Joint meeting

The 9th International Symposium on Neurocardiology

NEUROCARD 2017

The 8th International Symposium on Noninvasive Electrocardiology

SCIENTIFIC PROGRAM
&
BOOK OF ABSTRACTS

Editors:
Professor Dr. Branislav Milovanovic
Associate Professor Dr. Cristian Podoleanu

September 22nd – 23rd, 2017
Crowne Plaza, Belgrade, Serbia

Joint meeting

The 9th International Symposium on Neurocardiology

NEUROCARD 2017

The 8th International Symposium on Noninvasive Electrocardiology

September 22nd — 23rd, 2017
Crowne Plaza, Belgrade, Serbia

Organized by:

Serbian Neurocardiological Society, SNCS

Serbian Autonomic Society, SAS

Under auspices:

International Society for Holter and Noninvasive Electrocardiology (ISHNE)
European Academy of Science and Arts

Meeting endorsed by:

International College of Nutrition
International College of Cardiology
Russian Society for Holter Monitoring and Noninvasive Electrophysiology, ROHMINE
Russian Society of Cardiologists
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 Research (SAATVBR)
Cardiology Society of Serbia, CCS
University of Belgrade, School of Medicine
Serbian Medical Society
Noninvasive Electrocardiology Section PTK
Clinical Hospital Center Bezanijska Kosa
Ministry of Health Republic of Serbia
Ministry of Science and Technological Development, Republic of Serbia

Dear colleagues,

It is our great pleasure to welcome you to our Joint meeting of the 9th International Symposium on Neurocardiology, (Neurocard 2017) and the 8th International Symposium on Noninvasive Electrocardiology. The meeting will be held in Belgrade on September 22nd – 23rd 2017 and organized by Serbian Neurocardiological Society and Serbian Autonomic Society, under auspices of International Society for Holter and Noninvasive Electrocardiology (ISHNE) and Eurpean Academy of Science and Arts.
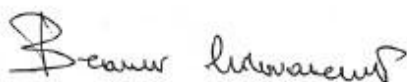
The previous NEUROCARD meetings and Joint Meeting on Noninvasive Electrocardiology, included participation of scientists from whole world, Europe and region and organized under the auspices of several international organizations. In order to improve scientific collaboration between experts from similar disciplines we decided to organize joint meeting of Neurocard 2017 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

Dragana Bajic
Nina Japundzic-Zigon
Vesna Bisenic
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Zorica Rasic Milutinovic
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Ljudmila Stojanovic

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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
Artificial Intelligence

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
Placebo effect
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   Posters will be published in Abstract book

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 and
                            around the Registration area. The working hours of the exhibition are the same as the Symposium working hours.

Opening ceremony   Crowne Plaza, Belgrade, Serbia

Gala dinner   Restaurant at Hotel Park, Belgrade, Serbia

SCIENTIFIC PROGRAM

NEUROCARD 2017 – FINAL PROGRAM

22nd –23rd September 2017, Crowne Plaza, Belgrade, Serbia

September 22nd

08:00-09:00   Registration

09:00-09:30   Opening Ceremony

Branislav Milovanovic
President of Serbian Neurocardiological Society, Chairmen of the meeting
Belgrade, Serbia

Zorica Rasic Milutinovic
President of Serbian Autonomic Society
Belgrade, Serbia

Nina Japundzic-Zigon
President of Serbian Working Group of Basic Neurocardiology
Belgrade, Serbia

Vesna Baltezarevic
Representative of European Academy of Science and Arts
Belgrade, Serbia

Nebojsa Lalic
Dean of Medical faculty, University of Belgrade
Belgrade, Serbia

Marija Zdravkovic
Director of University Clinical Center Bezanijska Kosa
Belgrade, Serbia

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

Thomas Klingenheben
Member of ISHNE board
Bonn, Germany

Emanuela Locati
Member of ISHNE board
Milan, Italy

Victor-Dan 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

Venevtseva Yulia
Tula State University
Tula, Russia

Tatiana Mironova
Yekaterinburg, Russia

09:30-10:30 Sudden Cardiac Death: Risk Stratification
Chairs: Branislav Milovanovic (Belgrade, Serbia), Thomas Klingenheben (Bonn, Germany)

09:30-09:50 Artificial inteligence and sudden death risk stratification:new challenge in science?
Branislav Milovanovic, Drasko Furundzic, Tatjana Gligorijevic, Zoran Matic
(Belgrade, Serbia)

09:50-10:10 - Inappropriate Sinus tachycardia - when is it "real"? How - if at all - should it be "treated"?
Thomas Klingenheben
(Bonn, Germany)

10:10-10:30 Role of prolonged ECG monitoring n the diagnosis of infrequent arrhythmic events
Emanuela Locati
(Milan, Italy)

10:30-10:45 Remote Monitoring of cardiac implantable devices (CIEDs): telemedicine for everyone?

Thomas Klingenheben

(Bonn, Germany)

10:45-11:00 Risk score to assess mortality risk in patients undergoing transvenous lead extraction

Ewa Topolska, Andrzej Kutarski, Andrzej Oszczygieł, Beata Mańkowska-Załuska, Michał Chudzik, Iwona Cygankiewicz, Jerzy K. Wranicz

(Lodz, Poland)

11:00-11:15 Mobile heart health platform: ECG for everybody

Stevan Jokic, Ivan Jokic, Branislav Milovanovic

(Belgrade, Serbia)

11:15-11:30 The role of CMR in the differential diagnosis of cardiomyopathies

Zdravković M, Hinić S, Popović M, Prijic S, Saric J, Djokovic A, Bisenic V , Gavrilovic, Mudrenovic V, Klasnja S, Omerovic A , Milovanovic B

(Belgrade, Serbia)

11:30-11:50 Coffee break

11:50-12:20 Lecture: Polypill concept in the prevention of atherosclerosis: does it work?

Miodrag Ostojic

(Belgrade, Serbia)

12:20-12:40 What new in the problem of sudden cardiac deaths in athletes

Leonid Makarov

(Moscow, Russia)

12:40-13:00 New Mechanisms of Perinatal Hypoxia and Perspectives of Pathogenesis-oriented Treatment

Balykova L.A., Ledyajkina L.V., Trofimov V.A., Vlasov A.P., Motorkina A.S.

(Saransk, Russia)

13:00-13:15 The case of spontaneous occlusive thrombosis in the soccer player with hereditary predisposition in a hot humid climate

Pavlov V.I., Gvinianidze M.V., Rezepov A.S., Odzhonikidze Z.G., Badtieva V.A., Yardoshvili A.E.

(Moscow, Russia)

13:15-14.10   Stroke-Risk Factors
Chairs: Ludovit Gaspar (Bratislava, Slovak Republic), Jorge Ignacio Celis Mejia (Medellin, Colombia)

13:15-13:35 Heart and brain: White matter disease, vascular dementia, and its risk for anticoagulation: a review

Jorge Ignacio Celis Mejia

(Medellin, Colombia)

13:35-13:55 Risk factors in stroke in real clinical practice

Ludovit Gaspar, Matej Bendzala, Andrea Komornikova, Iveta Gasparov, Veronika Vestenicka

(Bratislava, Slovak Republic)

13:55-14:10 Transient ischemic attack can be followed by stress induced Takotsubo cardiomiopathy

Marija Zdravkovic, Sasa Hinic, Vladan Mudrenovic, Jelena Saric, Nebojsa Ninkovic, Aleksandra Djokovic, Sergej Prijic, Goran Koracevic, Zoran Andric, Bogdan Crnokrak, Dragan Lovic, Branislav Milovanovic

(Belgrade, Serbia)

14:10-15:00 Lunch

15:00-16:30   Basic Neurocardiology
Chairs: Nina Japundzic-Zigon (Belgrade, Serbia), Dragan Djuric (Belgrade, Serbia),
Bassim I Mohammad (Al Qadisiyah, Iraq)

15:00-15:20 Subchronic Methionine load affected vitamin B12 level and Von Willebrand factor activity in blood of male Wistar rats and induced myocardial haemorrhagia

Djuric D, Micovic Z, Stevanovic A, Djuric M, Obrenović R, Labudovic Borovic M

(Belgrade, Serbia)

15:20-15:40 Pharmacological Protection Against Sepsis Associated Cardiac Dysfunction: Emerging Targets And Strategies

Bassim I. Mohammad

(Al Qadisiyah, Iraq)

15:40-15:55 Vasopressin V1AR expression in the paraventricular nucleus of the hypothalamus in borderline hypertension

Bojana Savić, Olivera Šarenac, Andrew Martin, David Murphy, Nina Japundžić-Žigon

(Belgrade, Serbia)

15:55-16:10 Statins in cardiorenal syndrome: why not?

Z. Todorović

(Belgrade, Serbia)

16:10-16:25 Significance of determination of BCL-2 and CASPASE-3 activity in ishemic heart disease patients

T. Ristic, B.V. Djordjevic, M. Deljanin-Ilic, P. Vlahovic., V. Cosic

(Nis, Serbia)

16:30-18:00 Genetic Aspects in Neurocardiology

Chairs: Zaklyazminskaya Elena (Moscow, Russia), Aleksandra Stankovic (Belgrade, Serbia),
Maja Zivkovic (Belgrade, Serbia)

16:30-16:50 Splicing mutations causing unusual early-onset dominant MYH7-related myopathy

 Zaklyazminskaya E.V., Rogozhina Y.A., Filatova A.Y., Polyak M.E., Skoblov M. Y.

(Moscow, Russia)

16:50-17:10 Prevalence of dilated cardiomyopathy in the Russian patients with Marfan Syndrome

Rumyantseva V.A., Rogozhina U.A., Bukaeva A.A., Charchyan E. R, Zaklyazminskaya E.V.

(Moscow, Russia)

17:10-17:30 Cardiovascular genomics: avenue of approach to the personalized medicine

Zivkovic M, Djuric Delic T, Alavantic D, Stankovic A.

(Belgrade, Serbia)

17:30-17:45 Chromosomal region 9p21 in cardiovascular disease: Results from Serbian population

Zivotic I, Stankovic A, Alavantic D, Zivkovic M.

(Belgrade, Serbia)

17:45-18:00 The association of AGTR1, AGTR2 and SCN5A genetic variants with arrhythmia in patients after the first myocardial infarction. Preliminary results of a prospective study

Kolić I., Đurić Delić T., Zivković M., Alavantić D., Dekleva M .Markovic Nikolic N., Stanković A.

