced are** sex, age, race, and ethnicity, heredity. **Risk factors that can be influenced and** *that are well-documented risk factors are* hypertension, diabetes mellitus and glicoregulation disturbances (hyperinsulinemia and insulin resistance), smoking, dyslipidemia, atrial fibrillation, and other cardiac disturbances.
Risk factors that can be influenced and *that are less-documented potential risk factors are* obesity, physical inactivity, diet, alcohol abuse, hyperhomocysteinemia, substitutional hormone therapy, use of oral contraceptives.

ATRIAL FIBRILLATION

Atrial fibrillation (AF) is atrial *tachyarrythmia characterised by the inconsistent depolarisation of atria with the disturbance of mechanical function and variable, irregular frequency of ventricles.Atrial fibrillation is the most common* arrhythmia *in clinical practice with an incidence from 0.4% to 1% in general population, up to 60 years of age. An incidence in those older than 65 is from 2-5%, and 8% in those older than 80.* When there is a preserved atrioventricular conduction, this atrial rhytm disturbance is joined with an irregular, often rapid, ventricular response. The most common consequence of atrial fibrillation in developed countries is hyperintensive and ischemic heart disease. Other causes include *hyperthyreosis*, cardiomiopathy, degenerative mitral insufficiency, atrial septal defectand constrictive pericarditis. Alcohol, obesity, diabetes, and pulmonary disease lead to the occurence of atrial fibrillation. Vagal or adrenergic stimulation can cause atrial fibrillation even in a healthy heart. About 30% (5-45%) of atrial fibrillation cases occur in healthy hearts and, in such cases, it is called isolated (lone) atrial fibrillation. According to its duration, atrial fibrillation can be divided into **paroxysmal, persistent, and permanent.** Paroxysmal atrial fibrillation is short-term; it is mostly stated that it lasts between two minutes and two days, but the definition of up to seven days is still sometimes acceptable. It spontaneously converts into sinus rhythm, even though the fibrillation that was converted soon after the application of antiarrhytmic is ofen defined as paroxysmal. Long-term atrial fibrillation is called persistent if there is an assumption that it can still be converted into a sinus rhythm with a theraphy. If there are no expectations of conversion into the sinus rhythm, atrial fibrillation is marked as permanent or accepted.

ATRIAL FIBRILLATION AND STROKE

Ischemic stroke incidence among patients with non-rheumatic atrial fibrillation is, on average, five percent per year, which is between two and seven times greater than in persons without atrial fibrillation. One in every six strokes occurs in patients with atrial fibrillation. When transitory ischemic attacks and clinically hidden, "silent", strokes (discovered radiographically) are also taken into account, the rate of cerebral ischemia which follows non-valvural atrial fibrillation exceeds seven percent per year. In patients with rheumatic heart disease and atrial

fibrillation, monitored in the Framingham study, the risk of stroke was 17 times greater compared with the corresponding age control group, while this risk was five times greater compared with the patients with non-rheumatic atrial fibrillation.
In the Manitoba follow-up study, atrial fibrillation doubles the risk of stroke, regardless of other risk factors. Relative risk for stroke at non-rheumatic atrial fibrillation was 6.9 percent in the Whitehall study and 2.3 percent in the Regional Heart study. During a mean follow-up period of 8.6 months among patients with atrial fibrillation, the French ALFA study determined the incidence of thromboembolism of 2.4 percent. Risk of stroke is associated with advancing age; in the Framingham study, the annual risk of stroke attributed to atrial fibrillation increased from 1.5 percent at the age of 50-59 to 23.5 percent at the age between 80 and 89. The incidence of stroke in patients with atrial fibrillation increases with age as much as 36 percent in patients 80-89 years of age. In the Stroke Prevention in Atrial Fibrillation (SPAF) study, the annual risk of ischemic stroke was similar in those with recurrent (3.2%) and permanent (3.3%) atrial fibrillation (AF). As for patients with previous strokes or transitory ischemic attacs, further follow-up showed the incidence of stroke of about 10% to 12% annually, even though they were taking aspirin, while oral anticoagulant therapy was significantly beneficial for those patients. Almost half of AF- associated strokes occur in persons older than 75, and AF is the most frequent cause of massive stroke in elderly. Multivariate analysis separates age and atrial fibrillation, as independent predictors of thromboembolism. Atrial fibrillation is the most frequent cause (in almost 50% of cases) of cardioembolic acute ischemic stroke (AIS) and makes one fifth of all acute ischemic strokes. Due to the fluttering, atria lose their cardiac pump function and a blood path occurs along with the conditions for the formation of thrombus, with consequential cerebral or systematic embolisation. Persons with permanent and paroxysmal non-valvular atrial fibrillation are at 4-5 times higher risk for AIS, with the annual risk of 5-8%, but much lower in those younger than 60 and if there are no joint risk factors for AIS.

2. AIMS OF RESEARCH

The connection between atrial fibrillation and stroke is very common in practice and imposes the need for further research in this important field of medicine. This research was made with the aim of providing valid information on atrial fibrillation as a risk factor for the occurrence of stroke, with the purpose of further application of the results gained in clinical practice too.
Knowledge of this important risk factor for stroke can help in identification of potential risk and high-risk stroke patients. Understanding mechanisms connecting stroke and atrial fibrillation would also define the first step in treatment or prevention of this disease, with the possibility of leading to some new therapeutic strategies and, that way, it would improve the course and prognosis of the disease.
According to those starting basis, following research aims were also defined:

1) Determine the connection between atrial fibrillation and stroke.
2) Determine the connection between atrial fibrillation after stroke and neurological functional status.
3) Determine the influence of atrial fibrillation afte stroke on the outcome of the disease.

3. MATERIAL AND METHODS

This research was conducted as a prospective study in the period from 2009 to 2015 at the Clinic of Neurology, University Clinical Centre Banja Luka. It included 2049 patients who were treated for stroke at the Clinic of Neurology, University Clinical Centre of the Republic of Srpska. One group of examinees was comprised of patients who suffered stroke joined with atrial fibrillation. Other group-control-of examinees was comprised of patients who suffered stroke, but do not have atrial fibrillation diagnosis. Patients were tested on their admission and on their release. The data from anamnesis, clinical examination, laboratory analysis, and targeting scanning were taken. The *questionnaire used in this research consisted of numerous questions, normed questionnaires, as well as the questionnaires designed for the needs of this research. All medical analysis were performed at the Clinical Centre Banja Luka.*
The criteria for the inclusion of patient in this research were:

- stroke verified with additional diagnostic methods: computed tomography (CT) of the brain and/or magnetic resonance (MR) of the brain.

By direct contact and by analysing hospital documentation, all relevant data were collected for each patient, including information on demographic characteristics, personal and family anamnesis, especially regarding vascular risk factors. Neurological examination, biochemical blood analysis, blood counts, CT or MR examinations of endocranium were all conducted for every patient on their admission. All patients also underwent the ultrasound examination of the blood vessels of the neck, transcranial doppler. By conducting neurological examination, patients were scored according to their NIHSS and Rankin scale on their admission and their release thus

measuring the degree of stroke difficulty. The degree of functional dependency and disability was evaluated based on mRS within the first 24 hours on hospital admission and on their release.
The data that were obtained are shown numerically, tabular and graphically. For testing statistically significant differences we used parametric and non-parametric tests-significancy (x2–test and Student's t-test).

4. RESULTS

Table 1.

Ischemic stroke	*Hemorrhagic stroke*	Total
1690 – 82.48%	359 – 17.52%	**2049**

Table 2. Mortality

Survived	Dead	Total	Total mortality
1314	735	**2049**	**35,87 %**

Table 3. Mortality of certain types of stroke

Ischemic stroke			Hemorrhagic stroke		
Dead	Total	Mortality	Dead	Total	Mortality
570	1690	**33,73%**	165	359	**45,96%**

Table 4. Presence of atrial fibrillation as a risk factor in patients with stroke

Atrial fibrillation	Total	Percentage
525	2049	**25,62%**

Table 5. Atrial fibrillation incidence in ischemic and hemorrhagic stroke

Ischemic stroke			Hemorrhagic stroke		
Atrial fibrillation	Total	Percentage	Atrial fibrillation	Total	Percentage
487	1690	**28,82%**	38	359	**10,58%**

Table 6. Mortality of patients with atrial fibrillation and stroke

Dead	Total	Mortality
225	525	**42,86%**

Table 7. Mortality of patients with ischemic stroke and atrial fibrillation

Dead	Total	Mortality
205	487	**42,09%**

Table 8. Mortality of patients with hemorrhagic stroke and atrial fibrillation

Dead	Total	Mortality
9	38	**23,68%**

Table 9. NIHSS on admission in patients with atrial fibrillation and without atrial fibrillation

NIHSS stroke with AF admission	NIHSS stroke without AF admission	NIHSS stroke with AF release	NIHSS stroke without AF release
14,80	13,08	7,5	5,86

Table 10. Rankin on admission in patients with atrial fibrillation and without atrial fibrillation

Rankin score with AF Admission	Rankin score without AF admission	Rankin score with AF release	Rankin score without AF release
4,36	3,87	3,72	2,54

6. DISCUSSION AND CONCLUSIONS

A total of 2049 patients were included in this prospective study of monitoring stroke patients. Among those patients, 1690 patients (82.48%) had ischemic stroke and 359 patients (17.52%) had hemorrhagic stroke, which matches the data from the liteature.

Of the total number of patients, 735 patients died and the mortality was 35.87%. Mortality of patients with ischemic stroke was 33.72%, and 45.96% in patients with hemorrhagic stroke.

By analysing atrial fibrillation as a risk factor for stroke we found that 525 patients, of the total number of 2049, had atrial fibrillation before the occurrence of stroke,that is, 25.62% of the total number of patients!!

As far as ischemic stroke is concerned, out of 1690 patients, 487 patients (28.81%) had atrial fibrillation as a risk factor and as for those with hemorrhagic stroke, out of 359 patients, 38 patients (10.58%) had artial fibrillation.

The total mortality in patients who had stroke and atrial fibrillation was 42.86% (out of 525 patients, 225 died) which has statistical significance greater than the total mortality (33.72%). In patients with stroke who did not have atrial fibrillation, the mortality was 33.05 % (of the total number of 1543 patients, 510 died). Therefore, it can be noticed that patients with atrial fibrillation have worse outcome compared with those without atrial fibrillation as a risk factor.

By analysing ischemic and hemorrhagic stroke in patients with atrial fibrillation, we noticed that the mortality rate was 42.86% in patients with ischemic stroke compared with 33.72% in patients without atrial fibrillation and hence concluded that far worse outcome was found in patients with ischemic stroke and atrial fibrillation as a risk factor.

By analysing NIHSS scores referring to the difficulty of stroke, we found that patients with atrial fibrillation had more severe neurological damage on admission (NIHSS 14.8 compared with 13.08), and that it remained even after patient's release (NIHSS 7.5 on release compared with 5.86).

When we, on admission, analysed the Rankin score, which refers to the patient's functional deficiency, we found that patients with atrial fibrillation had more difficult functional deficiencyon admission (Rankin score was 4.36 on admission compared with 3.87), and that deficiency remained on release too (Rankin score was 3.87 on release compared with 2.84)

In conclusion, it should be emphasised that fibrillation is an important risk factor for the occurrence of stroke and that this study showed that every fourth stroke patient had atrial fibrillation as a risk factor for stroke. If treated correctly and by identifying such patients, the number of stroke patients, especially in this population, could be significantly reduced.

The results showed that patients with atrial fibrillation have worse prognosis both when it comes to the final outcome of the disease, that is, surviving and when it comes to the functional recovery of those patients.

The aim of neurologists and cardiologists should be an early detection of rhythm disturbance and an adequate therapy of those patients which would also result in the improvement of both primary and secondary stroke prevention.