(Belgrade, Serbia)

18:00-18:15 Case report of patient with psoriasis during aplication of programming placebo aqueous solution with biochemical and XRD examination of serum samples
D. Jovanovic, B. Milovanovic, D. Zagorac, N. Stankovic, J. Zagorac, B. Babic, B. Matovic
(Belgrade, Serbia)

18:15-18:30 Quantum mechanics combined with XRD investigations of Sucrose as placebo used in medicine
D. Jordanov, D. Zagorac, J. Lukovic, J. Zagorac, B. Matovic, M. Rosic, B. Milovanovic
(Belgrade, Serbia)

18:30-18:45 The cytotoxic effect of Achillea S., L., Rosmarinus officinalis L. and Juniperus communis L. on squamous and basal cell carcinomas cells
Miloš Lazarević, Maja Milošević, Tatjana Gligorijević, Slobodan S. Petrović, Nada Petrovic, Branislav Milovanović
(Belgrade, Serbia)

20:00 Gala dinner, Restaurant Hotel Park

September 23rd

09:00-09:25 Heart-brain interactions: infectious, congenital heart disease and heart transplant: Beyond embolic sources
Jorge Ignacio Celis Mejia
(Meddelin, Colombia)

09:25-09:50 Pathogenesis of Parkinson's disease and microbiota - could we be wrong all the time?
Ilić TV
(Belgrade, Serbia)

09:50-10:10 Prognostic value of detrended fluctuation analysis in diferent disease states
Sanja Pavlovic, Dragana Bajić, Branislav Milovanovic, Zorica Stevic
(Belgrade, Serbia)

10:10-10:30 Cardiac involvement in dystrophinopathies

Osman Sinanovic

(Tuzla, Bosnia and Herzegovina)

10:30-11:00 Coffe Break

11:00:12-30 Autoimmune Disease in Neurocardiology
Chairs: Ljudmila Stojanovic (Belgrade, Serbia), L.Kalashnikova (Moscow, Russia)

11:00-11:20 Skin manifestations as independent predictors of stroke and total cardiopulmonal risk: a multidisciplinary study based on the Serbian national APS registry

Stojanovich Ljudmila, Djokovic Aleksandra, Banicevic Slavica, Bisenic Vesna, Danica Lisulov, and Zdravkovic Marija

(Belgrade, Serbia)

11:20-11:35 Sneddon syndrome (SS) and antiphospholipid syndroma (APS)

L.Kalashnikova, L.Stojanovich, L.Dobrynina, E.Alexandrova, A.Novikov, E.Nassonov, J.Chapman, ZS Alekberova

(Moscow, Russia, Belgrade, Serbia, Tel Aviv, Izrael)

11:35-11:45 Changing the conceptof antinuclear autoantibofies screening:a new laboratory algorithm in diagnosis of szstemic autoimmune rheumatic diseases

Dolores Pérez , Fernando Lozano, Boris Gilburd, Laura Naranjo, Manuel Serrano, Ora Shovman, Luis Morillas, Yehuda Shoenfeld, Antonio Serrano

(Madrid, Spain, Tel Aviv, Izrael)

11:45-11:55 Effects of training program on quality of life and fatigue in patients with systemic lupus erythematosus

G. Bogdanovic, L.J. Stojanovich

(Belgrade, Serbia)

11:55-12:05 Impact of valvular changes on cerebrovascular manifestations in patients with primary and secondary antiphospholipid syndrome

Djokovic A, Stojanovich L, Banicevic S, Smiljanic D, Zdravkovic M

(Belgrade, Serbia)

12:05-12:20 Autonomic nervous system activity and chronic autoimmune thyroiditis – is there a missing link?

Svetlana Jelić, Branislav Milovanović

(Belgrade, Serbia)

12:20-12:30 Brain-reactive autoantibodies from patients with Neuropsyhiatric Systemic Lupus alter calcium homeostasis in cultured hippocampal neurons

Bijelić D., Milošević M., Stojanović Lj., Šakić B., Andjus P.R.

(Belgrade, Serbia, Hamilton, Canada)

12:30-14:15 Heart Rate Variability
Chairs: Victor-Dan Moga (Timisoara, Romania), Tatiana Mironova (Yekaterinburg, Russia), Yulia Venevtseva (Tula, Russia)

12:30-12:45 Coronary artery disease and clinical neurocardiology

Tatiana Mironova, Vladimir Mironov

(Yekaterinburg, Russia)

12:45-13:00 Analysis of body posture changing, painfulness, regulation of the heart and breath during night sleep in experiment with a 5-day dry immersion

A.V.Slonov,,R.M.Baevsky.,I.V.Rukavishnikov.,L.E.Amirova,c.McGregor.,A.Zhmurchak., E.Yu.Bersenev

(Moscow, Russia)

13:00-13:15 Conventional and Complexity Analysis of RR Intervals Dynamics during Head-up Tilt Test

Ioana Cotet, Victor-Dan Moga, Andrei Beceanu, Mirela Lupu, Mariana Moga, Florin Vidu, Ciprian Rezus, Attila Frigy, Rodica Avram

(Timisoara, Romania)

13:15-13:25 Clinical, psychological characteristics and heart rate variability of persons with undifferentiated connective tissue dysplasia

Akimova A.V., Mironov V.A., Tarasova E.V., Palabugina P.A., Talankina A.A.

(Yekaterinburg, Russia)

13:25-13:35 The Chernobyl accident: 31 years later

Eliseev D., Venevtseva Yu., Melnikov A., Pomogaev I.

(Tula, Russia)

13:35-13:45 Heart rate variability and circadian rhythmicity in modern students

Kazidaeva E., Venevtseva Yu., Fedotova A.

(Tula, Russia)

13:45-13:55 Heart rate variability and academic performance in medical school

Putilin L., Venevtseva Yu., Melnikov A.

(Tula, Russia)

13:55-14:00 The relationship between subjective health evaluation and heart rate variability in students with different habitual physical activity

Nikolai Tcarev, Yulia Venevtseva, Aleksandr Melnikov

(Tula, Russia)

14:00-14:45 Lunch

14:45-15:05 Heart rate and blood pressure dynamics in hypertensive patients
Victor-Dan Moga, Ioana Cotet, Andrei Beceanu, Mariana Moga, Florin Vidu, Attila Frigy, Rodica Avram
(Timisoara, Romania)

15:05-15:25 Autonomous nerve system changes during deep SCUBA dive
Ante Obad, Tatjana Gligorijević, Duška Glavaš, Igor Glavičić, Maja Valić, Branislav Milovanović, Zoran Valić
(Split, Croatia)

15:25-15:45 The prevention of arrhythmias: HISPA program
Nebojsa Tasic
(Belgrade, Serbia)

15:45-16:00 Comorbidities associated with gender in patients with heart faillure with preserved and mindrange ejection fraction
A.I.Milaschenko, A.N. Andreev, M.S. Ibragimov, A.V.Akimova
(Yekaterinburg, Russia)

16:00-16:15 Data Preprocessing for ECG Signal Classification using Artificial Neural Networks
Slobodanka Stanojević Terzić, Zoran Ševarac, Tatjana Gligorijević, Branislav Milovanović
(Belgrade, Serbia)

16:15-16:30 Artificial neural networks for removing artifacts from heart rate variability signals
Zoran Matić, Tijana Bojić, Dejan Raković, Branislav Milovanović
(Belgrade, Serbia)

16:30-16:45 Benefits and risks of artificial intelligence in complex biomedical systems analysis: a review
Tatjana Gligorijevic, Branislav Milovanovic
(Belgarde, Serbia)

16:45-17:00 The artificial intelligence and cardiac autonomic patterns in patients with syncope
Branislav Milovanovic, Drasko Furundzic, Tatjana Gligorijevic, Zoran Matic
(Belgrade, Serbia)

17:00-18:00 Cardionephrology and Methabolic Neuropathies
Chairs: Natasa Markovic (Belgrade, Serbia), Zorica Rasic Milutinovic (Belgrade, Serbia)
Gordana Pekovic Perunicic (Belgrade, Serbia)

17:00-17:15 Optimal screening of cardiovascular system in renal patients at the begining of the dialysis

Nataša Marković-Nikolić, Milica Dekleva, Tatjana Damjanović, Goran Lončar, Milan Brajović, Maja Despotović-Nikolić, Nikola Dodić, Ana Čolić-Ozmo, Nada Dimković
(Belgrade, Serbia)

17:15-17:30 Analysis of 24-hour blood pressure and arterial stiffness in patients before and after renal transplantation

Minyukhina I. E., Kashaeva A. I., Posokhov I. N., Struchkov P. V.
(Nizhniy Novgorod, Russia)

17:30-17:45 Assotiation between HRV parameters and mortality in HD patients

Pekovic-Perunicic G., Rasic-Milutinovic Z., Milovanovic B.
(Belgrade, Serbia)

17:45-18:00 Association of Diabetes Related Complications with Heart Rate Variability in Type 2 diabetic patients

Zorica Rasic-Milutinovic, Branislav Milovanovic, Dragana Jovanovic
(Belgrade, Serbia)

18:00 -19.25 Biosignal Processing
Chairs: Dragana Bajic (Belgrade, Serbia), Konstantinos Katzis (Cyprius)

18:00-18:20 Totally Connected Healthcare with TV White Spaces

Konstantinos Katzis, Richard W. Jones and Georgios Despotou
(Cyprus)

18:20-18:35 Multivariate visualization of dependency structures via copula tomography

Sanja Milutinović-Smiljanić, Tamara Škorić, Nina Japundžić-Žigon, Dragana Bajić
(Novi Sad, Serbia)

18:35-18:50 Approximate entropy of PI-transformed signals

Tamara Škorić, Branislav Milovanović, Nina Japundžić-Žigon, Dragana Bajić
(Novi Sad, Serbia)

18:50-19:05 Copula as a quantifier of SBP-RR dependency measure in patients with diabetes

Sladjana Jovanović, Tamara Škorić, Zorica Rasić, Branislav Milovanović, Dragana Bajić
(Novi Sad, Serbia)

19:05-19:15 Effects of ranolazine on ultra low frequency heart rate fluctuations assessed from very shortterm recordings

Miljan Petrovic, Miljan Jeremić

(Nis, Serbia)

19:15-19:20 Task Force® Monitor signals in patients with Lyme disease

Katarina Ćoćić, Natasa Korčok, Vesna Kokotović, Tamara Škorić, Branislav Milovanović, Dragana Bajić

(Novi Sad, Serbia)

19:20-19:25 On error statistics in Portapres® signals

Marko Mozetić, Jelena Antelj, Katarina Otašević, Tamara Škorić, Branislav Milovanović, Dragana Bajić

(Novi Sad, Serbia)

19:30-19:45 Closing of meeting

POSTERS

1. Heart from the perspective of Neurocardiology

Zoran Matić, Tijana Bojić, Ana Žikić, Dejan Raković, Branislav Milovanović

(Belgrade, Serbia)

2. Heart rate variability in young men with autonomic dysfunction syndrome

A.V.Akimova, V.A.Mironov, A.I.Milaschenko

 (Yekaterinburg, Russia)

3. Changes in Raman spectra of programmed placebo samples

Hadžić, N. Romčević, B. Milovanović

(Belgrade, Serbia)

4. The response of the cardiovascular system to short-term and long-term methods to improve the performance of trained athletes

E.Yu. Bersenev, A.V. Suvorov, A.A. Gurov

(Moscow, Russia)

5. Theoretical and experimental investigation of pure water and aqueous solutions as placebo, and water based biological samples

D. Jovanovic, D. Zagorac, M. Prekajski, J. Zagorac, B. Milovanovic, B. Matovic

(Belgrade, Serbia)

6. Exposure of chronically stressed rats to treadmill running induces potentially positive adaptations of the catecholaminergic turnover in stellate ganglia

Ljubica Gavrilović, Vesna Stojiljković, Nataša Popović, Snežana Pejić, Ana Todorović, Ivan Pavlović and Snežana B. Pajović

(Belgrade, Serbia)

7. Changing the concept of antinuclear autoantibodies screening: a new laboratory algorithm in the diagnosis of systemic autoimmune rheumatic diseases

Dolores Pérez , Fernando Lozano, Boris Gilburd, Laura Naranjo, Manuel Serrano, Ora Shovman, Luis Morillas, Yehuda Shoenfeld, Antonio Serrano

(Madrid, Spain)

8. Direct oral anticoagulants in atrial fibrillation in elderly patients – time for the new challenges

Cejović N , Hinic, Milovanovic B, Zdravkovic M

(Belgrade, Serbia)

9. Stent loss during PCI and successful recovery using new approach

Sasa Hinic, Slobodan Klasnja, Zoran Andric, Bogdan Crnokrak, Branislav Milovanovic, Marija Zdravkovic

(Belgrade, Serbia)

10. Cerebrolysin in the treatment of acute ischemic stroke

Miljkovic S., Djajic V., Perišić M.

(Banjaluka, Republic of Srpska)

11. Case with lethal outcome at autonomic cardioneuropathy

Vladimir Mironov, Tatiana Mironova, Olga Nohrina, Elena Kuvatova

(Yekaterinburg, Russia)

12. Hypertension disease, heart rate variability. Some clinical possibilities

Vladimir Mironov, Tatiana Mironova, Branislav Milovanovic, Olga Nicolaenko

(Yekaterinburg, Russia)

13. Autonomic deregulation of sinus heart node pacemaker activity at occupational diseases

T. Mironova, T.Obuhova, O. Shmonina, E. Mordas

(Yekaterinburg, Russia)

14. Circadian chronology and number of deaths from acute coronary syndrome and acute myocardial infarction (a fragment of the study "RACSMI-Uz")

Nagaeva G.A., Mamutov R. Sh.

(Tashkent, Uzbekistan)

15. Low systolic arterial pressure in the evaluation of the frequency of registration of heart rhythm disturbances and ST-displacement according to the data of ambulance medical care (Fragment of the study RACSMI-Uz)

Nagaeva G.A., Mamutov R. Sh.

(Tashkent, Uzbekistan)

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BOOK OF ABSTRACTS

ORAL PRESENTATIONS

O1 Inappropriate Sinus tachycardia - when is it "real"? How - if at all - should it be "treated"?

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Inappropriate sinus tachycardia (IST) is an disorder characterized by persistent increased sinus rate or inadequate heart rate increase with minimal physical effort. Caused by an intrinsic impairment of sinus node function (increased SN automaticity) – often in combination with autonomic dysfunction, patients with IST report palpitations and symptomatic tachycardia. IST is a diagnosis of exclusion, particularly it is necessary to rule out potential causes of clinically adequate tachycardia.

Rate control therapy should be restricted to highly symptomatic patients whereas treatment of asymptomatic patients is highly controversial. Pharmacologically, ß blockers remain drugs of first choice. Recently, treatment with the If blocker Ivabradin – alone or in combination with ß blockers- has been shown to be effective as well. Sinus node modification by catheter ablation should be avoided due to very limited efficacy.

O2 Role of prolonged ECG monitoring in the diagnosis of infrequent arrhythmic events

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Electrocardiographic Ambulatory Monitoring (AECG) usually referred as "Holter" monitoring, now represents an essential tool in the diagnostic evaluation of patients with cardiac arrhythmias. From the first introduction in 1957, long-term monitoring systems underwent major technologic evolution, both for the acquisition and for the analysis of the ECG signals [1-2].

According to the "ACC/AHA Practice Guideline for Ambulatory Electrocardiology", released in 1999, AECG monitoring is recommended for the clinical evaluation of symptoms attributed to cardiac arrhythmias [1]. Very recently a new document entitled "ISHNE-HRS Expert Consensus Statement on Ambulatory ECG and External Cardiac Monitoring/Telemetry", has been developed in collaboration and endorsed by the International Society for Holter and Noninvasive Electrocardiology (ISHNE) and the Heart Rhythm Society (HRS), with the purposesto review how contemporary AECG devices acquire and process ECG signals and how they should be interpreted, the appropriate utilization of these devices in the management of cardiovascular disease; and how to promote standards that will improve the accuracy and appropriate use of the AECG in clinical practice [3].

Today AECG is typically used to evaluate symptoms such as syncope, dizziness, chest pain, palpitations, or shortness of breath, that may correlate with intermittent cardiac arrhythmias. Additionally, AECG is used to evaluate patient response to initiation, revision, or discontinuation of arrhythmic drug therapy, and to assess prognosis or risk of arrhythmias in specific clinical conditions, such as patients at risk of ventricular arrhythmias and sudden death, and in the evaluation of permanent or paroxysmal atrial fibrillation, and for the investigation of unexplained syncope or cryptogenic stroke [1-5].

Because certain rhythm abnormalities may be infrequent and paroxysmal, and may occur only during sleep or in association with mental, emotional, or exercise-induced perturbation in cardiac function, AECG is recorded over longerperiod of time, originally lasting 24 hours and now expanding up to several weeks and even months.
New algorithms for continuous beat-to-beat ECG monitoring, automatic arrhythmia detection and wireless transmission of data in near real-time, highly improved the ECG signals quality for very long-term recordings (up to one month) and the diagnostic yield for infrequent cardiac arrhythmias [3,5]. New wireless electrodes systems, such as patches, vest or belt greatly increased the tolerability, quality and feasibility of prolonged AECG, which is particularly useful in conditions of infrequent symptoms, such as unexplained syncope, palpitation or cryptogenic stroke.

Newer digital recorders will also have the capability for multichannel simultaneous digital acquisition, allow the recording of different biological signals by appropriate sensors, such as respiratory frequency, peripheral oxygen tension, arterial pulse pressure, EEG, and others. The estimation of respiratory signals together with the oxygen saturation and respiratory movements will allow an easy detection of the sleep apnea syndrome, and correlates it with arrhythmic events. This will transform conventional AECG in "ambulatory policardiography", allowing the comprehensive evaluation of patients with complex disorders, such as heart failure or sleep apnea syndromes. The comprehensive analysis of several parameters obtained from long-term Holter monitoring can provide a global evaluation of the cardiac substrate and of the risk of arrhythmogenesis in the individual patient. Thus, Holter analysis becomes a real "*noninvasive electrophysiological test*", to identify potential risk factors for life-threatening cardiac arrhythmias.

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O3 Remote Monitoring of cardiac implantable devices (CIEDs): telemedicine for everyone?

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Remote Monitoring (RM) of CIEDs has become a mainstay at least in patients with ICD and / or CRT devices. Several studies have shown that RM is able to reduce both appropriate and inappropriate shocks. Also, device safety can be enhanced by RM, since potential lead complications can be detected earlier. Furthermore, early detection of atrial fibrillation by RM will result in early initiation of AF-targeted therapy including oral anticoagulation.

In contrast to these advantages, there is still an underuse of RM in patients with CIEDs. More recently, studies have proven a survival benefit for patients with active RM. Accordingly, new guidelines strongly recommend RM at least in patients with ICD and CRT-d devices.

O4 Risk score to assess mortality risk in patients undergoing transvenous lead extraction

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Introduction: Transvenous lead extraction (TLE) is considered as the gold standard in the treatment of CIED-related infective complications. Main indications for TLE include infective endocarditis (IE), pocket infection (PI), lead malfunction, lead redudancy, or vascular stenosis with the upgrading indication.The mortality risk that is directly related to the CIED removal procedure is relatively small, but one-year mortality patients undergoing TLE procedure is larger. Risk factors for one-year mortality among patients undergoing TLE procedure vary between different studies and in general include comorbidities and IE. To our knowledge this is the first risk score to assess mortality risk in patients undergoing TLE. We report on one-year follow-up of patients undergoing lead extraction in a high volume center.

Purpose: The main aim of a study was to assess one-year mortality and its predictors in a cohort of patients who underwent ICD (implantable cardioverter-defibrillator) implantation.

Methods: Retrospective analysis of clinical characteristics and one-year follow up of patients referred for a TLE procedure in a single high volume center between June 2006 and October 2014 was performed.

Results: The studied population included 130 patients (82 males; mean age 64 ±15 years) implanted with pacemakers (74%), implantable cardioverter defibrillators (15%), or cardiac resynchronization therapy defibrillator (11%). Indications for the extraction included infective endocarditis (40.5%), pocket infection (18.5%), lead fault or failure (41%). Total radiological success rate was 90% while clinical success rate was 93.5%. The cumulative 1-year mortality was 28%.Mortality was higher in a group of older patients (94.4% vs 68%, p=0.001) and those with chronic kidney disease (33.3% vs 4.3 %, p=0.0002) as well as in patients after removal of high voltage lead (88.9% vs 26.3% p=0.01). Higher mortality was also related to infection as an indication for TLE (37.2% vs 13.5%, p=0.002).Following these findings a new risk model for predicting 1 year mortality in patients undergoing TLE procedure is proposed. The acronym of this model is IKAR (I= infective indications for TLE procedure 1 point; K= kidney dysfunction 2 points; A= age ≥56 years 1 point, R = removal of high voltage lead, 1 point). Such a model allows for predicting 5-fold higher mortality in patients undergoing TLE procedure.Patients with IKAR score≥3 points were characterized by 79% mortality as compared to 16% in those with a score 1-2 points

Conclusions: One-year mortality of patients undergoing TLE procedure can be predicted by using IKAR risk score. The proposed risk score may be helpful in making individual patient-tailored statements on risk for mortality prior to the TLE procedure in daily practice.

O5 Mobile heart health platform: ECG for Everybody

**Stevan Jokic, Ivan Jokic, Branislav Milovanovic**

ECG for Everybody is a mobile platform for heart health, fitness and stress level check, compare and track. In the ECG for Everybody we believe that mobile technologies and smart big data usage can struggle successfully with the leading cause of death - Heart Diseases. Heart diseases takes about half of all death around the world, still, WHO [1] claims that 80% of all heart diseases could be prevented. It requires only more work on early detection and life style improving.

We have designed Mobile ECG Sensing Extender which can be easily used without electrodes. Our approach is to extend nowadays smart phone to enable ECG sensing by using their own resources as much as it is possible and to minimize external components usage. We achieved this by transforming ECG signal to the audio signal which can be captured by smart phone audio interface, including microphone, so starting from the audio interface all following processing, analysis, storing, displaying, sending is performed using mobile device resources. Analysis are available through the mobile application which uses standard algorithms to check records as well as big data access to compare results with another appropriate users.

People networking by ECG for Everybody platform enables aggregation of a huge big data from various sources in one common goals - to help people to better understand and improve their health. The first big data usage, available through the mobile application for Android devices "Heart rate camera" [3], provides record scoring among other users records matched by age, gender and activity. Our further big data analysis will include finding life style patterns like exercise frequency, breathing pattern etc. which provide the best improvement in record results such as lowering resting heart rate and increasing heart rate variability. All patterns that we find in the big data will be available to our users as advising which will be matched by their age, gender and another preferences. Our platform provides Crowdsourcing portal [2] which enables collecting of opinions and comments regarding to user's recordings from various sources and various point of view, thus not only from physicians but also from people in sport.

For instance, after introducing the breathing advising in the mobile application for Android devices our users shows one to two grade better results in the average. This is advising from yoga, still from medicine research we know that that people with high HR and low HRV has greater probability to develop heat disease in coming years. Breathing advising does not provides permanent improvement if it does not become routine, still it may be good motivator to be more practiced as user will have a clear picture how it improve results. Our vision is to enrich advising set by inspecting big data and find patterns which leads to best results and best results improvement. Our inspection will track and degradation of results and our actions will be focused on finding reasons why results are downgraded as well as finding which patterns will improve results. For example, people in sport can practice too intensive which may develop overtraining injury. Overtraining may be avoided by proper results inspection. This is very important to optimize trainings before important competitions.