7. LITERATURE

1. A to Z of thrombosis. Editor Sylvia Haas. Originally produced for Thrombosis management: Transforming practice 24-25 May, 2013, Barcelona, Spain. Published by Remedica; books@remedica.com;
2. Radna grupa Američkog koledža za kardiologiju i Američkog udruženja za srce. Preporuke za lečenje atrijalne fibrilacije, prevod orginalnog rada objavljenog u: Eur Heart J 2001;22:1852-1923 Kardiovaskularna medicina: Preporuke (http://www.uksrb.org/pdf/7/Atrijalnafibrilacija.pdf)
3. Fuster V, Ryden LE, Cannom DS et al (2006). „ACC/AHA/ESC 2006 Guidlines for the Management of Patients with Atrial Fibrillation: a report of American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee fo rPractice Guidelines: developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society“. Circulation 114(7): e257-354.
4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke 1991; 22:983-8.
5. Hart RG, Halperin JL. Atrial fibrillation and thromboembolism: a decade of progress in stroke prevention. Ann Intern Med 1999; 131: 688-95.
6. Atrial fibrillation investigators. Riskfactors for stroke and efficacy of antithrombotic therapy in atrial fibrillation.Analysis pooled data from five randomised controlled trials. ArchInternMed 1994:154:1449-57.
7. Hobbs FD, Roalfe AK, Lip GY, et al. Performance of stroke risk scores in older people with atrial fibrillation not taking warfarin: comparative cohort study from BAFTA trial. *BMJ*. Jun 23 2011;342:d3653.
8. Gerth A, Nabauer M, Oeff M, et al. Stroke events in patients with CHADS2 scores 0 and 1 in a contemporary population of patients with atrial fibrillation: results from the German AFNET registry [abstract 4381]. Presented at: European Society of Cardiology (ESC) Congress 2013; September 3, 2013; Amsterdam, The Netherlands. *Eur Heart J*. 2013;34 (suppl):808.
9. Hughes S. CHA2DS2-VASc score best for stroke risk assessment in AF. *Medscape Medical News* [serial online]. September 19, 2013;Accessed September 29, 2013. Available a thttp://www.medscape.com/viewarticle/811332.
10. Hart RG, Benavente O, McBride R, et al. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. Ann Intern Med 1999;131:492–501.
11. Connolly S, Pogue J, Hart R, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. Lancet. 2006; 367: 1903-12.
12. Connolly S, Pogue J, Hart R, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. N Engl J Med. 2009; 360:2066-78.
13. Stiles S. 'New' Oral Anticoagulant Stroke-Protection Benefits in AF Cut Across Subgroups in Meta-Analysis. Medscape Medical News. Available at http://www.medscape.com/viewarticle/815453. Accessed December 17, 2013.
14. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet*. Dec 3 2013;

P8 IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN PREVENTION OF SUDDEN CARDIAC DEATH IN ISCHEMIC HEART DISEASE AND CORONARY ARTERY BYPASS GRAFT SURGERY

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INTRODUCTION: More than 7 million people die of sudden cardiac death worlwide.High incidence of sudden cardiac death is present among the patients with a heart failure. The most common cause of sudden cardiac death is coronary artery disease (80%). It can develop any time after myocardial infarction due to onset of ventricular fibrillation or fast prolonged ventricular tachycardia which alterates to ventricular fibrillation.Present literature has showed that medical therapy with beta blockers and amiodarone hasn't yielded satisfying results compared to prophylactic ICD implantation.

AIM: To compare arrhythmic mortality in patients with EF≤ 35%, after CABG surgery, who had prophylactic ICD implantation, and patients from control group.

METHODS: Patients were divided into two groups, one group with 29 patients who had prophylactic ICD implantation at least a month after CABG surgery, and control group of 36 patients who were only on medical therapy for rhythm disturbances after CABG surgery.

RESULTS: Overall survival was 81,8%. In ICD group 74,4%, and in control group 87% (Log-Rank;p=0,27). Death of VT/VF was higher in control group 11,1% , than in ICD group 10,3% (p=0,92).

CONCLUSION: Prophylactic ICD implantation in patients with EF≤ 35%, one month after CABG surgery showed better VT/VF survival compared to patients only on medical therapy, but without statistical significance.

P9 A rare presentation of myocarditis in young patient: clinical conundrum

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Background

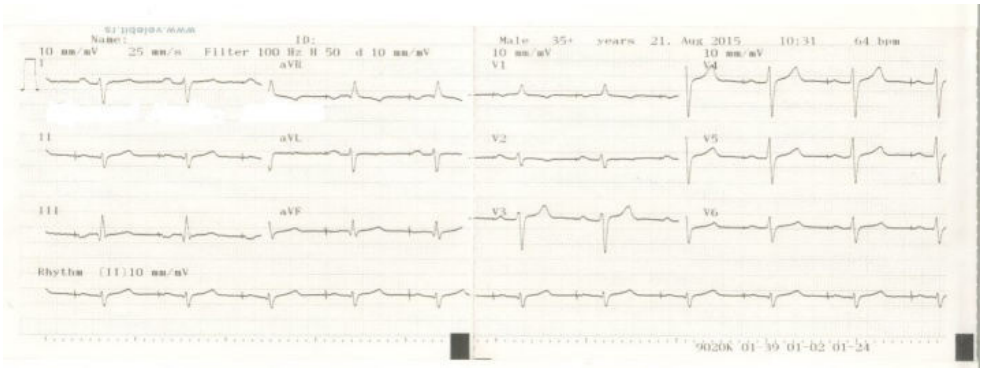
Myocarditis is defined as active inflammatory destructionof the myocardium. A large variety of infectious agents, systemic diseases, drugs, and toxins can cause myocarditis, but still the etiology in many particular cases remains undetermined. (1,2) Despite broad array of etiological causes of myocarditis still viral myocarditis remains the prototype, therefore when we consider myocarditis we usually refer to viral myocarditis as its most common form. (3) Epidemiological studies suggest that during the lifetime around 70% individuals in general population will be in contact with cardiotropic viruses, and half of exposed will have an episode of acute viral myocarditis. (4) Recent studies show that most frequent causal agents are Parvovirus B1, Human Herpes Virus 6, Enterovirus (Coxsackie Virus) respectively. (5, 6) Clinical manifestations range from asymptomatic ECG abnormalities with elevated values of cardiac enzymes to fulminant myocarditis presenting as new-onset cardiomyopathy to life-threatening ventricular arrhythmia. Clinical experience showed that most patients remain asymptomatic. (7)

Case presentation

A 20-year-old female was transferred to Department of Heart Failure from Coronary Unit, presenting with acute chest pain, 3 hours after a cocktail consumption (vodka and energy drink).

Medical history: at the age of 15 she was hospitalized at Neurology Department ofInstitute for Mother and Child Health Care due to ischemic cerebral insult with right-sided hemiplegia, facial nerve paresis and motor aphasia, a week after flu-like symptoms with fever. Previously she actively practice athletics and consumed energy boosters (Coenzyme Q10, L- Glutamyl, anabolic minerals, L-Carnitine extreme, Arginine ornithine lysine). A week before CVI occurred she was treated forheavy alcohol intoxication. Echocardiography examination revealed enlarged left ventricle (5.2/4.0cm) with reduced contractility and ejection fraction of around 40%, with three thrombi in apical region of LV. Laboratory showed increase in troponin I, CK –MB and serum transaminases, high antibody titer for Coxackie B4 and increased titer for B. Burgdorferi. She was diagnosed and treated as myocarditis. Blood coagulation tests revealed homozygous C677T mutation for MTHFR gene, which increases risk of thrombosis. Since sinus node dysfunction with extreme bradycardia was detected, she had an ICD implanted.She was discharged with anticolagulant therapy. Neurological deficit completely regressed after rehabilitation.
Six months after discharge she had an unsuccessful RF catheter ablation of paroxysmal VT, after which ICD was implanted. In 2012 oral anticolagulant therapy was discontinued due to normal coagulation status, and left ventricular function.

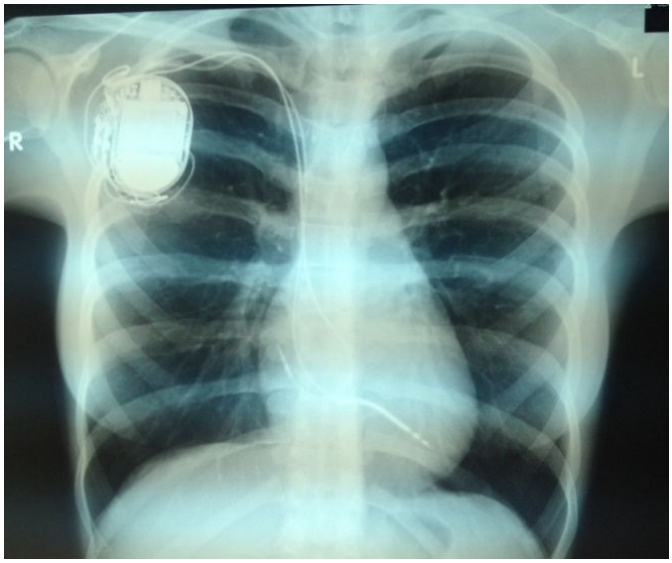
In the mean time she was asymptomatic. Several months before ER admission she had erogospirometry test performed that showed normal functional capacity without evidence of myocardial ischemia.
At admission, physical examination revealed a blood pressure of 110/70 mmHg, heart rate of 80 bpm, discreet systolic murmur at the apex, with no evidence of decompensation.
The electrocardiogram revealed sinus rhythm with regular pacemaker pacing, 64 bpm, right heart axis, qR in leads D3 and aVF, negative T wave in lead V1, V2.



Laboratory parameters revealed elevated troponin I (49 ug/L), CK (1193 U/L) and LDH (731 U/L) levels. Inflammatory parameters and D-dimer values were in normal ranges. All tests for standard narcotis were also negative.

Echocardiographic examination demonstrated

normal left ventricle diameters (4.9/3.7cm),interventricular septal fibrosis with hypokinesia, ejection fraction around 50%, without intracardial thrombi, and normal right heart parameters.
Chest x-ray: without pathological characteristics with visible pacemaker silhouette.



Readings from ICD-DR device showed no significant rhythm and conduction disturbances.
Homocysteine level measured through a routine blood test was 14.9 umol/L wich is considered moderately elevated. Lipoprotein (a) level of 67.3 mg/dl implicates an increased risk for atherosclerosis, heart attack, or stroke. The other parameters (Antithrombin and Protein C) of hemostasis were in normal range.
During hospitalization she was treated with aspirin, low molecular heparin, beta-blockers, mineralocorticoid receptor antagonists and ACE inhibitors. She was discharged 12 days after initial hospitalization, asymptomatic and in stable condition, with beta blocker, Aspirin, folic acid and vitamin B complex therapy and the advice to avoid intensive physical activity.

Discussion
Intracardiac thromosis is rare in younger age. In the last few decades, the incidence of intracardiac thrombosis increased, especially in cases with preexisting hypercoagulable state. (8) The most important predisposing factors for left heart throbosis are dilated cardiomyopathy, atrial fibrillation, endocarditis, prosthetic heart valves, intracardiac tumors and rheumatic mitral stenosis. Left ventricular systolic dysfunction and dilatation are contributing the formation of intracardial trhombi by altering the hemostatic state. Besides that, heart failure is associated with abnormalities of endothelial function, which is also prothrombogenic. In addition, MTHFR gene provides instructions for enzyme methylenetetrahydrofolate reductase synthesis. This enzyme is a part of multistep conversion process of amino acid homocysteine to methionine (conversion of a molecule called 5,10-methylenetetrahydrofolate to a molecule
5-methyltetrahydrofolate). Dysfunction of MTHFR gene leads to elevated homocysteine serum levels (hyperhomocysteinemia). Hyperhomocysteinemia increases risk for atherosclerosis and arterial and venous thrombosis. (9-14). Studies have shown that mean values of homocysteine depend on MTHFR genotype. The most common finding in the general population is mutation of MHTR gene with normal homocysteine and lipoprotein levels. While cases of elevated homocysteine and lipoprotein levels are rare. (19)

In reported case, two of the above mentioned risk factors for intracardial thrombosis were present- left ventricle disfunction caused by myocarditis and predisponing hypercoagulation state. In addition, the risk for instravascular thrombosis was also present, making it plausable as a cause of CVI. Conduction and rhythm disturbances are expected as a complication of myocarditis, and in this patient lead to initial antibradycardial and later, on a permmanent ICD-DR implantation.