One of our work is addressed on Cuff-less, continuous blood pressure measurements by measuring blood transiting speed (Pulse Wave Speed, PWS). PWS estimated by combining ECG and PPG (PhotoPlethysmoGraphy) signal. This approach is based on several lows of physic which connects PWS and pressure in tubes. Relations in between pressure and PWS are not linear and they are person dependent, thus typical approach is to collect several measurement of the blood pressure with traditional equipment and to use them as a calibration values. Our idea is to provide it integrated in the ECG device shown on the following image, as well as to focus only on classifying blood pressure as a higher or lower than reference value. Person will specify reference value and check further blood pressure values against this reference value. Detecting trend of the blood pressure is useful in clinics when it is needed to find which medication will provide wishful change in the blood pressure, usually it is very important to lower quickly blood pressure to patients who have extremely high blood pressure value.
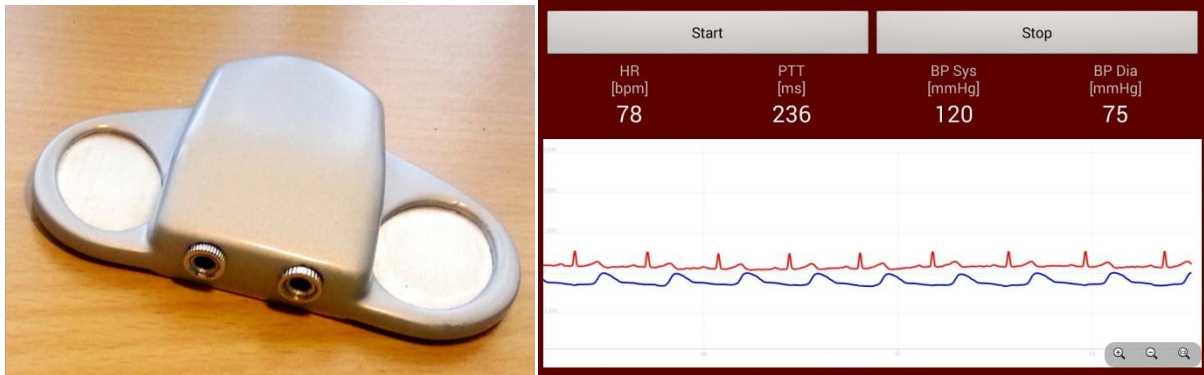
New ECG device and blood pressure measurement derived from ECG(red) and PPG(blue) signal

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O6 The role of CMR in the differential diagnosis of cardiomyopathies

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Cardiovascular magnetic resonance (CMR) is known to be an excellent noninvasivediagnostic procedure, ideal for the evaluation of many cardiovascular disorders due to its ability to differentiate normal from abnormal tissue and to identify the underlying abnormality of diseased tissue. It provides unique and accurate data representative of cardiac structure, function, and perfusion both at gross anatomical and myocardial levels.

Late gadolinium enhancement is an accurate method used in the diagnosis of ischemic and nonischemic cardiomyopathies. Nonischemic cardiomyopathies include a variety of diseases where the primary pathology directly involves the myocardium excluding CAD, and in this paper we would like to present examples of:Apical hypertrophic cardiomyopathy,Arrhythmogenic right ventricular cardiomyopathy andMyocarditis.

Apical hypertrophic cardiomyopathy (AHCM) is a rare form of hypertrophic cardiomyopathy (HCM) which usually involves the apex of the left ventricle.

Case report: A 47-year-old white man with weakness, was admitted in ICU. He had no complaints of chest pain, dyspnea or palpitations. On examination his blood pressure was 140/95 mmHg, heart rate 51 bpm with no heart murmur or any signs of congestive heart failure. The cardiac enzymes and chest X-ray were normal. An Electrocardiogram (ECG) showed an inverted T-waves in D1, AVL, V2 to V6 leads. A transthoracic echocardiogram (TTE) showed septal hypertrophy with dyskinesia of the apical segments of the front, lateral and posterior wall (the entire apex) and decreased systolic function EF 45-50%. 24-Hour Holter monitoring and Coronary angiography were normal. The ECG and TTE findings were attributed to AHCM and a CMR was indicated, which showed isolated asymmetric apical left ventricular hypertrophy, most prominent in the apical segment of the septum, to 15mm (in the basal and the medial segment 9mm). Along the septum we observed areas of late gadolinium enhancement, which could be classified as intramyocardial fibrosis. Since the patient wasasymptomatic, no further medical intervention was nedeed.
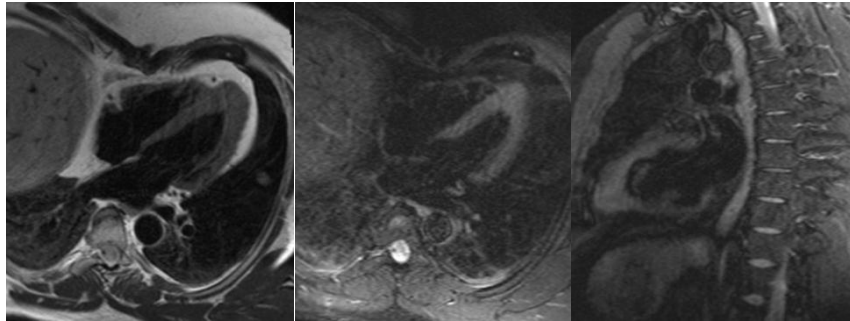
Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an uncommon cardiac disease caused by replacement of myocardial cells by adipose cell and fibrocytes and risk of sudden cardiac death from malignant arrhythmias.

Case report: A 63-years old woman with a history of non-sustained ventricular tachycardia of right ventricular outflow configuration, left bundle-branch block morphology with inferior axis, syncope and successful cardiopulmonal reanimation, was admitted for further cardiological diagnostics. She had recurrent palpitations with one documented incident of pharmacologically treated ventricular tachycardia 6 years ago. Upon admission her blood pressure was 130/75mmHg, heart rate 66 bpm with no heart murmur or any signs of congestive heart failure. The cardiac enzymes and chest X-ray were normal. ECG showed sinus rhythm without malignant arrhythmias. TTE revealed right ventricular dilation with areas of fibrous trabeculas and wall thinning with numerous recesses. Her coronary angiography result was normal. CMR showed markedly dilated right ventricle with large areas of fatty degeneration of the myocardium in

the area of the free wall of the right ventricle, disturbed kinetics with reduced right ventricular ejection fraction (42%) and septum (middle and apical segments) with zones of fibrosis. Due to the recurrent character of the arrhythmia and CMR findings the patient received an implantable cardioverter defibrillator (ICD). Genetic testing was not performed.
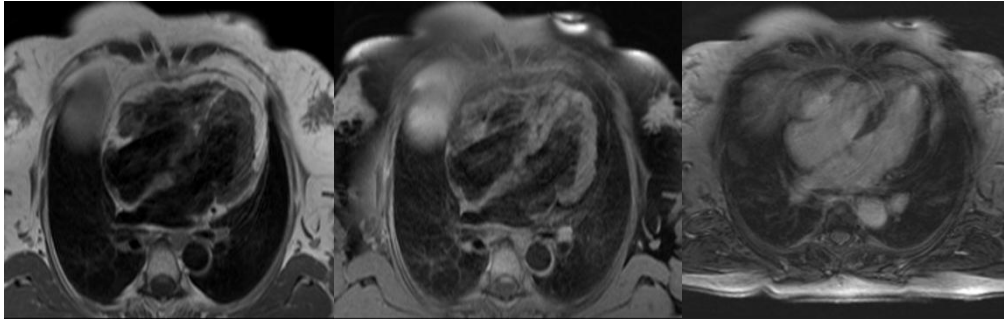
Myocarditis is an inflammatory disease characterized by the presence of inflammatory infiltrate in the myocardium and present degeneration and necrosis of myocytes in the histological examination. It can be manifested in different ways, from chest pain and palpitations accompanied by changes in the ECG until ventricular arrhythmia and cardiogenic shock.

Case report: A 26-year-old man was admitted to the coronary care unit for chest pain by type of contraction with propagation in both hands and sweating. Four days prior to admission, he was observed at the Infective Clinic for acute tonsillitis and antibiotic therapy (broad-spectrum penicillin) was introduced. At admission he was afebrile, oxygen saturation neat, heart rate 66 bpm, blood pressure 125/ 85mmHg, chest X-ray was normal. ECG showed normal sinus rhythm with a convex precordial ST segment elevation. Laboratory findings are recorded elevated levels of inflammatory parameters with elevated levels of cardiac enzymes. TTEs howed the left ventricle border dimension, global hypocontractile, left ventricular ejection fraction 40-45%, pericardium layered behind the posterior wall. His coronary angiography result was normal. CMR showed myocardial edema in the anterior wall (basal, mid and apical segments) and inferior wall (apical segment) of the left ventricle, also in apical septum. Late gadolinium enchament was seen in the mentioned segments. Pericardium inflammatory changed on the apical part with layering. According to diagnostic procedures was suspected acute Myo-pericarditis.
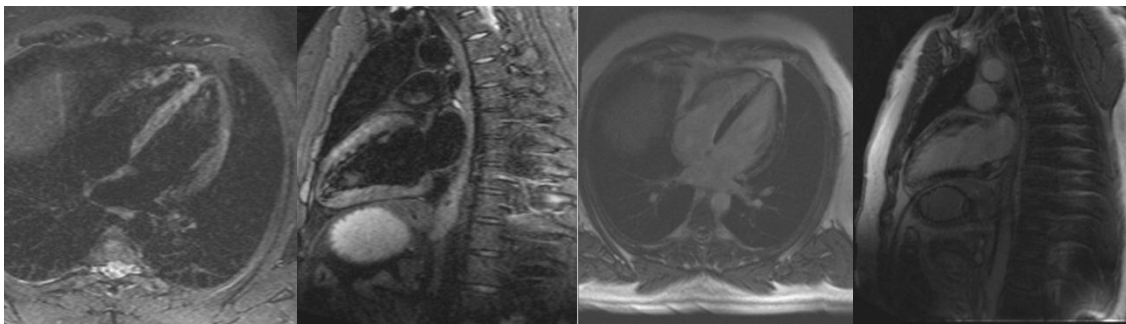
Conclusion: Cardiac magnetic resonance imaging (CMR) is an ideal method for the noninvasive evaluation of cardiomyopathies of unknown etiology because it is not limited by anatomic barriers and is able to characterize tissue abnormalities that previously could often be identified only through biopsy.

O7 What New in the Problem Sudden Cardiac Death in Athletes

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Sudden Cardiac death (SCD) is the most dangerous and irreversible outcome of diseases in clinical as well as in sport medicine. Between 1980 and 2011, the Sudden Death in Young Athletes Registry in the United States, which was developed based on mass media information, recorded 2406 cases of sudden death, which were observed in 29 diverse sports. In the USA 80% of all SD occurred in high school/middle school or collegiate student athletes, 20% were engaged in organized youth, postgraduate.

Statistical data vary greatly in some regions: in the USA as 7.47 and 1.33 per 1,000,000 exercising male and female school-age athletes, respectively, whereas the SCD incidence rate in Italy, is 2.6 cases in men and 1.1 in women per 100,000 individuals per year that are involved in active competitive sports.