Vasospasm can be, also, a possible cause of prolonged ischemia, myocardial infarction or cerebrovascular insult. Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by reversible narrowing of the cerebral arteries. It is usually associated with use of vasoactive agents (drugs that modulate dopamine or serotonin system or sympathomimetics), but can be idiopathic, as well. The most common symptoms are acute headache followed with neurologic deficit. (15) Energy drinks are one of most commonly used substances which have sympathomimetic effects Thier main compound –cafeine is an antagonist of adenosine and presynaptic α1 receptor and it causes the increase in catecholamine release and vasoactive effects. (16) Energy drinks usually contain additional herbal ingredients (ginkgo biloba leaf extract, Siberian ginseng root extract,) with significant sympathomimetic properties. Worrall et al published a report of cerebral vasculopathy and stroke after single consumption of an herbal energy drink. (17,18) Wilson et al. presented a case of 17-year-old male who had been diagnosed with transient coronary vasospasms as a result of drinking a disproportionate amount of caffeinated energy drinks.

During second hospitalization for suspected myocarditis, the acute coronary syndrome was also taken into consideration as a cause of chest pain and elevation of cardiac specific enzymes. Coronary angiography wasnt perfomed due to atypical clinical presentation, absent ECG signs of ischemia, normal echocardiographic findings and patient's age.

Patient was discharged with folic acid and B- vitamin complex therapy of elevated homocysteine and lipoproteine a levels and Aspirin was adviced as permament treatment. Since she has history of energy boosters and alcohol consumption before both hospitalizations of interest, she was adviced to avoid energy drinks consumption in the future.

With respect to mentioned findings there were not enough criteria for myocarditis nor enough sings of acute myocardial ischemia. It remains unclear whater thromboembolic CVI at age of 15 was a direct consequence of myocarditis and embolisation from LV trombi precipitated by reduced LV function and coagulation disorder. It is also uncertain, wheater a nonspecific chest pain at the age of 20 was caused by energy booster-induced vasoconstriction, premature atherosclerotic disease in the coronary arteries, or was it a combination of all these factors.

Keywords: myocarditis, CVI, coagulation disorder, MTHR gene mutation, hyperhomocysteinemia, energy drinks

References

1. Richardson et al. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies.Circulation1996;93:841–842.
2. Leone O et al. 2011 Consensus statement on endomyocardial biopsy from the Association for European Cardiovascular Pathology and the Society for Cardiovascu- lar Pathology. CardiovascPathol 2012;21:245–274.
3. Baboonian C, Treasure T. Meta-analysis of the association of entero- viruses with human heart disease. Heart. 1997;78:539 –543.
4. O'Connell JB: The role of myocarditis in end-stage dilated cardiomy- opathy. Tex Heart Inst J 1987, 14:268–275
5. Kuhl U, Pauschinger M, Noutsias M, et al. High prevalence of viral genomes and multiple viral infections in the myocardium of adults with "idiopathic" left ventricular dysfunction. Circulation 2005;111:887-93
6. Caforio AL[1] at al.European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: aposition statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases.Eur Heart J. 2013 Sep;34(33):2636-48, 2648a-2648d. doi: 10.1093/eurheartj/eht210. Epub 2013 Jul 3
7. Dec GW. Introduction to clinical myocarditis. In: Cooper LT, ed. Myocarditis: From Bench to Bedside. Totowa, NJ: Humana Press; 2003: 257–281. However when the disease has more severe form we should be aware of possible complications and try to prevent them.
8. Atalay S, Akar N, Tutar HE, Yilmaz E. *Factor V 1691 G-A mutation in children with intracardiac thrombosis: a prospective study. Acta Pa-ediatr 2002;91:168-71.*
9. Kádár K, Hartyánszky I, Király L, Bendig L. *Right heart thrombus in infants and children. PediatrCardiol 1991;12:24-7.*
10. Ross P Jr , Ehrenkranz R, Kleinman CS, Seashore JH. *Thrombus associated with central venous catheters in infants and children. J PediatrSurg 1989;24:253-6*
11. Tegeler CH, Downes TR. *Thrombosis and the heart. SeminNeurol 1991;11:339-52.*
12. Lip GY, Gibbs CR. *Does heart failure confer a hypercoagulablest-ate? Virchow's triade revisited. J Am CollCardiol 1999;33:1424-6.*7) Meltzer RS, Visser CA, Fuster V. *Intracardiac thrombi and systemic embolization. Ann Intern Med 1986;104:689-98.*
13. Treasure CB, Vita JA, Cox DA, et al. *Endothelium-dependent dilation of coronary microvasculature is impaired in dilated cardiomyopathy. Circulation 1990;81:772-9.*
14. Varga EA[1], Sturm AC, Misita CP, Moll S. Cardiology patient pages. Homocysteine and MTHFR mutations: relation to thrombosis and coronary artery disease. Circulation. 2005 May 17;111(19):e289-93.
15. Chen SP, Fuh JL, Wang SJ. Reversible cerebral vasoconstriction syndrome: current and future perspectives. *Expert Rev Neurother*. 2011;11:1265-1276.
16. Benowitz NL. Clinical pharmacology of caffeine. Annu Rev Med. 1990;41:277-288.
17. Wilson, R. E., Kado, H. S., Samson, R., & Miller, A. B. (2012). A case of caffeine-induced coronary artery vasospasm of a 17-year old male. Cardiovascular Toxicology. doi:10.1007/s12012-011- 9152-9.
18. Debopam S. Reversible cerebral vasoconstriction syndrome: another health hazard of energydrinks? ClinPediatr (Phila). 2015 Feb;54(2):186-7. doi: 10.1177/0009922814541675. Epub 2014 Jul 7
19. Intessar ES, Effect of Methylenetetrahydrofolate Reductase Gene Mutation on Plasma Homocysteine Level and its Prevalence in Arterial Diseases. J. Taibah Uni. Med. Sci. Volume 1, Issue 1, 2006, Pages 20–29

P10 Autonomic nervous system is affected in children with atopic dermatitis

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Background. Atopic dermatitis is a common, genetically predisposed, inflammatory and pruritic skin disease and has been shown to be associated with neurogenic and psychosocial factors. There is increasing evidence that stress influences disease processes and contributes to the inflammation through modulating hypothalamic-pituitary-adrenal axis. But papers devoted clarifying the significance of autonomic nervous system (ANS) in pathogenesis of atopic dermatitis is scarce.

Aim and methods. We aimed to investigate the ANS state and reactivity measured by heart rate variability (HRV) in 35 children aged 3-14 years (22 girls and 13 boys) with atopic dermatitis. The severity of disease was calculated according to EASI (Eczema Area and Severity Index). HRV has been obtained with 5-min EEG recording in supine and standing (3 min) position (NeuroSoft, Ivanovo, Russia). Analysis in time, frequency domain and according to R.M.Baevskiy algorithm was conducted. 10 children were investigated after treatment.

Results. 29 children had mild 6 - moderate severity of dermatitis. All patients were divided into 3 groups according to sympatho-vagal balance (LF/HF). Parasympathetic predominance (LF/HF=<0.6) was seen in 51.5%, eytonia (LF/HF 0.6-1.9) was registered in 36.4% and sympathetic predominance (LF/HF>1.9) obtained in 12.1% of patients. Stress-index <120 units had 72.7% of children. This fact also suggests high parasympathetic activity in pathogenesis of atopic dermatitis.

We found only one significant negative correlation between severity of disease detected by EASI and power of LF band in standing position ($r = -0.33$; $p<0.05$) due to altered cardiac autonomic modulation upon postural change with increasing severity of disease.

After treatment there was tendency to decreasing total HRV power both in boys (5909+/-1898 vs 2838+/-877 ms2) and girls (6516+/-1145 vs 4103+/-820 ms2).

Conclusion. This study supports the concept that atopic dermatitis is a stress-responsive disorder and involves autonomic nervous system dysfunction. Parasympathetic predominance in children with atopic dermatitis may be served as indicator of chronically influenced stress with altered sympathetic reactivity.

P11 Acute inflammatory response after Scaffold stent implantation and impact of Trimetazidine

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Background. Coronary heart disease is a condition in which atherosclerotic plaque builds up within the wall of the coronary arteries result in narrowing and development of atherosclerotic lesions.If these lesions, unstable or clinically significant are frequently treated by PCI. Bioresorbable coronary scaffold stent have been considered as the fourth revolution in interventional cardiology due to immediate and long term results of PCI have been improved very significantly.TMZan anti-ischemic drug protects the myocardial cell from the harmful effects of ischemia and minimizes the myocardial damage induced by PCI.
Objective. To assess the effect of Trimetazidine on the acute inflammatory response after bioresorbable coronary scaffold stent implantation in patients with coronary heart disease.
Materials and Methods. A total of 40 diabetic patients with stable coronary artery disease were assigned to two groups: control and TMZ treated ,admitted at AL-Najaf center for cardiac surgery and trans catheter therapy and underwent to elective coronary scaffold stent implantation . Serum blood from the peripheral vein was collected before, 12 hrs,24 hrs after implantation of stent and used to measure IL-6,IL-8,IL-10,hs-CRP ,cTn-I,PTX3,MMP-9 ,C5a and VCAM-1 levels by sandwich ELISA method .
Results. The implantation of scaffold stent resulted in significant changes in serum level IL-6, IL-8, hs-CRP, cTN-I, PTX3,C5a and VCAM-1($p< 0.05$)while non significant changes in serum levels IL-10 and MMP-9 were found ($p>0.05$).similarly three days of TMZ treatment produced significant decrease in IL-6, hs-CRP, cTn-I and PTX3levels while serum IL-10 was significantly increased ($p<0.05$). It was found that serum IL-8, MMP-9, C5a and VCAM-1were non significantly changed by TMZ treatment ($p>0.05$).
Conclusions. It can be concluded that administration of Trimetazidine reduce the systemic inflammatory response induced by implantation of bioresorbable coronary scaffold stent.
Kew words. Coronary heart disease, Percutaneous coronary intervention, Bioresorbable coronary scaffold stent, inflammatory markers ,Trimetazidine.

P12 Is there any corelation between severity of the obstructive sleep apnea and endothelial dysfunction?

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BACKGROUND: Obstructive sleep apnea (OSA) is a common disorder and is associated with adverse cardiovascular consequences, including hypertension and coronary artery disease and the mechanisms responsible for increased risk of cardiovascular events in OSA have not yet been fully elucidated. Studies have directly measured vascular endothelial function in patients with OSA and found a muted response compared to controls.
AIM: to elvaluate is there any relationship between severity of the obstructive sleep apnea syndrome and endothelial dysfunction as a marker of cardiovascular risk.
METHODS: One hunderd and seven consecutive patients with polysomnographic criteria for OSA were enrolled in the prospective study (aged 25-80 years, mean age 52 ± 1 years): 17% had mild OSA (AHI 6-15), 37% moderate OSA (AHI 16-30), and 46% severe OSA (AHI > 30). Coronary artery disease was excluded in al of them by noninvasive testing (maximal test of physical exertion or Dobuamine stress test), 22% of them were diabetics and 66% of them had hypertension. Flow-mediated dilatation (FMD) and nitroglycerin-mediated dilatation (NMD) were assessed to evaluate endothelial dysfunction and vascular smooth muscle dysfunction, respectively by using a novel ultrasound device. Difference in vasodilatation less than 5% was used as cut-off value for endothelial dysfunction in both tests. Microaluminuria was detected by standard laboratory procedure.
RESULTS: Impaired FMD was detected in 59 % of patients with OSA: severe dysfunction in 59 %, moderate in 38% and mild in 10 % of them. More statistically frequently presence of the endothelial dysunction was related to the most severe grade of the OSA and there was n a high statistically significant relationship beween the severity of the OSA and FMD , (X2 = 11.72, p=0.003). On the other side, microalbuminuria was detected in 14 % of the patients with OSA: 40% of them were with severe OSA, 40% with moderate and 20% with mild OSA. There was no correlation between the impaired FMD and presence of microalbuminuria (Pearson p=0,590 p>0,05), so the microalbuminuria is an independent marker of endothelial dysfunction.
CONCLUSION: Our study shows that the severity of OSA is an important factor of impaired endothelial function and hence an important risk factor for higher risk of atherosclerosis and cardiovascular complications. Early detection of the endothelial dysfunction is very important in prevention of cadiovascular complications in patients with OSA.

P13 Conduction disturbances as predictors of adverse cardiovascular events for 30 days in patients with acute coronary syndrome undergoing percutaneous coronary intervention

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Introduction: Stratifying patients with acute coronary syndrome (ACS) using the most accurate risk score can contribute to more effective therapeutic treatment of patients. Variables that make up the score increases sensitivity score in the prediction of major adverse cardiovascular events (MACE). Acute bundle branch block (1, 2) and complete atrioventricular block (3, 4) are important predictors of poor outcome in patients with ACS.

Methods: The study enrolled two hundred patients with the admission diagnosis of acute ST-elevation and non ST-elevation myocardial infarction and unstable angina pectoris undergoing percutaneous coronary intervention (PCI). Follow-up data were obtained by history ofdisease and telephone interviews of patients. Composite 30-day MACE comprising death and urgent myocardial revascularization for ischemia were the primary end point. These patients were calculated TIMI, GRACE on admission and discharge and RISK-PCI risk scores and compared their predictive value using c-statistic, logistic regression, Cox's regression and ROC curve analysis. Internal validation of risk models was performed using Hosmer-Lemeshow chi-square test.

Results: This study enrolled 200 patients with ACS, the average age of 62.3 ± 10.8 years, 140 males and 60 females. RISK-PCI score and the GRACE score was excellent prognostic value and discriminative ability for mortality within 30 days with much better discrimination RISK-PCI score (c-statistic 0.96) compared to the GRACE score on admission (c statistic 0 88) and GRACE score at discharge (c-statistic 0.78). The analysis of the scores in the prediction of MACE during the same period, the best predictive value with good discriminative ability was a RISK-PCI score (c-statistic 0.79), followed by GRACE score on admission and discharge (c-statistic 0.66 and 0.62). TIMI score was no significant prognostic value. Multivariable regression RISK-PCI score is confirmed as an independent predictor of death, the composite MACE and was the only reliable record in quantitative assess urgent revascularisation. Internal model validation Hosmer-Lemeshow goodness-of-fit test has proven to be good for all the observed scores ($p > 0.05$).

Conclusion: RISK-PCI score proved to be superior predictive to the GRACE and TIMI scores for composite 30-day MACE comprising death and emergency myocardial revascularization for ischemia. Acute bundle branch block and complete atrioventricular block as part predictors RISK-PCI score increase its prognostic value compared with other scores.

References:

1. Go AS, Barron HV, Rundle AC, Ornato JP, Avins AL. for the National Registry of Myocardial Infarction 2 investigators. Bundle-branch block and in-hospital mortality in acute myocardial infarction. Ann Intern Med 1998; 129:690–7.
2. Addala S, Grines CL, Dixon SR, et al. Predicting mortality in patients with ST elevation myocardial infarction treated with primary percutaneous coronary intervention (PAMI risk score). Am J Cardiol 2004; 93:629–32.
3. Van de Werf F, Bax J, Betriu A, et al. ESC Committee for Practice Guidelines; ESC Committee for Practice Guidelines. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. The Task Force of the management of ST-elevation acute myocardial infarction of the European Society of Cardiology. Eur Heart J 2008; 29:2909–45.
4. Harpaz D, Behar S, Gottlieb S, et al. Complete atrioventricular block complicating acute myocardial infarction in the thrombolytic era. J Am Coll Cardiol 1999; 34:1721–8.

P14 Treating hypertension using the basic principles of Traditional Chinese Medicine

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***Introduction*.** Hypertension is an important global public -health issue. Having high mortality and disability, it affects general life quality. It is one of the main culprits to cardiovascular and cerebrovascular events such as heart failure, stroke, kidney failure, blindness and cognitive impairment [1]. Worldwide prevalence for hypertension is about 40 % [1]. In China it is about 29.6 % [2].Nowadays, many hypertensive patients, especially in Asia, have turned to traditional Chinese medicine (TCM). Despite the fact that hypertension is not a TCM concept, it can be treated using TCM principles [3]. A variety of approaches, and a number of clinical studies have been conducted in China, for treating hypertension. TCM has a unique way to diagnose and treat diseases, as a result of long observation of nature, society and the human organism interactions [3].

Application of TCM on hypertension. In clinical use, methods of TCM are acupuncture and moxibustion, Chinese herbal medicine, cupping, qigong, Tai Chi, and diet. TCM asserts that a sedentary lifestyle, persistent stress, unhealthy diet, organ damages, and constitutional defects are all contributed to the raised blood pressure (BP). As according to a *theory of five elements* all organs are interconnected, hypertension is result of misbalance of heart, liver and kidney systems. There may also have dysfunctions of the Thoroughfare Vessel (Chong Mai) and Girdling Vessel (Dai Mai). According to holistic concept and treatment based on syndrome differentiation TCM principles for reducing BP are:
1. Eliminating dampness and resolving phlegm: this promotes excess body fluids and wastes to eliminate through urination.The action also lowers blood lipids, and promotes blood flow throughout the body.

2. Soothing liver and extinguishing wind: This can calm down and regulate the nervous system, expand blood vessels, promote urination, and regulate calcium metabolism.

3. Activating blood and resolving stasis:This can expand blood vessels, free blood circulation, also soothe the central nerve system, slow down heartbeat, and inhibit blood platelets clotting.

4. Clearing heat and purging fire: This can expand blood vessels, promote excretions, and calm down the body.

Treatment.
1. Traditional Chinese Medical Formulas. The exploration of Chinese herbal formulas (HF) for curing hypertension is the most fruitful research field in TCM and integrative medicine in China. According to the clinical manifestations of patients with hypertension, TCM physicians diagnose certain syndromes and prescribe certain HF. The most used HF according to syndrome differentiation are: Tianma Gouteng Yin (decoction of Gastrodia and Uncaria), Huanglian JieDu Tang (detoxicant decoction of Coptis), Zexie Tang (decoction of Alisma), BanxiaBaizhuTianmaTang (decoction of Pinelliaternata, Atractylodesmacrocephala and Gastrodiaelata), ShenqiWan(kidney qi pill), LiuWeiDihuangWan (pill of Rehmannia).. [4]. Modern research are indicating chemical components of Chinese HF can reduce BP (by α1 receptors), reduce blood pressure variability, block sympathetic nerves, inhibit sympathetic and rise vagus activity [4], regulate the function of Renin-angiotensin-aldosterone system, inhibit the level of inflammatory factor, prevent and reverse left ventricular hypertrophy caused by high BP, influence vasoactive substances significantly, and so on [5-8].

2. Acupuncture is an ancient technique of TCM that appeared about 5 200 years ago. Results of the recent trials are showing a tendency that acupuncture can decrease high BP. Numerous case studies and uncontrolled trials provide evidences for efficacy of acupuncture for treating hypertension [9]. In many of them, systolic BP was more beneficially affected then diastolic BP [10]. The commonly used acupuncture points for curing are: Baihui (DU20), Quchi (LI11), Taichong (LV3), Taixi (KI3), Sanyinjiao (SP6), Hegu (LI4), Renying (ST9) with uniform reinforcing-reducing method [11, pg 59].

3. Moxibustion is a TCM therapy using moxa made from dried mugwort (Artemisia argyi). Moxa is used to warm regions and meridian points with the intention of stimulating circulation, through the points and inducing a smoother flow of qi and blood. It can causelowering of BP, once stagnation of qi and blood is removed.
4. Cupping therapy is a method of TCM where a glass cup is placed over a painful area or an appropriate acupuncture point. It cause the skin to pull into the cup and under pressure exerted on the skin irritates subcutaneous muscles. By removing the stagnancy of quid and blood, and influencing their un-obstructively movements through meridians, it is used to lower BP and relieve hypertension-related symptoms.
5. Qi Gong, as an ancient Chinese healing art, where movement and breathing are harmonized. It is widely used in Chinese hospitals nowadays. According to the theory of TM, it opens meridians, and increase the healthy flow of quid throughout the body. Documented positive effects of quid gong on heart rate variability and BP might mean that certain breathing, mind and body movements produce sympathetic and parasympathetic balancing [12].
Conclusion. Traditional Chinese medicine focuses on holistic and personal healthcare, in many cases, integrated treatment methods by using both Traditional Chinese and western medicine have had better outcomes then using either alone. TCM methods for hypertension are not as quick and steady as conventional methods but they can be incorporated as part of the hypertension management, and may even be the first line therapies for mild to moderate cases. The final purpose of Chinese medicine in treating hypertension is to reduce blood pressure variability and risk factors, modulate factors difficult to control blood pressure, relieve symptoms to improve patients' quality of life, improve long-term survival, and reduce the morbidity and mortality maximally [13].

*Keywords***:** Hypertension; Traditional Chinese medicine; Acupuncture; Chinese herbal formulas;

References:

[1] A global brief on hypertension: Silent killer, global public health crisis. World Health Organization. 2013; 1-40 (cited 2015 August 31). Available from: http://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en/;
[2] Wang J, Zhang L, Wang F, Liu L, Wang H. Prevalence, awareness, treatment and control of hypertension in China: results from a national survey. Am J Hypertens. 2014; 27 (11): 1355-1361.
[3] Xiong X,, Yang X, Liu W, Chu F, Wang P, Wang J. Trends in the treatment of hypertension from the perspective of traditional Chinese medicine, Evidence-based complementary and alternative medicine. 2013; 1-13.
[4] Xiong X, Yang X, Liu Y, Zhang Y, Wang P, Wang J. Chinese herbal formulas for treating hypertension in traditional Chinese medicine: perspective of modern science. Hypertension Research. 2013; 36: 570-579.
[5].Y. H. Zhao, Y. H. Xu, Y. Guan, et al., "Effects of Yinian Jiangya Decoction containing serum on cytokines secretion of vascular endothelium of spontaneously hypertensive rats," Chinese Journal of Integrative Medicine. 2010; 16 (8): 344-347.
[6].H. Li, W. M. Zhao, Y. X. Han. Effect of an integrative medical regimen on levels of vascular endothelial function and hypersensitive C-reactive protein in elderly patients with isolated systolic hypertension. Zhong Guo Zhong Xi Yi Jie He Za Zhi. 2009; 29 (2): 115-119 (in Chinese).
[7].J. Y. Jiang, X. Z. Wang, S. S. Luo, et al. Effect of Banxia Baizhu Tianma Decoction on the left ventricular hypertrophy of hypertrophied myocardium in spontaneously hypertensive rat. Zhong Guo Zhong Xi Yi Jie He Za Zhi. 2010; 30 (10): 1061-1066 (in Chinese)
[8] L. L. TAO, X. C. MA, and K. J. Chen. Clinical study on effect of Qingxuan Tiaoya Recipe in treating menopausal women with hypertension. Zhong Guo Zhong Xi Yi Jie He Za Zhi. 2009; 29 (8): 680-684 (in Chinese)
[9] Macklin EA,Wayne PM, Kalish LA, Valaskatgis P, Thompson J, Pian-Smith MC et al. Stop hypertension with the Acupuncture Research Program (SHARP): results of a randomized, controlled clinical trial. Hypertension. 2006; 48 (5): 838-845.
[10] Guo W, Ni G. The effects of acupuncture on blood pressure in different patients. *J Tradit Chin Med*. 2003;23:49 –50.
[11]Zhang Ren , Xu Hong . Acupuncture Treatment for Hypertension. Shanghai Scientific and Technical Publishers. 2007.
[12] Jahnke R, Larkey L, Rogers C, Etnier J, Lin F. A comprehensive review of health benefits of qigong and tai chi. Am J Health Promot. 2010; 24 (6): e1-e25.
[13] Y. Lei. Train of thought and strategy over strengthening the research of treating hypertension by integrative Chinese and western medicine. Chinese Journal of Integrative Medicine. 2004; 10 (1): 4-6.

P15 Acute myocardial infarction with chronic myeloid leukemia – a case repost

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The patient 64 years appeared in the emergency service due to suffocation, pain in his right shoulder, numbness of both hands, fatigue, denies chest pain. It is not diabetic. Otherwise it is the patients who had a myocardial infarction 2 so far (2000 yr. and 2008.) In 2008. built her two stents and 2013 years. diagnosed chronic myeloid leukemia in a regular control, taking Imatinib 400 mg.