European Heart Rhythm Association (EHRA) position paper concluded that overall estimate, 1 to 2 out of 100 000 athletes between of age of 12 - 35 years old die suddenly each year. It was shown that the risk of SCD is significantly higher in athletes than in non-athletes with the same heart condition in the general population - by more than five times for ARVD/ARVC, 2.6 times for coronary artery disease, 1.5 times for myocarditis, and more than 2 times for cardiac conduction system diseases.

O8 New Mechanisms of Perinatal Hypoxia and Perspectives of Pathogenesis-oriented Treatment

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Introduction. Perinatal hypoxia is thought to be a universal mechanism of impairment of both fetal and neonatal organs and systems. Antenatal hypoxia and birth asphyxia is one of the leading causes of newborn and infant mortality and morbidity across the world. Hypoxic/ischemic encephalopathy continues to be the most clinically significant signs of perinatal hypoxia and is the main cause of neurological consequence in remote periods in full-term and pre-term babies. Some aspects of PH pathogenesis and its consequences have not been thoroughly investigated. In recent years there have appeared new data about a potential role of hemic disorders in development of HI impairments.

Aim. To study the contribution of structural and functional hemoglobin (Hb) disorders into the pathogenesis of perinatal hypoxia / asphyxia (PH) in newborns.

Patients and methods. 90 full-term newborns with PH and 30 healthy ones were examined by clinical methods, electroencephalography (EEG), neurosonography (NSG) and by spectroscopy of Hb combined dispersion. Newborns blood was testing on RAMAN-spectrograph "Renishaw". All the patients were randomize into 2 group: group1 neonates (n=45) receive standard therapyonly, group2neonates (n=45) – additionally – L-carnitine 100 mg/kg/24 hour during month. The indices, indicating Hb affinity to ligands (oxygen) (1355/1550)/(1375/1580) and Hb ability to bind them (1355/1550) were less in hypoxia-affected newborns than in healthy ones. They got reduced at increased severity of PH. The indices showing Hb ability to reject ligands (1375/1580), and Hbconformative alterations (1375/1172) were higher in hypoxia-affected neonates and increased simultaneously with the increase in PH severity. It means that in severe PH oxygen binding to Hb becomes insufficient, which may aggravate hypoxia. Besides, along with oxygen concentration increase, pyrrole ring configuration (conformative alterations) of Hb escaladed. This may lead to decrease in Hb ability to bind oxygen and to disorders its function. In "in vitro" studies with oxygen-aerated blood, Hb affinity to oxygen and Hb ability to bind it were lower than in tests without oxygenation. These indices reduced proportionally to oxygen concentration increase. Besides, along with oxygen concentration increase, conformative alterations of Hb escalated. This may lead to decreased Hb ability to bind oxygen and to a rise of Hb transportation function disorders. We have established the correlation between the indices of Hb properties and some clinical features in newborns with PH: Apgar scoring, oxygen saturation, neurological status, ischemic changes on EEG, NSG. Additional use of L-carnitine promoted restoration of Hbcomformative properties and improvement of neurologic status.

Conclusion. Our dates confirm the contribution of disorders in the structural and functional properties of Hb into PH pathogenesis. The obtained results may suggest, that the Hb spectroscopy data could be used as one the novel criteria to assess hypoxia severity in newborns, particularly in those who are on ventilation. Hb spectroscopy indices could be used for assessing pharmaco-therapy efficiency.

O9 The Evolution of the views on ventricular arrhytmias in athletes

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The ventricular arrhythmias (VA) in trained athletes are the most frequent phenomena and have been considered a clinically benign expression not infrequently associated with the physiologic athlete's heart. On the contrary, exercise-induced ventricular tachyarrhythmias raise clinical concern as a marker of increased risk in the presence of underlying cardiovascular disease.. In Recommendation of Study Group on Sports Cardiology of the European Association for Cardiovascular Prevention and Rehabilitation in 2006 it is said that athletes with VA more than 2000/24h or polymorphic VA or couplets need deconditioning 3-6 month because early in researched by A. Biffi et al has been showed VA reduced after period of detrening. In recent years in some study (L.Verdile, 2015, P.Delise 2013) were demonstrated that exercise-induced VA were present in a sizable minority of highly trained athletes without heart disease. These arrhythmias proved to be benign and not associated with adverse events or later development of cardiovascular disease.

O10 The case of spontaneous occlusive thrombosis in the soccer player with hereditary predisposition in a hot humid climate

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There are situations where the pathological condition of an athlete simulates injury or its consequences. They are generally not less severe, and are complicated in the plan of differential diagnosis. Athlete L., the goalkeeper of the football club of the Russian Premier League, played for his soccer team in difficult climatic conditions. After 4 days after the game a football player was hospitalized complaining of swelling and a feeling of "fullness" in the upper left limb.

During the ultrasound scan of veins right upper extremity vena brachialis is passable to the upper third of the arm, blood flow is slowed down; in the upper third vena brachialis occlusive thrombosis observed. Axillary and subclavian the veins on the right is totally thrombosed and occluded.

Diagnosis. Occlusive thrombosis of the right subclavian and axillary vein (Paget-Schroetter syndrome) .

Athlete received conservative treatment, including anticoagulant therapy, with a positive effect.

After 5 days, swelling of the right upper extremity regressed, the pain does not disturb. Thrombosis rate, according to the results of ultrasound, is not growing.

The athlete was made genetic testing "plasma factors of blood coagulation" designed to identify genetic polymorphisms in genes encoding plasma coagulation factors (table).

Table. Genetic testing "plasma clotting factors of the system," the soccer player L., 20 years old.

GENE	The protein produced by gene	Polymorphism	rs	Risk allele	Patient results	Comment
F7	Coagulation Factor VII	R353Q G>A	rs6046	*G*	*G/A*	*Heterozygotes the mutant type*
FGB	Fibrinogen	455 G>A	rs1800790	*A*	*G/G*	*Homozygous the normal type*
SERPINE 1	Plasminogen activator inhibitor	−675 5G>4G	rs1799768	*4G*	*4G/4G*	*Heterozygotes the mutant type*

Polymorphism R353Q G> A rs6046 assumes high level of coagulation factor VII in the blood, which is associated with an increased risk of thrombosis.

Polymorphisms of 4G (-675) 5G (rs1799768) are mutations encoding ratio "protective allele 4G» / «5G allele risk», leading to an increase in gene activity. In this case there is an increase rate of platelet adhesion, which may lead to an increased risk of thrombophilia due to platelet hyperaggregation.

Conclusion
- Some of the role of athletes in common sports, such as football goalkeepers, may have a predisposition *Paget-Schroetter syndrome*, which is not characteristic of other categories of players in this sport.
- *Paget-Schroetter syndrome* develops with a combination of predisposing external (e.g., hot humid environmental conditions) and internal (e.g., a genetic predisposition to hypercoagulability) factors with the specificity of athletic activity.

O11 Heart and brain: White matter disease, vascular dementia, and its risk for anticoagulation: a review

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White matter disease (WMD) is a chronic condition due to vascular function alterations which produce several forms of damage, mainly divided into: 1- *Lacunar infarcts* (lacunar infarcts, lacunar hemorrhages and dilated perivascular spaces) and 2- *Diffuse white matter damage.* The first group can compromise some areas critically involved in the process of learning and memory which are called strategic infarcts. The second group is due to chronic hypoperfusion and hypoxic conditions which produce a damage in the interconnecting fibers which is now evaluated in tractography studies. There are several factors implicated in this damage: aging, hypertension, hypotension, diabetes, chronic kidney disease, inherited alterations, migraine.

The neurovascular unit (NU) is the key damage target, compound by neurons, glial cells, perivascular and vascular cells which function as a whole to control cerebral blood flow, metabolism through brain blood barrier (BBB), throphicand immune functions. Brain vessels diminish their diameter from pial arteries and arterioles which are extrinsic innervated by trigeminal and autonomic nerves bathing in CSF, then penetrating arteries lying in Virshow Robin space with lesser extrinsic innervation and finally parenchymal arterioles without extrinsic innervation but with intrinsic innervation forming the NU. Risk factors produce change in the vessel wall, BBB rupture, and in some amyloid deposition; altering the perfusion to local areas where there is a great change in diameter from a parent vessel to small one generating a segmental occlusion with proximal and distal occlusions producing a lacunae, which can be a complete or partial infarct, thenlacunarinfarcts are classifiedintopartialor complete. In others the low perfusion generates confluent hyperintense lesions visualized on MRI-T2 or hypodense lesions on NCCT producingchronic hipoxiaand inducingactivation of metabolicpathwaysgenerating vasoconstriction, inflammation, increase in permeability, atherosclerosis, and thrombosis. Thispathophysiologicalevents are known as endothelial dysfunction formostthe earliest event in the initiation of vascular disease playing a key role throughout the disease process.Thesefunctional changes in endothelial functioncontribute to reductions in resting blood flow producinghypoperfusion, impairment of vasodilator responses, and subsequent cellular injury. Chronic reductions in cerebral blood flow in a levelnotproducingischemia have functional consequences traducing in behavioral, motor, balance, memory, speed in mental processes and sphincterdisturbances. Oligodendrocytes are affectedconductingto loose in the myelin sheet of tracts where thalamic cortical connections are crucial in cognition, behavior, gait and movement. The patients with SMD extensive confluent pattern have slow gait, rigidity in the lower extremities producing vascular parkinsonism (VP) and alteration in balance, this is key in the differential diagnosis between Parkinson Disease and VP, in the first it begins affecting one side of the body with the involvement of upper and lower extremities and after both sides of the body, VP affects lower extremities. With strategic infarcts or with extensive confluent WM lesions behavioral changes occur and cognitive decline mainly the executive function is affected, also have been reported problems with memory, visuo-constructional and nomination functions.

WMD clinical manifestation can be associated in crosssecctionalstudies as: 1- cognitiveimpairment and reduced test performances, 2- depressive symptoms, 3- gaitand balance disturbances, impaired mobility, falls and 4- urinary disturbances; in longitudinal studies WMD is predictor of: dementia, depression, disability and death. There are correlation betweenlocalisation of WM lesions and their volume; the periventricular lesions have been reported associated with slow speed in processing and memory. Predominance of WM hyperintensities in occipital lobe / posterior regions or enlarged perivascular spaces in the centrum semiovale are associated with cerebral amyloid angiopathy and are an imaging marker. Behavioral changes occur with affection of: 1- basal ganglia, thalamus and cerebellum, and 2- fibers interconennecting those with cortical structure and between cortical areas; cerebral microbleeds are associatedwith a worsecognitivefunction.

Vascular dementia (VaD), vascular mildcognitiveimpairment and mixeddementia are classified as vascular cognitiveimpairment (CVI) forits diagnosis clinical, behavioral, cognitive and neuroradiologicalaspects are considered. Thepresence of a cognitivedisorder in theneuropsychologicalevaluation, pasthistory of strokeordemonstration of radiologicalalterations as theabovedescribedshouldput VCI diagnosis onattention, memorylostaloneis no longerpart of diagnosis of VaD. Neuroradiologicalalterations of WMD criteria are basedon ARWMC (age- related white matter

changes) score: 0: no lesions, 1: focal lesions, 2: beginning of confluentlesions, 3: diffuselesionsafecting a total of a region, withorwithout U fibersinvolvement.