On physical examination conscious, oriented, eupnoic in peace, acianotic, anirectal, pale color of the skin and visible mucous membranes, withought signs of hemorrhagic syndromes and peripheral lymphadenopathy. CV compensated for and gives the impression of medium heavy patient. The objective findings on the head and neck in the physiological range. Thorax cylindrical, mutually respiratory mobile. Cardiac function rhythmical, clear tones, present regurgitate systolic murmur at the top of propagation to the left axillas volume 2-3 / 6. On auscultation of the lung normal respiratory sound. TA on receipt of 140/100 mmHg. ECG sinus rhythm, rate 84 / min, left position of heart PK 0.16; KT 0.32; R / S - V 4 kr Cr-D2-D3-KR avf with apl T HS-V1.

Abdomen soft, painful on palpation no pain. Liver and spleen not palpated.L insensitive to the essence. Inferior extremitas : mobile, without swelling, deformity and varices. Peripheral arterial pulsations mutually symmetrically palpable at the typical places.

She was start with Lorazepam tbl. x 1 and Zodol amp. x 1 in ER. The internal department was located in the coronary care unit on a continuous TA and ECG monitoring . Administered dual antiplatelet and anticoagulant therapy with oxygenation of the organism with a long-acting nitrates and below the treatment baths blocker, statin, diuretic and sedative occasionally. to the administered therapy patients as treatment progresses without pain rhythmically stable without clinical signs of heart failure. The internal department underwent abdominal ultrasound: liver is homogeneous structure. Gall bladder B. O. pancreas spleen and two kidneys, central retroperitoneum are normal TO caracetristics. No fluid in abdomen. Ray of the heart and lungs: Heart shadow magnified, enhanced port of the left ventricle, pulmonary filds without pathology. Laboratory: Hb-141…148…151; RBC-4,64; WBC-4,8; Trombocytes-116; Troponin-0,10…0,11: The therapy at discharge: Monizol 20+20+0 mg; Tensec 5 mg x1; Cardiopirin 100 mg x1; Prexanil 5 mg x1, Sortis 20 mg at night, Sortis at night Trimetacor tbl. 2x1, Lasix tbl 1x1+ Spirinilacton 25 mg on third day + hematology therapy. The patient was discharged from hospital with diagnosis: Infarctus myocardii subendocardialis acutus NSTEMI, Cardiomyopathia ishaemica dilatativa comp, Hypertensio arterialis essentialis, Leukemia myeloides .

P16 Adverse drug reaction to Ticagrelor – a stumbling stone of dual antiplatelet therapy – case report

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Introduction: According to the definition given by the WHO, adverse drug reactions are defined as an adverse body reaction appearing as a result of an adverse (unwanted and often harmful) effect of a drug properly administered and in correct dose for prophylactic, diagnostic or therapeutic purposes. From a clinician's perspective the effects are representing a stumbling stone of any medicamentous therapy. Ticagrelor-induced dyspnoea, as the most common given adverse effect is usually manifested as mild (easy tolerable) or moderate (interrupting the normal habitus) dyspnoea, and as such is not a reason for cessation of therapy.

Case report: A 39-year-old male presented himself with a typical angina chest pain (treadmill test was positive), just two months after he had suffered from inferior wall STEMI, when he was treated primary PCI RCA with implantation of three bare metal stents. After the infarction, patient was treated by the STEMI treatment protocol. Performed recoronarography showed in-stent restenosis of a right coronary artery. After administration of a ticagrelor "loading" dose four drug-eluting stents were implanted. Several days after a ticagrelor therapy introduction, mild there was appearance of mild dyspnoea with a few episodes of worsening. During the hospitalization metabolic status was normal, lab results showed no increase of inflammatory parameters what so ever. Conducted cardiology diagnostic and pulmonary function tests have excluded the existence of cardiologic or pulmonary substrate as a potential cause of aforementioned symptom. As concluded, the adverse event was most probably the case of an adverse effect on initiated ticagrelor therapy.

Discussion: In acute coronary disease dual antiplatelet therapy with aspirin and P2Y12 inhibitor is a standard care[1]. Ticagrelor is the first reversibly binding, oral P2Y12 receptor antagonist. Its effects, manifested through direct inhibition without the need for enzym activation, are faster and more consistent platelet inhibition as opposed to clopidogrel and prasugrel[2,3].

In the phase III PLATO trial, it is shown that ticagrelor significantly reduces the composite rate of death from cardiovascular causes (CV death), myocardial infarction, or stroke at 12 months, without increasing the rate of PLATO-defined overall major bleeding. These findings are the result of comparison with clopidogrel in patients with ACS, with or without ST-segment elevation[4].

Ticagrelor-related dyspnoea is generally defined as sudden and unexpected „hunger" for air or insuffitient inspiration. Its pattern may vary widely, from very brief episodes (generally starting in the first week of treatment) to sustained or intermittent episodes occurring over several weeks, with most episodes being reported as mild[6]. It usually occurs at rest, often is not related to exertion and it doesn't limits an exercise capacity.

Dyspnoea, as one of the most common and distressing symptoms experienced by patients, can result from a variety of conditions,including cardiac, pulmonary, renal and liver diseases, anaemia and metabolic abnormalities etc. As opposed to heart failure, it's not associated with wheezing, orthopnoea, paroxysmal nocturnal dyspnoea nor chest pain. There is also neither increase in serum NT-pro-BNP level and regarding echocardiogram findings, there is no change in left ventricular systolic function[5]. In differentiating ticagrelor-related dyspnoea from other pathological causes, many tests are helpful like chest X-ray, and pulmonary function tests[6], lab results to exclude inflammation etc.

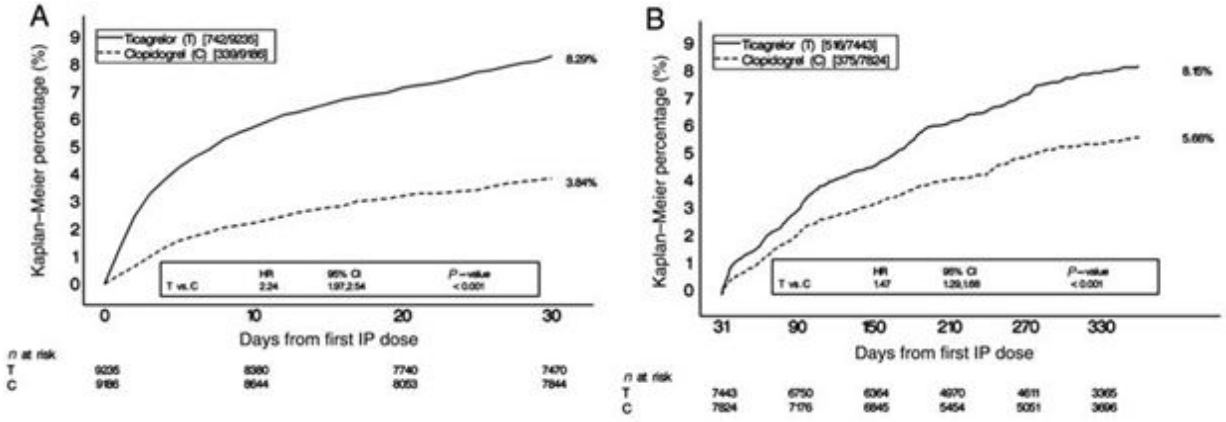

Figure 1Landmark analyses of the incidence of new dyspnoea AE post investigational product, (IP) showing (A) onset of any episodes of dyspnoea AE in the first 30 days; (B) onset of any dyspnoea AE from 31 days onwards[6]

The exact mechanism of ticagrelor-related dyspnoea has not been definitively proven, although preliminary data indicate that ticagrelor has an off-target effect on adenosine reuptake[7]. It is known that intravenous adenosine infusion can cause transient dyspnea in the absence of bronchoconstriction[8]. However, some experimental evidence indicates that it is biologically plausible that inhibition of P2Y12 increases the conductivity of vagal C-fibers and, hence, the sensation of dyspnea.

Conclusion: In a modern medicine it's a known fact that there is no such thing as a medication without an adverse effect; there are only the ones with different manifestation of adverse effect forms, according to their propensity to act with a certain tissue or organ. Then again, relying on the published research results and overall benefit, PLATO study in cases of manifested mild dyspnoea supports the perpetuation of therapy. Patients who cannot tolerate dyspnoea, believed to be an adverse effect of ticagrelor, may be switched to prasugrel.

REFERENCE:

1. Wright RS, Anderson JL,Adams CD, Bridges CR, Casey DE, Ettinger SM, Fesmire FM,Ganiats TG, Jneid H, Lincoff AM, Peterson ED, Philippides GJ, Theroux P, Wenger NK, Zidar JP, Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE, Chavey WE, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK, Zidar JP, American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction: a report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines developed in collaboration with the American Academy of Family Physicians, Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons. J Am Coll Cardiol 2011;57:e215–e367.

2. Storey RF, Husted S, Harrington R, Heptinstall S, Wilcox RG, Peters G, Wickens M, Emanuelsson H, Gurbel P, Grande P, CannonCP. Inhibition of platelet aggregation by AZD6140, a reversible oral P2Y12 receptor antagonist, compared with clopidogrel in patients with acute coronary syndromes. J Am Coll Cardiol 2007;50:1852–1856.

3. Gurbel PA, Bliden KP, Butler K, Tantry US, Gesheff T,Wei C, Teng R, Antonino MJ, Patil SB, Karunakaran A, Kereiakes DJ, Parris C, Purdy D, Wilson V, Ledley GS, Storey RF. Randomized double-blind assessment of the ONSET and OFFSET of the antiplatelet effects of ticagrelor vs. clopidogrel in patients with stable coronary artery disease: the ONSET/OFFSET study. Circulation 2009;120:2577–2585.)

4. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA; PLATO Investigators, Freij A, Thorse´n M. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009; 361:1045–1057.)

5. . Storey RF, Bliden K, Patil SB, Karunakaran A, Ecob R, Butler K, Teng R, Wei C, Tantry US, Gurbel P. Incidence of dyspnea and assessment of cardiac and pulmonary function in patients with stable coronary artery disease receiving ticagrelor, clopidogrel or placebo in the ONSET/OFFSET study. J Am Coll Cardiol 2010;56: 185–193.

6. Storey F.R, Becker C.R, Harrington A.R, Husted S,. James K.S, Cools F., Gabriel Steg P, Khurm S.N, Emanuelsson H, Cooper A, Cairns R, Cannon P.C, Wallentin L.Characterization of dyspnoea in PLATO study patients treated with ticagrelor or clopidogrel and its association with clinical outcomes. European Heart Journal (2011) 32, 2945–2953 doi:10.1093/eurheartj/ehr231)

7. Bjorkman J-A, Kirk I, van Giezen JJ. AZD6140 inhibits adenosine uptake into erythrocytes and enhances coronary blood flow after local ischemia or intracoronary adenosine infusion (abstr). Circulation 2007; 116:II28.

8. Burki NK, Dale WJ, Lee LY. Intravenous adenosine and dyspnea in humans. J Appl Physiol 2005;98:180 –5.)

P17 Adverse drug reactions as the cause of hospitalization – case report

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Introduction: According to the definition given by the WHO, adverse drug reactions(ADR) are defined as an adverse body reactionappearing as a resultof an adverse (unwanted and often harmful) effect of a drug properly administered and in correct dose for prophylactic, diagnostic or therapeutic purposes[1].From an economic viewpoint they are an ineluctable stumbling stone of any medicamentous therapy and a substantial burden to healthcare system. Drugs most commonly associated with adverse drug reactions include antibiotics, anticoagulants, antineoplastic drugs, non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics.

Case report: A 70-year-old woman, diabetic, presented herself with a severe dyspnoea and mild case of heart failure, just two days after she had suffered an inferior wall STEMI, when she was treated primary PCI RCA with implantation of two bare metal stents. After the infarction, significant heart failure wasn't detected sonographically (EF was preserved 55%); patient was treated by the STEMI treatment protocol. An inferior antiplatelet response to clopidogrel, proven by the platelet aggregation test, led to ticagrelor therapy introduction. During the rehospitalization, metabolic status was normal, lab results showed no increase of inflammatory parameters what so ever, prognostic markers for congestive heart failure were within acceptable limits considering a current condition and the age of patient. Conducted cardiology diagnostic and pulmonary function tests excluded deterioration of current cardiopulmonary state as a potential cause of aforementioned symptom. As concluded, the adverse event was most probably the case of an adverse effect tointroduced ticagrelor therapy.The assumption was confirmed by switching back to clopidogrel.

Discussion: Drug-related hospitalizations represent a bigger issue as it seems at first glance. Reasons for such statement are numerous.