Recently interest in ACO has been increased due the new DOAC and ASSERT 1 and 2, CRYSTAL-AF trials, with new NVAF found; then patients with WMD are challenge for decision on ACO:

1- As mentioned above those patients with a lobar pattern has an increased risk for bleeding due amyloid deposition. Also the imaging pattern of WMD should be taked in account, a ARWMC: 3 is a great risk for bleeding.

2- Gait disorder is also one of the clinical manifestations of patients with WMD, recent information about falls and bleeding risk has helped to view the risk with another perspective, a lower risk than previous thought.

3-Microbleeds on MRI are not a contraindication for OAC.

O12 Risk Factors of Stroke in Real Clinical Practice

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Aim of the study: Identify the most important risk factors in patients hospitalized for stroke.Point out the need to improve their early identification, elimination and treatment according to the valid recommendations of European Society of Cardiology.

Materials and Methods: Retrospectively, we analyzed acohort of patients hospitalized for stroke during a three month period (July-September 2016) at the IstDepartment of Neurology, Comenius University and University Hospital Bratislava. The group consisted of 104 patients, with ischemic strokediagnosed in 88 subjects (84.6%) and hemorrhagicstroke –cardiovascular accident (CVA) in 16 subjects (15.4%). The average age was 70.7 years.

Results: Among the most important risk factors in addition to age and concomitant atherosclerosis, we found that arterial hypertension as the most common risk factor occurred in 96 subjects (92.3%), whereas 14 subjects (87, 5%) were diagnosed with hemorrhagic CVA. Atrial fibrillation occurred in 34 patients (32.7%), of whom only 14 (41.2%) had an anticoagulation therapy before hospitalization (3 VKA, 11 DOACs). In the group of patients with anticoagulation therapy a hemorrhagic event occurred in 1 subject, the rest of the subjects (13)were diagnosed with ischemic CVA. It should be mentioned that 7 of the patients treated with DOACswere given smaller doses than recommended by guidelines.

Conclusion: Our results from real clinical practice show that arterial hypertension and atrial fibrillation are the most commoninfluenceable risk factors ofCVA. Arterial hypertension occurred in up to 92.3% of the cohort. Atrial fibrillation occurred in 32.7% of subjects, but only 41.2% of the group were treated with anticoagulant therapy before hospitalization, most of whom (63.6%) were under-dosed. Our results point to the fact that it is necessary to improve the effective prevention of CVA.

O13 Transient ischemic attack can be followed by stress induced Takotsubo cardiomyopathy

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Abstract:
Takotsubo cardiomyopathy is a cardiological syndrome with symptoms and clinical signs explicitly mimic acute coronary syndrome, and, as such, represents an important differential diagnostic entity. The incidence of this rare disease is between 1.2% and 2.2% of patients who suffer from a myocardial infarction. Although the process of entity onset remains unknown, there is an assumption of the role of brain-heart axis in the pathogenesis of the disease. A female patient, aged 57, with neither prior cardiac or neurological history, nor use of any drug therapy, was admitted to emergency room with the clinical picture which usually corresponds to acute coronary syndromes. Charasteristic angiographic and echocardiographic findings indicated an ongoing Takotsubo cardiomyopathy. On the second hospital day, the patient developed a neurologic episode, which was manifested as an cessation of speech, and the inability to establish verbal communication for about 10 min, without the loss of consciousness. Conducted neurological diagnostics, which included the multislice computed tomography of endocranium, Color Doppler sonography of carotid arteries and a computed tomography angiography of blood vessels of neck and endocranium were normal. Based on the above stated, as well as the normal findings in neurological follow-up and with a subjective improvement of the patient, the neurological event was concluded to be a transitory ischemic attack (TIA). It is not uncommon that Takotsubo cardiomyopathy correlates with some form of central nervous system ischemic processes. However, the causality between these two medical entities should be more carefully studied.

Keywords: Takotsubo cardiomyopathy, transient ischemic attack, brain-heart axis

INTRODUCTION

Takotsubo cardiomyopathy is a cardiological syndrome with symptoms and clinical signs explicitly mimic acute coronary syndrome, representing an important differential diagnostic entity. It is characterized by chest pain, positive enzyme response, characteristic changes in the electrocardiogram, and transient and completely reversible segmental kinetic disorders of the left ventricle. However, what makes it absolutely unique by the differential diagnosis is a discrepancy in the clinical and angiographic findings, i.e. the absence of changes in angiographically visible coronary blood vessels, which is also the first hint in favor of further differential diagnostic thinking in this direction. The incidence of this rare disease is between 1.2% and 2.2% of patients who suffer an acute myocardial infarction. The name comes from the shape of the left ventricular cavity captured on sonography and ventriculography (as shown in Figure 2), which irresistibly reminded its founder Sato of the Japanese octopus traps [1]. Such morphological subtype i.e. apical subtype occurs in 81.7% of cases. Other subtypes of Takotsubo cardiomyopathy include medial-ventricular subtype in 14.6%, reverse basal subtype in 2.2%, and focal subtype in 1.5% of cases [2-4].

Researching the literature gives a clear insight into the fact, that the entity, most commonly, occurs in postmenopausal women in about 90% of cases [5, 6]. The literature also describes additional synonyms, such as stress-induced cardiomyopathy, apical ballooning syndrome and the "broken heart syndrome" − a name that is certainly the most adequate one, explaining the etiology of the case about to be presented. Namely, a great stress (in this case the emotional one) that leads to the development of disorders is the main cause of this problem. Among other stressogenic factors showed to be the cause are: other emotional stressors (death of a loved one; emotional reaction due to bad financial news, legal problems, newly diagnosed significant medical condition), physical stressors (secondary occurence due to severe burns, organ transplatation, severe infections) or neurological injury (intracerebral hemorrhage, seizure or intracerebral infarction) [7, 8].

The pathophysiological mechanism of the syndrome onset has remained at the level of the various theories or hypotheses, given the fact that the syndrome itself has never been caught up in the moment of pathophysiological development, which would prove or deny the existence of the theories themselves. The considered theories are: a) multivessel coronary spasm, b) acute microvascular coronary spasm, c) catecholamine-induced myocardial regional numbness, d) transient left ventricular outflow tract (LVOT) obstruction [9].

Although the process of entity onset remains unknown, there is an assumption of the role of brain-heart axis in the pathogenesis of the disease, which only seems to be illogical. Such derivative is justified by the fact that this type of acute myocardial dysfunction occurs in susceptible individuals as a consequence of an acute stress, and as such represents a neurocardiac lesion which on the level of hypothesis triggers a neurohormonal response that results in characteristic left ventricular wall-motion abnormality.

CASE PRESENTATION

A female patient, aged 57, postmenopaused, with neither prior cardiac or neurologic hystory, nor use of any drug therapy, was admitted to the internal medicine clinic with the clinical picture which usually corresponds to acute coronary syndromes, *GRACE SCORE 121.* She was transported in an emergency vehicle to the emergency department and during transport, in accordance with the protocol, was administered a *"loading"* dose of antiplatelet therapy: acetylsalicylic acid 300 mg, clopidogrel 600 mg, with nitroglycerin spray application. At the clinic, she complained of a recurrent chest pain, lasting one hour without ceasing or changes of intensity. The patient described the pain as dull, clutching, without propagation, in the intensity of 7/10. She also stated to having suffered a similar manifestation of pain, lasting for about 2 hours, with a similar intensity, two days prior to admission, after being told that her husband had a car accident, and was taken to the Clinical Center of Serbia, Emergency Room in a serious condition (data obtained after coronarography, after emphsizing questions about the family problems). Objectively, during admission, she was conscious, oriented, eupnoeic, afebrile, acyanotic, anicteric, pale, with no signs of heart failure and visible diaphoresis of milder degree. Auscultation of lungs showed a slightly adventitious respiratory sound without pathological findings, heart sounds and blood pressure were normal. Admission electrocardiogram at a frequency of 130 bpm registered sinus rhythm, QS in precordial leads V_{1-3}, clearly ST elevation V_{3-5}, negative T waves in the inferior and in the left precordial leads.

Laboratory results verified an increase in cardiospecific enzymes (troponin I 2.00..2.08, creatine kinase 384..444). Without further delay, a therapy was initiated according to STEMI treatment protocol and the patient was referred to the cathlab for percutaneous coronary intervention. The total time, from the pain manifestations until the cathlab procedure, was less than 90 minutes! The angiographic findings were normal, which brought suspicion on further differential diagnostic thinking about this type of pathology.

Echocardiography confirmed the apical balloonization of the left ventricule with akinesia of the distal half of all walls with a reduced global systolic function and the ejection fraction of 35%, with no thrombotic masses detected in the akinetic apex. Since all Mayo Clinic criteria for Takotsubo cardiomyopathy were met, the diagnosis was made [13].

On the second hospital day, the patient had an episode of the cessation of speech, and the inability to establish verbal communication for about 10 min, without the loss of consciousness. An ECG monitoring showed no cardiac rhythm disorder as a potential cause of the neurological deficit. A neurologist was consulted. Objectively, at the examination, the pacient was conscious, oriented, communicative, with fluent speech, and a preserved prosody with signs of anomic dysphasia. The findings: on the cranial nerve, the tongue was slightly deviated to the right; free neck; normal motor reflexes on upper and lower limbs, without assymetry; motor: normal tone and bulk; the Wartenberg sign was negative and Mingazzini test showed no lateralization, the sensibility was preserved. Initially, an antiedematous therapy was introduced, according to the protocol. The multislice computed tomography of endocranium ruled out hemorrhage, edema, and displacement of medial sagittal structure. Color Doppler sonography of magistral blood vessels of the neck ruled out the existence of significant stenosis on the carotic artheries and a hemodynamically significant acceleration of flow. Angiographic examination of the blood vessels of the neck and endocranium in 3D sequences showed neither signs of occlusion, stenosis, reduction of flow, pathological vascularization, aneurysmal enlargement, nor arterio-venous malformations. According to the conclusion of the neurologist, this was most likely a transient ischemic attack (*TIA*). After a 24-hour observation, based on the normal neurological findings, normal readings of diagnostic procedures (multislice computed tomography, Color Doppler, angiography) and a subjectively better condition of the patient, the transient ischemic attack (*TIA)* diagnosis was confirmed. On the fourth hospital day, echocardiogram showed no signs of apical ballooning. The hypokinesis of the apex (all the cross sections) was described and the global systolic function was estimated at about 55%. In the further course of the hospitalization, there was a regression of cardiac specific enzymes in approximately reference range value. Holter ECG, among other findings within the spectral analysis, determined the domination of the sympaticus. On the day of the discharge (the tenth day from admission), electrocardiogram features with sinus rhythm and frequency around 60 bpm were observed. However, a negative deflection of the T wave (with a slightly smaller amplitude) was retained in the inferior and left precordial leads, but without ST elevation changes in apical leads, as presented on the day of admission.

The patient was discharged in good condition. Six months later, the control echocardiogram showed a complete recovery of contractile function of the left ventricle without any traces of previous illnesses whatsoever.