Such events, resulting in hospital admission, are more likely to be manifested as severe reactions, especially in elderly population[12]. Factors known to influence the severity of reaction include a patient's age and sex, the presence of comorbidities, the number of drugs a patient is taking, recent introduction of new drug therapy etc. Studies have shown that the highest risk of an adverse drug reaction(ADR) is likely to occur in the days shortly after introduction of a new drug therapy[9-11]. The numbers are the most obvious when it comes to opioids. Among ADRs associated with opioids, 33.2% occurred within 30 days of a patient starting therapy, while 8.4% occurred with anticoagulants, respectively. A longer period of drug usage is associated with a development of tolerance to certain side effects of the drug and therefore is less likely to cause an ADR.

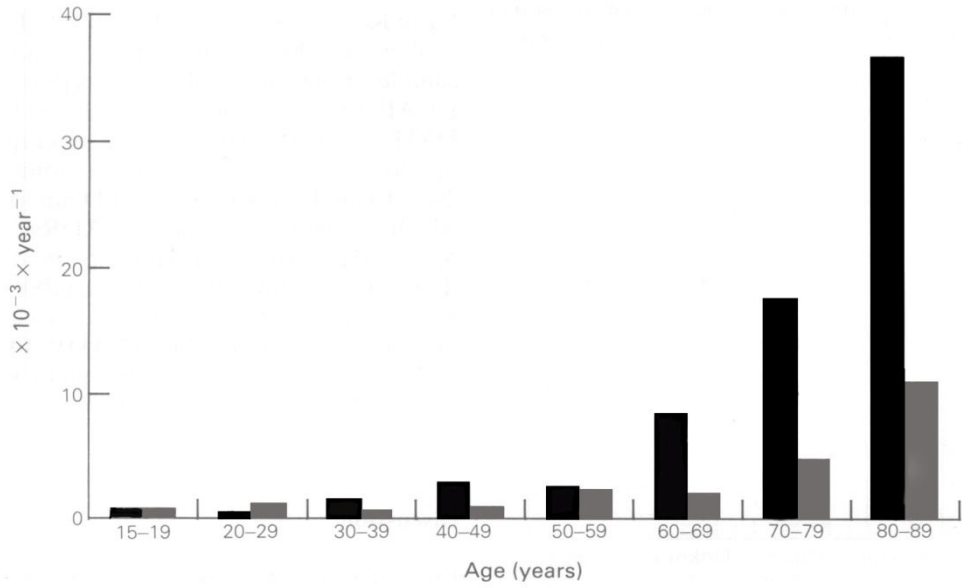
In a research done by the Canadian Institute for Health Information, anticoagulants were the drug class most commonly associated with ADR-related hospitalizations with their 12.6%, respectively. According to the provided data, hemorrhagic syndrome is the most common diagnosis associated with adverse drug reactions of anticoagulants[8].

Drug Class	Common Uses	Most Common Diagnosis Related to Hospitalization	Percentage of ADRs
Anticoagulants	Heart attack and stroke prevention	Hemorrhagic disorder (bleeding) due to circulating anticoagulants	12.6%
Antineoplastic drugs	Cancer	Neutropenia (low white blood cell count)	12.1%
Opioids and related analgesics	Pain management	Constipation	7.4%
Glucocorticoids and synthetic analogues	Asthma	Chronic obstructive pulmonary disease with acute lower respiratory infection	6.9%
NSAIDs* (excluding salicylates)	Arthritis, pain management, inflammation	Gastric ulcer, chronic or unspecified with hemorrhage (bleeding)	4.9%
Beta-adrenoreceptor antagonists, not elsewhere classified	Heart failure, high blood pressure, angina (chest pain)	Bradycardia (low heart rate), unspecified	4.6%
Other (non-thiazide, low-ceiling) diuretics	Heart failure, high blood pressure	Hypo-osmolality and hyponatremia (low blood sodium)	3.6%
Benzothiadiazine derivatives (thiazide diuretics)	High blood pressure	Hypo-osmolality and hyponatremia (low blood sodium)	3.2%
Cardiac-stimulant glycosides and drugs of similar action (e.g. digoxin)	Heart failure, arrhythmia (irregular heartbeat)	Bradycardia (low heart rate), unspecified	3.1%
Antipsychotics	Symptoms of dementia, schizophrenia, bipolar disorder	Disorientation, unspecified	2.7%

Discharge Abstract Database and Hospital Morbidity Database, Canadian Institute for Health Information

Reason for such claim is to be searched in a narrow therapeutic window, especially in the case of vitamin K antagonists such as warfarin. Finding a proper warfarin dose schedule represents itself a clinical challenge and usually requires careful monitoring.

Other drugs generally associated with ADR-related hospitalizations were antineoplastic drugs and opioids and related analgesics. The most common diagnosis associated with ADR-related hospitalizations due to antineoplastic drugs was neutropenia, while the most common diagnosis associated with opioid-related hospitalizations was constipation.



adverse drug reactions – black, dose related therapeutic failure (defined as a lack of therapeutic effect ascribed to recent dose changes) – grey
Drug related admissions to medical wards: a populationbased survey – Hallas et al

A modified chart by Hallas et al, given above is demonstrating an age-specific incidence of drug related hospital admissions. Correlation between a patient's age and ADR-related hospitalization is more than obvious, taking in consideration all abovementioned risk factors being correlated with an old age. "Polypharmacy" is a common practice as increasing numbers of individuals live longer and a spectrum of possible therapeutic options for a large number of illness increases. A clear risk of ADRs in this situation should be considered in the context of interactions among prescribed drugs, inadequate monitoring, inappropriate drug selection, overdosage, underprescribing etc.

As one of the common causes of hospitalization ARDs lead to large costs to society. The cost of hospitalization is, however, only a part of the total costs as most adverse reactions barely come to clinical attention[13]. Thereforelimitations of tracking such records are more than obvious. Identifying ADRs retrospectively using administrative hospital data is likely to underestimate the prevalence of ADR-related hospitalizations, as necessary data may be missing or inaccurately recorded and thus precise records of such evidence are hard to find.

Conclusion: The prevalence of drug-related hospitalizations has been reported to be as high as 31%, with large heterogeneity between different studies, depending on various conditions[1-4]. Therefore, comprehensive knowledge on drug pharmacological characteristics, especially the ones causing the most adverse events, deprives us of meaningless quest for disease causing agents and needless prolongation of hospitalization.It is also believed that a good preventive strategy consisted of educational programmes, implementation of a good drug practice, risk groups identification and a proper running of evidence can bring desired improvement on this matter[4]. After analyzing all abovementioned facts and because of the substantial annual estimated cost of ADRs in modern world countries, one may conclude that avoidance of such burden is impossible, but to hone it down to the bare bones is definitely an economical imperative of a healthy and stable healthcare politics.

REFERENCE:

1. World Health Organization. *International Drug Monitoring: The Role of National Centres. Report of WHO Meeting*. Geneva, Switzerland: WHO; 1971. World Health Organization Technical Report Series, 498.
2. Patel H, et al. Trends in Hospital Admissions for Adverse Drug Reactions in England: Analysis of National Hospital Episode Statistics 1998-2005, *BMC Clinical Pharmacology*. 2007;7:9.
3. Patel P, Zed P. Drug-Related Visits to the Emergency Department: How Big Is the Problem?. *Pharmacotherapy*. 2002;22(7):915-923
4. Gautier S, Bachelet H, Bordet R, Caron J. The cost of adverse drug reactions. Expert Opin Pharmacotheraper 2003;4:319-26.
5. Wu C. Adverse Drug Reactions in the Emergency Department Population in Ontario: Analysis of National Ambulatory Care Reporting System and Discharge Abstract Database 2003-2007. *University of Toronto*. 2009.
6. Patel P, Zed P. Drug-Related Visits to the Emergency Department: How Big Is the Problem?.*Pharmacotherapy*. 2002;22(7):915-923.
7. Hogan DB, Juby A, Peterson M et al. Adverse Drug Reaction–Related Hospitalizations Among Seniors, 2006 to 2011. *The Canadian Institute for Health Information (CIHI) 2013*
8. Hanlon JT, et al. Suboptimal Prescribing in Older Inpatients and Outpatients. Journal of the American Geriatrics Society. 2001;49:200-209.
9. Ineke Neutel C, et al. Medication Use and Risk of Falls, *Pharmacoepidemiology and Drug Safety.* April, 2002:97-104.
10. Coupland C, et al. Antidepressant Use and Risk of Adverse Outcomes in Older People: Population Based Cohort Study. *BMJ*. August 2, 2011:343(d4451). accessed on August 15, 2011
11. Routledge P, O´Mahony S et al. Adverse drug reactions in elderly patients. *Br J Clin Pharmacol.* 2004 Feb; 57(2): 121–126.
12. Lundkvist J, Jönsson B, et al. Pharmacoeconomics of adverse drug reactions, *Fundam Clin Pharmacol.*2004 Jun;18(3):275-80.

P18 MULTIDISCIPLINERY APPROACH IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEAAND OBESETY HYPOVENTILATION SYNDROME

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Introduction
Obesity hypoventilation syndrome (OHS) is defined as obesity with alveolar hypoventilation present when all other causes of hypoventilation are excluded. 11-15% of all obese patients with obstructive sleep apnea (OSA) have hypercapnia. It is well known that obesity represent one of the risk factors for OSA.

A 38 years old patient was admitted for polysomnography. He presented with dyspnea during the sleep and sleepiness. He was hospitalised several times forloss of consciousnessand unstable blood pressure. Extremely obese, BMI 53 kg/m^2, with cardiac failure, smoker. Auscultatoryexamination revealeddecreased breathing with inspiratory cracks. TA 150/90 mmHg. Epworth score 16. Spirometry with restrictive values and pCO_2 6.9kPa in arterial blood gases.
Polysomnography was performed, patient had severe OSA with OHS, apnea-hypopnea index (AHI) 85/h, desaturation index (ODI) 104/h, average saturation 79%. Saturation below 90% was recorded for 62% of time.
Due to financial difficulties patient couldn'tobtaine Bi-level as recommended, he obtained CPAP instead.He was referred to endocrinologist and cardiologist.
First control was six months after. He was feeling better, lost 42kg, BMI 35.3kg/m^2. Epworth score 2. Still obese but without cardiac failure. Auscultatory findings were normal, TA 130/80 mmHg. Polysomnography was performed, AHI 11.3/h, ODI 12.2/h. Saturation 96%.

CONCLUSION
We report a case of patient with OSA and OHS who underwent CPAP therapy with diet and cardiological therapy. Results of polysomnography were significantly better after this treatment. Multidisciplinary approach in treatment of this disease is recommended and proved by these results.

P19 Is there any connection between obstructive sleep apnea and glycated hemoglobin?

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Introduction. Obstructive sleep apnea syndrome (OSAS) is an independent risk factor for cardiovascular and cerebrovascular morbidity and mortality. Intermittent nocturnal hypoxemia and sleep fragmentation are associated with insulin resistance and diabetes. Plasma glycated hemoglobin (HbA1c) concentration is an indicator of mean glycaemia over 2-3 month period (increased HbA1c may precede diabetes).
We aimed to assess relationships between plasma HbA1c and OSAS severity in subjects without diabetes.
Methods. Cross-sectional study of consecutive cases of a Clinical Hospital Center Bezanijska kosa in Belgrade, within one year.
A total of 35 patients were studied (26 men and 8 women), the mean age was 54.2±12.7 years. All of them had no self-reported prior diagnosis of diabetes mellitus. Patients have undergone a sleep study (overnight polygraphy) so as it was possible to calculate the AHI. Blood sampling was performed for analysis of HbA1c levels, elevated were regarded as HbA1c> 6%.
Summary statistics were calculated and statistical tests used were Spearman's correlation test and odds ratio (OR) and 95% confidence interval (CI95%).
Results. There is a correlation between the severity of OSAS demonstrated by apnea-hypopnea index (AHI/ h) and serum levels of HbA1c.
The results of the study showed a medium positive correlation between the variables AHI and HbA1c by Spearman's correlation coefficient =0.45, p=0.0075 and odds ratio: OR=1.08 (CI 95%=1.01 to 1.15; p=0.0165).
Conclusion.These data suggest that the severity of OSAS may be associated with abnormal HbA1c levels in non-diabetics. There is an association between the severity of OSAS, measured by AHI/h, and serum levels of HbA1c .
Well-defined protocol test enables the selection and follow-up of these patients in order to reduce cardiovascular risk.

P 20 Incidence of carotid artery stenosis in persons with heart diseases

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Abstract
Given the consequences of a stroke, it is extremely important to prevent it. In order to prevent it, it is necessary to detect persons with risk factors for stroke and to determine if there are any pathological changes in the blood vessels of the head and neck. Heart diseases are one of the known risk factors.
The aim of this paper was to detect pathological changes in the head and neck blood vessels of persons with heart diseases as the risk factor and to prevent a stroke from occuring.
Material and methods: We organised a recruitment of patients with heart disease and did the ultrasound examination of the blood vessels of the neck and head and determined if there was a narrowing in the aforementioned blood vessels.
Results: A total of 20 240 patients were examined, out of which 6164 (30.5%) suffered from heart disease. The degree of carotid circulation stenosis equal to or greater than 20% was found in 8493 (42%) of the examinees, out of which 3614 (42.6%) also suffered from heart disease. Conclusion: On the basis of previous studies and our research we have come to the conclusion that there is a statistical correlation between the degree of carotid artery stenosis and the presence of heart disease.

Introduction
Stroke is one of the most difficult and one of the most common diseases of modern man causing over 4.5 million deaths a year in the world. Due to the consequences of stroke (it is the third cause of death and the leading cause of disability of modern man), it is extremely important to prevent it. In order to prevent it, persons at risk for a stroke need to be detected and any pathological changes in the blood vessels of the head and neck determined since its treatment can lead to the prevention of stroke [2-7]. The incidence of stroke is higher in underdeveloped than in developed countries [8]. Discovery of the so-called asymptomatic carotid disease is of great importance for the ultrasound examination of the blood vessels. [9, 10]. Patients with atherosclerotic asymptomatic disease have an increased risk of heart attack and stroke [11]. Data on the prevalence of asymptomatic carotid occlusive disease vary according to different authors. The cause of this variation in results is a consequence of different study designs, the differences in determining the degree of the stenosis of the lumen to be included in the examination study, the use of screening techniques, recruitment of examinees, etc. [12]. In a study conducted by Korean authors the prevalence of asymptomatic carotid stenosis was analysed in 20 712 examinees. The examinees were recruited randomly. Elderly age, males, hypertension, diabetes and ischemic heart disease were significantly higher in groups of over 50% of lumen stenosis($p = 0.001$, 0.001, 0.001, 0.048 i 0.001, respectively) [13]. In a study of the prevalence of asymptomatic carotid occlusive disease of Ignat'ev 624 patients were examined. Carotid artery stenosis greater than 50% were statistically significantly more frequent in a group of examinees with risk factors [14]. Persons with symptomatic or asymptomatic heart disease, regardless of the blood pressure value, have twice the risk of development of ischemic brain stroke than persons without heart disturbances. A clear connection has been eastablished a long time ago between increased risk of ischemic brain stroke and the following heart diseases: atrial fibrillation, heart valve diseases, heart attack, coronary artery disease, heart defect failures, electrocardiographic evidence of left ventricular hypertrophy and mitral valve prolapse [15]. The presence of carotid stenosis greater than 50%,especially if it is a plaque with the signs of instabilities (intraplaque hemorrhage) is connected with unstable angina pectoris and the development of myocardial infarction [16]. As for the patients undergoing coronary artery bypass surgery, current guidelines recommend a carotid artery ultrasound. In Cheng's study, published in 2005, it was concluded that in 21.2% of patients undergoing bypass surgery, an ultrasound examination of the carotid arteries finds the stenosis lumens 50% and higher [17].In Johri's

study, both ultrasound of the carotid arteries and coronarography were performed at the same time in patients examined. It was established that the increased intima-media complex (0.82 mm and higher) and the presence of plaque were indicative of the presence of coronary artery stenosis [18]. The most recent study by Rossi et al. examines the correlation between the aortic valve sclerosis and carotid artery stenosis greater than 50%. Both the ultrasound of heart and the ultrasound of carotid arteries were performed in 1065 patients. Atherosclerosis of aortic valve diagnosed with a heart ultrasound is significantly connected with the carotid artery stenosis greater than 50%. It was also established that the atherosclerosis of aortic valve is an independent risk factor for cardiovascular disease [19]. Similar as in aortic valve sclerosis, the mitral valve sclerosis was also examined. Mostowik examined 127 patients with angiographically-proven occlusive coronary artery disease. After that, all patients did an ultrasound of heart and the carotid arteries. Joint calcifications of aortic and mitral valves were found in 59% of patients. Intima-media complex of carotid arteries was significantly higher in the group of patients with calcifications of mitral valves as well as in the group with joined calcifications of both mitral and aortic valves. It was concluded that the presence of mitral valve calcifications in coronary artery occlusive disease patients is in correlation with the development of an increased carotid artery intima-media complex [20]. The study of Sannin et al. proves the connection between the acute coronary syndrome, calcifications of mitral valves, occlusive atherosclerotic carotid artery disease and the occlusive atherosclerotic disease of the peripheral arteries [21]. There has been a development of ultrasound machines, which are getting better and better and therefore providing some new diagnostic possibilities. More and more authors are getting involved in research of new parameters during the ultrasound examination and also trying to determine a predictive value of those parameters. Moreo et al. did an analysis of some new ultrasound parameters during the echocardiography. The study included 457 patients. It was established that three factors have the predictive value in determination of occlusive coronary disease. These are as follows: semi-quantitative score of cardiac calcifications, intima-media complex of the carotid arteries and the blood flow velocity registered with Doppler in the left anterior descending coronary artery [22].

Aim of the paper

The aim of the paper is to detect pathological changes in blood vessels of the head and neck in persons with heart diseases as a risk factor for stroke and to prevent a stroke from occuring.

Material and methods

Professional lectures were organised and held for citizens and health personnel, as well as the media appearance, radio, TV and newspapers. Posters and leaflets were designed, printed and distributed and promotional contents placed on the bilboards. These marketing measurements were used to organise a recruitment of patients with heart diseases and we performed ultrasoundexaminations of blood vessels of the neck and head and also determined any potential narrowing in the blood vessels [23].

The results obtained were compared with another group of examinees who did not suffer from heart diseases. They were analysed and presented through the descriptive statistics and the adequate statistical tests and were graphically presented and edited in a software package for statistical analysis SPSS (Originally: Statistical Package for the Social Sciences, later modified to read Statistical Product and Service Solutions) [24].

During the ultrasound examination of the blood vessels of the neck and head General Electric Vivid 4 ultrasound machines with a linear and transcranial probe were used.

Results

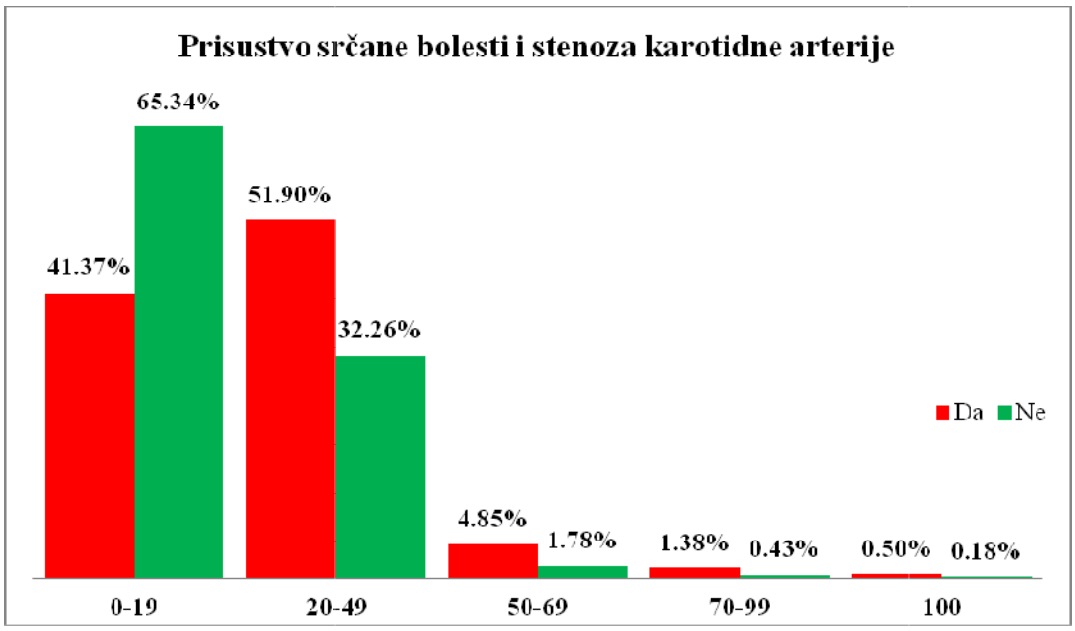
A total of 20 240 patients were examined, out of which 6164 (30.5%) suffered from heart disease. The degree of carotid circulation stenosis equal to or greater than 20% was found in 8493 (42%) of the examinees, out of which 3614 (42.6%) also suffered from heart disease. (Table 1.)

The use of χ^2 test showed highly statistically significant difference ($\chi^2 = 1011.257$, $p = 0.000$) in the presence of heart disease and the degree of carotid artery stenosis.

Table 1. The presence of heart disease in patients examined and the degree of carotid artery stenosis

Heart diseases		Carotid circulation (%)		Total
		0 - 19	≥ 20	
Yes	N	***2550***	***3614***	***6164***
		41.4%	58.6%	30.5%
		21.7%	42.6%	
No	N	***9197***	***4879***	***14076***
		65.3%	34.7%	69.5%
		78.3%	57.4%	
Total	N	***11747***	***8493***	***20240***
		58.0%	42.0%	100.0%

By observing the presence of heart disease in patients examined as well as the degree of carotid artery stenosis by the groups, it can be found that only in the group with the lowest stenosis (0 – 19%) there is, in terms of percentage, a higher number of patients (65.3% of the total number of patients with no heart disease) who did not have heart disease, compared with patients who did have heart disease (41.4% of the total number of patients with heart disease).
In slightly more than half (3199 or 51.9%) of patients who had heart disease, the degree of stenosis was from 20 to 49%. The degree of stenosis from 50 to 69% was registered in 299 (4.9%) of patients who had heart disease, while the degree of stenosis from 70 to 99% was registered in85 (1.4%) patients with heart disease. Complete obstruction was found in 31 (0.5%) patients with heart disease – Graph 1.



Graph 1. Presence of heart disease in patients examined and the degree of carotid artery stenosis (group)

Carotid artery stenosis ranged from 0 to 100%. The average stenosis of carotid circulation for all 20 240 examined patients was 18.36% (the average stenosis of carotid circulation in patients who had heart disease was 23.29%, while the average stenosis of carotid circulation in patients who did not have heart disease was 16.20%).The average stenosis of carotid circulation in patients whose stenosis of carotid circulation ranged from 0 to 19% was 9.73% (in patients who had heart disease the average stenosis of carotid circulation was 11.11%, while the average stenosis of carotid circulation was 9.36% in patients who did not have heart disease). The average stenosis of carotid circulation in patients whose stenosis of carotid circulation ranged from 20 to 100% was 30.29% (in patients who had heart disease the average

stenosis of carotid circulation was 31.89%, while the average stenosis of carotid circulation was 29.10% in patients who did not have heart disease).
By observing the degree of carotid circulation stenosis from 0 to 19% and by applying the Mann-Whitney U-test, highly statistically significant difference in the degree of carotid circulation stenosis in patients with heart disease was obtained (N = 2.550, Md = 12.00), compared with the patients with no heart disease (N = 9.197, Md = 10.00), z = -13.779, p = 0.000, r = 0.127. For the degree of stenosis of carotid circulation from 20 to 100% and by applying the Mann-Whitney U-test, highly statistically significant difference in the degree of carotid circulation stenosis in patients with heart disease was obtained (N = 3.614, Md = 27.00), compared with the patients with no heart disease (N = 4.879, Md = 25.00), z = -10.264, p = 0.000, r = 0.111.
By observing all patients and applying the Mann-Whitney U-test, highly statistically significant difference in the degree of carotid circulation stenosis in patients with heart disease was obtained (N = 6.164, Md = 21.00), compared with the patients with no heart disease (N = 14.076, Md = 14.00), z = -35,643, p = 0.000, r = 0.251.