DISCUSSION

As previously stated, although it is not common that Takotsubo cardiomyopathy correlates with some form of central nervous system (CNS) ischemic processes, it should be very carefully evaluated. Indications for such claims are to be sought in the following. Grabowski and colleagues examined the correlation existence between cerebrovascular attacks in patients with Takotsubo cardiomyopathy, and showed that 6.4% of the total number of patients with this cardiomyopathy had some kind of cerebrovascular obstruction [14]. Ischemic attack in 75% of cases is the most common form of cerebrovascular pathology. Yoshimura and colleagues complement that more than 30% of cases associated with Takotsubo cardiomyopathy are manifested by severe neurological deficits [15]. A definite connection between these two medical entities (Takotsubo cardiomyopathy and cerebrovascular event) is also reflected in the fact that there are cases with reverse causal relationship, where the formation of Takotsubo cardiomyopathy is interpreted as a possible consequence of cerebrovascular attacks [16, 17]. Reviewing similar cases, issued by Porto and associates, who were examining the causal connection between some form of ischemic neurological event and transient, regional left ventricular dysfunction (TRLVD), suchlike trend was depicted in 20,5% of cases [18].

The question that remains open is the actual cause of TIA, since the angiographic examination of the blood vessels of the neck and endocranium showed neither signs of occlusion, stenosis, reduction of flow, plaque formation, pathological vascularization, aneurysmal enlargement nor arterio-venous malformations. Also, whether the thromboembolic potential of akinetic apex could be „the answer to the riddle" as described by some authors [19, 20], in this case wasn't actualy proved. The existence of the cardioembolic potential of the akinetic apex, as a possible source of thrombotic masses is undeniable, due to the fact that the well-known factors of Virchow's triad in the pathophysiological process of forming the endoluminal thrombus are the hemodynamic changes (stasis and turbulence) and endothelial injury/dysfunction. The above hypothesis is justified by the assumption that the absence of synchronous contraction of a left ventricle, caused by dyskinesic ballooned apex is leading to the two pathophysiological phenomena. On the one hand, it leads to the reduction of the contractile ability of the weakened i.e. ballooned akinetic myocardium, followed by a notable drop of ejection fraction and the occurance of the "sludge" phenomena (a similar analogy could explain conceptually much closer and more frequent cardioembolic potential of fibrillation affected left atrium). On the other hand, the emergence of highly turbulent flow in the left veticule

potentially leads to a further formation of microlesions in the endothelium and thus to the formation of thrombotic masses in akinetic segments of myocardium. Both phenomena are leading to the formation of microemboli which could give a clinical presentation as described in the case.

CONCLUSION

Here is presented another fine example of a correlation of Takotsubo cardiomyopathy with some form of neurological ischemic process. Although it is not the usual pattern, neurological presentation should be always carefully evaluated in these patients. Unfortunately, at this moment the issue of causality between them remains a mystery and a matter on the level of hypothesis and assumpsions, needed to be carefully seek.

CONFLICTS OF INTEREST
The authors have no conflict of interest to declare.

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O14 Subchronic Methionine load affected vitamin B12 level and Von Willebrand factor activity in blood of male Wistar rats and induced myocardial haemorrhagia

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Aims: Hyperhomocysteinemia (HHC) is involved in the pathogenesis of atherosclerosis and other illnesses. HHC, both basal or after methionine load, may occur due to genetic disorders or deficiencies of certain nutrients that affect pathways in methionine metabolism. The aim was to examine the effects of subchronic methionine load on standard biochemical parameters, levels of homocysteine, folate and vitamin B12 as well as on the levels of different haemostatic parameters (fibrinogen, D-dimer, vWF Ag, vWF Ac) in rat serum or plasma.

Methods: The research was conducted during a three-week period (male Wistar albino rats, body weight of approximately 160 g), and the animals were divided into a control and experimental groups, consisted of 10 animals each: a) control group (0.1ml/day 0.9% NaCl, i.p.); b) methionine (0.8 mmol/kg/bw/day, i.p.).

Results: Regarding biochemical analysis there were statistically altered levels of certain parameters in methionine load group vs. control (BUN, CREA, URCA, TBI, TP, ALB, AHDLA, TGL, Na, K, AMY, ACRP, respectively). Interestingly, homocysteine level in this model was not increased (control 9.98±0.65 vs. methionine load 9.51±0.59 μmol/L, P>0.05), folate was also unaltered (35.25±2.04 vs. 32.11±2.13 μg/L, P>0.05) but vitamin B12 level was significantly decreased (882.00±32.00 vs. 742.50±25.70 ng/L, P<0.01). Furthermore, levels of certain haemostatic parameters (fibrinogen, D-dimer and vWF Ag) were unaltered however vWF Ac was dramatically decreased in methionine load group vs. control (4.16±0.21 vs. 27.25±11.20, P=0.001). However the spots of myocardial haemorrhagia were found in histological preparations.

Conclusions: The obtained results indicated that monitoring of standard biochemical parameters, levels of homocysteine, folate and vitamin B12 as well as the levels of different haemostatic parameters (fibrinogen, D-dimer, vWF Ag, vWF Ac) could provide a valuable marker for distinguishing between toxic and non-toxic doses of methionine load, which may be useful for further research. In addition, it has been proposed that decreased vWF Ac following subchronic methionine load could be responsible for myocardial haemorrhagia.

O15 Pharmacological Protection Against Sepsis Associated Cardiac Dysfunction: Emerging Targets And Strategies

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Myocardial dysfunction is an early and serious complication of severe sepsis and septic shock which associated with a high mortality rate reaching up to 70-90%. It occurs due to the functional and structural injury in the myocardium and it is characterized by impaired contractility, left ventricular dilatation and decrease in ejection fraction. In the intensive care unit, about 60% of severe sepsis patients exhibit cardiac dysfunction and the mortality for those patients range from 70-90%. In contrast, the mortality in patients who is not showing any signs of myocardial dysfunction due to sepsis is 20%.

No specific therapy for sepsis induced myocardial injury. Recently, general therapeutic strategies include infection control, hemodynamic support, host response modulation and critical care support.Septic shock patients need the use of inotropes and/or vasopressors to maintain adequate mean arterial pressure, oxygen delivery, and cardiac contractility. Additionally, sepsis causes profound metabolic alterations and exposes vital organs to high risk of energy failure, so several strategies explain the ways in order to reduce the cellular energy crisis. Regarding immuno-modulatory therapy, none of the available imuno-modulatory strategies, proven to be highly effective in sepsis, design specifically to target myocardial injury.The molecular pathophysiology of sepsis is highly complex and thus provides many molecular targets for therapeutic intervention. Therefore approaches for therapeutic intervention of sepsis may be subdivided into two classes, namely experimental and clinical approaches. Strategies that preferentially target cardiac injury in sepsis are emerging and fruitful cardioprotective agentsare promising to alleviate cardiac remodeling and injury.

O16 Vasopressin V1AR expression in the paraventricular nucleus of the hypothalamus in borderline hypertension

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Paraventicular nucleus (PVN) has a pivotal integrative role in neuroendocrine control of the circulation. It is a major source of neuropeptide vasopressin and co-expresses V1a receptor (V1aR) in abundance. Recent evidence suggests that V1aR in PVN are involved in salt induced sympathoexcitation[1]. It has also been shown that rats overexpressing V1aR in PVN exhibit exaggerated cardiovascular response to stress[2]. The aim of the present study is to investigate the level of expression of V1aR in PVN of borderline hypertensive rats (BHR) under baseline conditions and when exposed to salt load with and without stress. Twelve week old male BHRs and their normotensive Wistar (WR) controls equipped with radiotelemetry device for direct blood pressure (BP) recording were used for experimentation. Animals were randomized in four experimental groups for 29-weeks-long follow up: 1gr: WRs drinking tap water; 2gr: BHRs drinking tap water; 3gr: BHRs drinking 0.9% saline; 4gr: BHRs drinking 0.9% saline exposed to repeated combined environmental stress (shaker stress + crowding stress followed by isolation stress + air-jet stress + tilt stress). Hemodynamic parameters, BP and heart rate (HR) and autonomic markers, baro-reflex sensitivity (BRS) and HR variability (HRV) were monitored throughout the whole period. BRS and HRV were assessed by the sequence method and spectral analysis, respectively. At the end of the follow up period animals were sacrificed and the PVN tissue samples were harvested by micro-punching. Expression V1aR in PVN was evaluated using qPCR technique. Under baseline conditions BHRs had significantly higher BP and lower HR than WR, comparable BRS and HR variability (HRV) and reduced expression of V1aAR in PVN. In salt loaded BHRs, BRS increased in respect to baseline while V1AR expression remained reduced. In BHRs exposed to stress, overt hypertension developed, as well as the increase in low-frequency HRV. Interestingly, in these rats the level of V1aR expression in the PVN was higher than under baseline conditions and salt load exposure. It follows that changes in neurocardiogenic control of BHRs accompany the changes in V1aR expression in the PVN.

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O17 Statins in cardiorenal syndrome: why not?

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The intriguing concept of cardiorenal syndrome (CRS) has triggered a widespread research efforts in cardiovascular medicine since 2010. It was defined and classified into five subtypes six years ago. In particular, the deteriorating interplay between the heart and kidneys may be modulated by different pharmacological agents. Statins are well known lipid lowering drugs with additional pleiotropic effects. Even a single dose of statins was confirmed to be beneficial in different acute kidney injury (AKI) models while clinical trials with statins in patients with AKI and CRS offered controversial results. Of note, high-dose lipophyllic statins may affect the autonomic nervous system (ie. reduce adrenergic outflow) and contribute to the treatment of CRS. Such an interplay between the heart, kidneys and autonomic nervous system may improve condition in patients with CRS. Translational research and proof-of-concept studies are needed in order to clarify such an issue.

O18 Significance of determination of BCL-2 and CASPASE-3 activity in ishemic 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 characteristics in patients with SAP and USAP 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 between areas of Bcl-2 curves of these two patient groups. These results suggest that simultaneous determination of caspase-3 activity and Bcl-2 can indicate plaque evolution from 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.

O19 Splicing mutations causing unusual early-onset dominant MYH7-related myopathy

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Introduction. Dominant mutations in the *MYH7* gene cause allelic series of diseases including various cardiomyopathies and myopathies usually manifesting in adulthood.

<u>Clinical case.</u> We had under our observation the boy 2y.o. manifestedwith predominant axial muscles weaknesses, "dropped head syndrome", and mild dilatation of the heart chambers. Parents and older brother (10y.o.) are healthy.

Methods. Clinical investigation was performed by ECG, EchoCG, neurological examination, and muscular biopsy. The DNA-diagnostics had included whole exome sequencing with following Sanger resequencing, bioinformatic analysis, and cascade familial screening. Functional analysis of the variants of interest had included RT-PCR and expression analysis in HEK293N cell line transfected with 4 plasmids containing fragment of the MYH7 gene from exon 37 to exon 39 (*wt*, c.5655+5G>C, c.5655G>A, and c.5655+1G>A).

Results. We revealed new *de novo* mutation c.5655+5G>C in the *MYH7* gene in the 2 y.oproband. In-frame skipping of the exon 38in the proband'smRNA was confirmed. This variant and two previously published mutations (c.5655G>A and c.5655+1G>A) also leading to the 38 exon skipping were studied using expression system. Surprisingly we had found that *wt* plasmid expressed two RNA isoforms: full-length and shortened (skipping of the 38 exon). All mutant plasmids had expressed only shortened isoform. Quantitative difference in expression was shown for mutant plasmids.

Conclusion. We consider the variant c.5655+5G>C in the *MYH7* gene as a pathogenic mutation causing early-onset myopathy and dilated cardiomyopathy. All patients with those mutations seem to have similar phenotype.