Conclusion

Based on the previous studies and our research, we have come to the conclusion that there is a statistical correlation between the degree of carotid artery stenosis and the presence of heart disease.
The results obtained indicate that there is highly statistically significant difference between the degree of carotid circulation stenosis in patients with heart disease compared with those without heart disease.

Literature

[1] World Development Report: Investing in Health, New York: Oxford University Press; 1993.
[2] Bonita, R., Beaglehole, R., Asplund, K.: The worldwide problem of stroke. Current Opinion in Neurology, 1994; 7:5-10.
[3] Prati, P., Kanel, W. B., Sorlie, O., McNamara, P.: Asymptomatic carotid Bruit and risk of stroke: the Framingham study. JAM. 1981; 245:1442.
[4] Yasaka, M., Yamaguchi, T., Shichiri, M: Distribution of atherosclerosis and risk factors in atherotrombotic occlusion. Stroke. 1993; 24:206.
[5] Whisnant, J. P., Homer, D., Ingall, T. I. et al.: Duration of cigarette smoking is the strongest predictor of severe extracranial carotid artery atherosclerosis. Stroke. 1990; 21-707.
[6] Bogousslavsky, J., Van Melle, G., Despland, J. A. et al.: Alchohol consuption and carotid atherosclerosis in the Lausanne stroke registry. Stroke.1990; 21-715.
[7] Caplan, L. R., Gorelick, P. B., Hier, D. B.: Race, sex and occlusive cerebrovascular disease: A review. Stroke. 1986; 17:648.
[8] World Health Organisation: World Health Annual Statistics, Geneva: WHO; 1993.
[9] Camerlongo M, Casto L, Censori B, Servalli MC, Ferraro B, Mamoli A. Prognostic use of ultrasonography in acute non-hemorrhagic carotid stroke. Ital J Neurol Sci. 1996; 17: 215-8.
[10] Miljković S, Vujković Z, Žikić M, Đajić V, Račić D, Arbutina A. Senzitivnost i specifičnost transkranijalne Dopler sonografije u poređenju sa magnetno-rezonantnom i digitalno suptrakcionom angiografijom, Scripta Medica, 2006; 37 (1): 1-6.

[11] Bonaca MP, Beckman J. Management of asymptomatic carotid artery stenosis. Curr Treat Options Cardiovasc Med, 2013 Apr;15(2):252-63.
[12] M. de Weerd, J. P. Greving, B. Hedblad, M. W. Lorenz, E. B. Mathiesen, Daniel H. O'Leary, Maria Rosvall, M. Sitzer, E. Buskens, M. L. Bots, Prevalence of Asymptomatic Carotid Artery Stenosis in the General Population An Individual Participant Data Meta-Analysis. Stroke. 2010; 41: 1294-1297
[13] Roh YN, Woo SY, Kim N, Kim S, Kim YW, Kim DI. Prevalence of asymptomatic carotid stenosis in Korea based on health screening population. J Korean Med Sci, 2011 Sep;26(9):1173-7.
[14] Ignat'ev IM. Asymptomatic stenoses of carotid arteries. Angiol Sosud Khir., 2012;18(4):72-84.
[15] Arbutina M, Đajić V, Račić D, Miljkocić S, Vujković Z, Cerebrovaskularne bolesti, Medicinski fakultet u Banjaluci, Banjaluka, 2007.
[16]GaigalaiteV, OzheraiteneV, KalibateneD, LaurikenasK, SabaliauskeneZ. Association between structure of atherosclerotic plaques in carotid arteries and myocardial infarction. Kardiologiia. 2013;53(9):21-5.
[17]Cheng Y, Gao J, Wang J, Wang S, Peng J. Risk Factors for Carotid Artery Stenosis in Chinese Patients Undergoing Coronary Artery Bypass Graft Interventions. Medicine (Baltimore). 2015 Jul;94(28):e1119. doi: 10.1097/MD.0000000000001119.
[18]Johri AM, Behl P, Hétu MF, Haqqi M, Ewart P, Day AG, Parfrey B, Matangi MF. Carotid Ultrasound Maximum Plaque Height-A Sensitive Imaging Biomarker for the Assessment of Significant Coronary Artery Disease. Echocardiography. 2015 Jun 29. doi: 10.1111/echo.13007.
[19]Rossi A, Faggiano P, Amado AE, Cicoira M, Bonapace S, Franceschini L, Dini FL, Ghio S, Agricola E, Temporelli PL, Vassanelli C. Mitral and aortic valve sclerosis/calcification and carotid atherosclerosis: results from 1065 patients. Heart Vessels. 2014 Nov;29(6):776-83.
[20]Mostowik M, Palka I, Gajos G, Nessler J, Gackowski A. Mitral and aortic annular calcifications and cerebrovascular ischemic episodes in patients with coronary artery disease. Pol Arch Med Wewn. 2014;124(7-8):373-9.
[21]Sannino A, Losi MA, Giugliano G, Canciello G, Toscano E, Giamundo A, Scudiero F, Brevetti L, Scudiero L, Prastaro M, Perrino C, Perrone-Filardi P, Galderisi M, Trimarco B, Esposito G. Aortic and Mitral Calcification Is Marker of Significant Carotid and Limb Atherosclerosis in Patients with First Acute Coronary Syndrome. Echocardiography. 2015 Jun 29. doi: 10.1111/echo.13006.
[22] Moreo A, Gaibazzi N, Faggiano P, Mohammed M, Carerj S, Mureddu G, Pigazzani F, Muiesan L, Salvetti M, Cesana F, Faden G, Facchetti R, Giannattasio C, Rigo F. Multiparametric carotid and cardiac ultrasound compared with clinical risk scores for the prediction of angiographic coronary artery disease: a multicenter prospective study. J Hypertens. 2015 Jun;33(6):1291-300.
[23] Đajić V, Preradović Lj, Bogdanić D, Tomaš D, Rabi Žikić T, Obrazac nacionalnog projekta prevencije moždanog udara u ranom otkrivanju patoloških promjena na krvnim sudovima vrata i glave, Aktuelnosti, 2014; 22 (1-2): 7-14.
[24] Preradović Lj, Đajić V. Analitičko-statističke tehnike u savremenim istraživanjima, Arhitektonsko-građevinski fakultet, Banja Luka, 2011.

P21 Early signs of impaired systolic and diastolic function of the right ventricle in patients with OSA

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Heart failure increase morbidity and mortality of OSA. OSA can accelerate disease progression of current decompensated heart and leads to the worsening of heart failure and death.

Aim: The aim of our study was to assess whether obstructive sleep apnea (OSA) directly contributes to regional diastolic and systolic dysfunction of the right ventricle in patients with newly diagnosed OSA and normal ejection fraction.

Methods: 160 consecutive patients (mean age 58 ± 11) with newly diagnosed OSA who were questioned in our Reference Center for Sleep Apnea are included in the study, 65% of men and only 35% of women. The control group consisted of 78 healthy subjects. All patients with newly diagnosed OSA were without the existence of coronary disease. Patients were divided into groups: group I mild OSA-AHI 5-15/h; group II 16-30/h; group III AHI >30/h. Echocardiography was done to all patients in the standard left lateral position as recommended by the ASE. Pulsed Doppler tissue imaging (TDI) was done from the apical four-chamber section.

Results: 81 (51%) patients had newly diagnosed severe OSA. There was a statistically significant difference in diastolic diameter of right ventricle, FAC%, and late diastolic velocity A' were significantly less. No difference was found between OSA patients and control group global systolic function of the right ventricle measured with TAPSE. Regional systolic function of the right ventricle is not significantly different in relation to the degree of severity of OSA. The amplitude of the A' wave on the lateral tricuspid anulus was less in OSA patients compared to the control group. The degree of OSA affects the initial disturbance of diastolic function of the right ventricle (A’ wave on lateral tricuspid annulus). There was a statistically significant inverse relationship between AHI and amplitude A' waves septum and free wall (p <0, 05). The initial diastolic dysfunction of the right ventricle (A', IVA, FAC%) are correlated with the severity of OSA.

Conclusions: Disorders of breathing during sleep in OSA patients are associated with the development of subclinical systolic and diastolic dysfunction. Diastolic dysfunction of RV begins before systolic. Patients with OSA should make echocardiographic review at an early stage of the disease for appropriate treatment and prevention of development of heart failure.

P22 Masked hypertension in patients with obstructive sleep apnea – OSA

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The relationship between OSA and hypertension is well documented, especially when it comes to nighttime hypertension. Studies have shown a connection between severe OSA with fatal and non-fatal cardiovascular events and all deaths. Masked hypertension is pressure that occurs during ambulatory blood pressure measurements while maintaining the established hypertension in more measurements in ambulatory conditions. The prevalence of masked hypertension are on average about 13% (range 10-17%), greater than 135/85 mmHg.

AIM: The aim of our study was to determine the prevalence of hypertension in patients with newly diagnosed OSA.

METHODS: 81consecutive patients (mean age 56.7) with newly diagnosed OSA and who were being questioned in our Reference Center for Sleep Apnea are included in the study. Sixty-five percent of men and only 35% of women. According to previous medical documentation, ambulatory measurements and pressure measurements before and after polysomnography studies, 59.3% of patients were diagnosed with hypertension (> 14o / 90 mmHg). 33 patients without previously diagnosed hypertension, are included in 24h ambulatory blood pressure monitoring. We analyzed the occurrence of high blood pressure according to the European Guide for hypertension, the relationship between daytime and night-time pressure, "Dipper and nondipper".

RESULTS: 22 patients (66.7%) of the test group were diagnosed as hypertensive. This means that even in patients with de novo diagnosis of OSA, with no previous medical data on hypertension and with normal hospital values of arterial blood pressure, had masked hypertension. Episodes of increased systolic and diastolic blood pressure were significantly more frequent during the night ($p > 0.05$). All patients with masked hypertension were divided into groups according to severity of OSA by AHI index. 80% of patients with OSA and masked hypertension had severe OSA, which was highly statistically significant ($p < 0.001$). This means that even in patients with newly diagnosed OSA, with no previous medical data on hypertension and normal hospital values of arterial pressure, 27.6% have masked hypertension. "Nondipping" to 27.16% with newly detecting hypertension.

CONCLUSIONS: In the group of patients who were tested, high pressure existed at night in 67% of patients. As the masked hypertension is very common in patients with OSA, in the evaluation of the cardiovascular risk profile of patients with OSA ambulatory blood pressure measuring during 24 hours needs to be done for the prevention of cardiovascular complications.

P 23 RELATION OF DIASTOLIC FUNCTION AND THE DEGREE OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH OSA

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Introduction: According to current knowledge OSA in a unique way initiates a series of pathophysiological changes leading to acute and chronic cardiovascular disorders. Hypoxia and hypercapnia, compensatory activation of the sympathetic nervous system and oxidative stress leads to endothelial disfunction and myocardial ischemia.

AIM: The aims of the study were to examine the relationship of diastolic function and the degree of endothelial dysfunction in patients with the syndrome of cessation of breathing during sleep.

Methods: 81 consecutive patients (mean age 56.7) with newly diagnosed OSA who were being examined in our Reference Center for Sleep Apnea are included in the study. All studied individuals have undergone the complete night polysomnography and complete standard transthoracal echocardiographyc and Doppler examination, as well as the pulse tissue Doppler (TDI) examination. The examination of the endothelial dysfunction degree by the method of brachial artery vasodilatation caused by the flow was conducted in all studied individuals of OSAS group, with and without diabetes, and in individuals of control group.

Results: We detected the relation of the breathing syndrome cessation severity degree during sleep and the initial systolic dysfunction of left chamber (S'Sm, S'Lm) and diastolic function of both chambers (E'Sm, E'Lm, E'Lt). We found the statistically important correlation between FMD and initial diastolic dysfunction of heart chambers (E'Sm, E'Lm E'Lt) and initial longitudinal systolic dysfunction of left chamber (S'Lm). There was no established correlation of FMD and systolic longitudinal function of right ventricle.

Conclusions: There is a correlation between diastolic dysfunction and endothelial dysfunction in patients with the syndrome of cessation of breathing during sleep. Disorder of breathing during sleep due to obstruction of the upper airways (OSA) is independently associated with these changes in the function of heart chambers.

Contents:

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