O20 Prevalence of dilated cardiomyopathy in the Russian patients with Marfan Syndrome

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Introduction. Usually dilated cardiomyopathy (DCM) in patients with Marfan syndrome (MFS) is explained by volume overloading due to aortic or mitral valve regurgitation, and progressive aortic root dilatation. Recent studies of J.R.Cook et al. "Abnormal muscle mechanosignaling triggers cardiomyopathy in mice with Marfan syndrome" have shown that fibrillin-1, a structural component of the architectural ECM, is a force-transmitting molecule protecting the mammalian heart against cardiomyopathy.

Materials and methods. We have performed clinical (Standard and 24-hours Holter ECG, EchoCG, Dopplerography, chest radiography) and genealogical examination of the 40 probands with MFS, 6 of them were children. All probands had met the Ghent's criteria for MFS. Affected relatives were found in 13 families. Mutational screening in the *FBN1* gene was performed by PGM Ion Torrent followed capillary Sanger sequencing.

Results. We had detected 30 mutations in the *FBN1* gene in 31 (77,5%) index cases. Cardiomegaly was found in 30 (88%) adult probands and in 2 out of 6 children. All heart chambers enlargement, increased end-diastolic volume of the LV and reduced ejection fraction were found in 15 (37,5%) index cases.

Conclusion. The prevalence of DCM is very high in probands with MFS. The influence of this complication for the long-term prognosis in this clinical group might be underestimated. We suggest that mutations in the *FBN1* gene may play a direct causative role in cardiac remodeling in MFS patients. This work was supported by grant RNF № 16-15-10421.

O21 Cardiovascular genomics: avenue of approach to the personalized medicine

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As a common multifactorial disease with vast of sub-phenotypes cardiovascular disease (CVD) had always been great challenge for human geneticists. Main objectives of human genetic research are to uncover the genetic variants that play a significant role in development and/or complication in CVD. Since 80's most of the candidate gene association studies in CVD have identified the genes and variants affecting lipid levels, inflammation, and biology of the vascular wall as the underlying markers for disease. During last decade the breakthrough of non-candidate driven approach in genetics, genome wide association studies (GWAS) traced new paths in complex diseases among which are CVD. The integrative approach in analysis of heterogeneous types of data in genetic studies has become imperative. In order to distinguish functionally relevant genetic variants, especially non-coding, new strategies have been applied by combining genomics and transcriptomics data. The expression quantitative trait loci (eQTL) analysis indicated the widespread regulation of gene expression mostly by cis acting genetic variants. A further direction of research is to link the genetic variants to protein level, either in plasma or tissue specific. Other regulatory molecules such as microRNAa also became the targets for both, research and therapy in atherosclerosis and CVD. In parallel to genomics a development of novel tools for the statistical analysis and visualization of complex data sets is inevitable to allow advances in the research and knowledge translation. In further years we can expect to maximize our ability to move from associated genes, to pathways, to biology and clinical translation aiming at personalized medicine.

O22 Chromosomal region 9p21 in cardiovascular disease: Results from Serbian population

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The chromosome 9p21 locus was identified and now it is even considered the most robust genetic marker of CAD. It has also been associated with other phenotypes, such as carotid plaque (CP) presence, CAD-associated myocardial infarction, abdominal and intracranial aneurysm. Despite compelling genetic evidence for its association with CAD, the direct mechanistic link between the 9p21.3 risk alleles and atherosclerosis remains obscure. Several functional links to atherosclerosis have been proposed including regulation of proximal genes (*ANRIL*, *CDKN2B*, *CDKN2A* and *MTAP*) expression.

The kick off investigation of 9p21 region in Serbian population was performed by our group. Up to date two previously well characterized, lead genetic variants from two haplotype blocks (rs10757278, rs518394) and two eQTL variants (rs36212560, rs2275888) are explored in association with coronary and carotid atherosclerosis in patients from Serbia. The research have has been strengthened with the relative expression analysis of genes in/or close to 9p21 region in patients.

Analysis of DNA and RNA samples was performed by PCR and real-time PCR in order to determine investigated genotypes and gene expression. The sole genetic variants as well as their haplotypes were investigated in association with disease susceptibility and phenotype.

Our results suggest a gender specific association of two investigated variants with atherosclerosis, one of them was significantly associated only with carotid disease (rs10757278) while the other (rs36212560) showed significance in both carotid and coronary patients. Among variants hypothesized to influence 9p21 genes expression the strongest association was found for between rs10757278 and CDKN2B in CAD patients.

In conclusion, despite extensive research of 9p21 chromosomal region during the last decade further replication as well as functional studies are desirable in order to completely enlighten the mechanisms of its action in pathophysiology of cardiovascular diseases and to specify particular cardiovascular sub-phenotypes, which are modulated by this genetic locus.

O23 The association of AGTR1, AGTR2 and SCN5A genetic variantswith arrhythmia inpatients after the first myocardial infarction. Preliminary results of a prospective study

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Background: Patients who suffer myocardialinfarction (MI) have an increased risk of sudden cardiac deathif they experiencesome type of arrhythmiasearly after MI (up to 2 months), have a history of previous MI or experience syncope at the time of the first documented episode of arrhythmia.The arrhythmic effect of the renin–angiotensin–aldosterone system (RAAS) activation involves alterations in cardiac SCN5A sodium channel expression mediated in part by increased oxidative stress. Electrophisiological abnormalities in cardiomyocytes, caused by altered function of sodium channels, may predispose to arrhythmic storm during MI. TheAGTR1 rs5186 variant has been associated with diastolic heart failure and coronary heart disease.The AGTR2 rs1403543 variant has been associated with a moderate increase in left ventricular mass in young hypertensive males, with above median sodium intake.SCN5Ars1805124 variant was associated with lone atrial fibrillation, and may increase susceptibility to sodium channel blocker-induced proarrhythmia.

The aim: The aim of our study was to investigate the association of AGTR1, AGTR2 and SCN5A genetic variants with ECG parameters ofarrhythmia, heart rate and abnormal heart beatsamongst patients with first MI.

Methods: This study encompassed 136 patients with acute MI that were followed up for 6 months. ECG parameters were obtained by 2 D Doppler echocardiography at baseline (3-4 days afterr MI) and 6 months post MI. Rs5186, rs1403543 and rs1805124 were detected by TaqMan® technology.Statistical analysis was performed using SPSS software (SPSS 17.0).

Results: There were no significant associations of theinvestigated genetic variants with ST-segment depression, ST-segment elevation, T-wave inversion, heart rate, both at baseline as well as after the six months of follow up. There was also no association with Q-waveandabnormal heart beats at a baseline.

Conclusions: Preliminary results suggest no association of theAGTR1, AGTR2 and SCN5A variants witharrhythmia among the patients with first MI. Since the power of the study is moderate, further studies on larger study sampe is invitable to accurately estimate the effect of investigated genetic variants on post MI arrhythmia.

O24 Case report of patient with psoriasis during application of programming placebo aqueous solution with biochemical and XRD examination of serum samples

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Introduction: Psoriasis is a disease whose cause and effective treatment for complete healing is still not well known. Programming of aqueous solutions as a placebo has in practice provided good results for the suppression of this disease.

Purpose: to investigate the effects of programmed placebo solutions on patient's condition and possible changes of extracellular fluid structure.

Material and methods: programmed placebo aqueous solution, blood samples, biochemical analyzes and X-ray diffraction method. A patient with psoriasis has been oral administered a programmed placebo aqueous solution for 2.5 months. We monitored the dermatological changes, the results of blood tests and investigated structure of extracellular fluid by XRD method.

Case description: The patient is a 42-year-old male with psoriasis and present dermatological changes over 20 years without any other chronic illness. Dermatological changes are most present in the area of the back, legs and arms. Biochemical analyzes were made prior to the onset of the application of placebo solution and gave results of increased Holesterol values. The patient uses a programmed placebo solution of code Z|600. Since the blood serum contains 90% water, we analyzed solid serum samples by XRD method, at atmospheric pressure, prepared by freezing in the lyophilizer at a temperature of -40°C. After two weeks of oral administration of placebo solution, we have repeated biochemical analyzes and XRD examinations of serum samples. The results of the biochemical analyzes are presented in Table 1. The results of the XRD characterization before application of placebo solution were compared with the results obtained after two weeks of application of placebo, which were both compared with data of pure water, available in ICSD database (see Table 2).

Table 1. The results of biochemical analyzes prior to the onset of application of placebo solution and after two weeks of oral administration.

Biochemical analysis	Results		Units	Reference values	Method
	Prior to administration	After 2 weeks of administration			
Holesterol	**5.99**	5.06	mmol/L	<5.2	SPFT
HDL Holesterol	1.36	1.38	mmol/L	>1.0	SPFT
NON-HDL Holesterol	**4.63**	**3.68**	mmol/L	<3.37	SPFT
LDL Holesterol	3.98	3.32	mmol/L	<4.1	RN
Tryglicerides	1.42	0.79	mmol/L	<1.7	RN

Table 2. The cell parameters and volumes of the unit cell of the H_2O samples (In Ice form) from XRD characterization.

Modification		Ice Ih(c)		
Sample		ICSD-pure H_2O	H_2O-serum-1	H_2O-serum-2
Space group (no.)		$P6_3cm$ (185)	$P6_3cm$ (185)	$P6_3cm$ (185)
Unit Cell Parameters (Å)	a	7.82	7.839(2)	7.873(2)
	b	7.82	7.839(2)	7.873(2)
	c	7.36	7.370(3)	7.405(2)
	α	90	90	90
	β	90	90	90
	γ	120	120	120
Volume (Å³)	V	389.78	392.21	397.49

*H_2O-serum-1 – sample before administration of placebo solution
*H_2O-serum-2 – sample after 2 weeks of oral administration of placebo solution

Figure 1. Patient images displayed prior to the onset of application of placebo solution (left) and after 2.5 months of oral administration (right).

Conclusion: After two weeks of oral administration increased biochemical analyzes parameters of Holesterol and NON-HDL Holesterol were reduced. The results of XRD characterization suggest that there has been a slight increase in the parameters and volume of the unit cell of solid serum samples after two weeks of oral administration. Dermatological changes disappeared to a large extent after 2.5 months of oral administration of placebo solution.

O25 Quantum mechanics combined with XRD investigations of Sucrose as placebo used in medicine

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Sucrose is naturally occurring carbohydrate found in many plants. The molecule is a disaccharide combination of the monosaccharide glucose and fructose with the formula $C_{12}H_{22}O_{11}$. Sucrose structure has been solved as crystal structure, showing monoclinic symmetry (Fig. 1). Sucrose is currently under extensive research due to its potential application in medicine. In this study we have performed *ab inito* modeling of sucrose (placebo), using various quantum mechanical methods: Hartree-Fock approximation (HF), Density Functional Theory (DFT) with Local-Density Approximations (LDA) and Generalised Gradient Approximation (GGA), and hybrid (Becke, three-parameter, Lee-Yang-Parr, B3LYP) functional. In order to investigate possible influence of placebo effect on sucrose, in our earlier work we have performed nano-technological testing of structure of sucrose [1]. Furthermore, we have experimentally studied the nanostructure of medicaments by X-ray methods and compared to placebo forms obtained from sucrose and sucrose as control parameter [2-4]. The all samples were monitored by X-ray powder diffraction on a Siemens D-500 XRPD difractometer. The XRPD results were characterized using Ritveld refinement, while theoretical analysis has been performed using VESTA and Kplot software. Our calculations were in very good agreement with previous experimental and theoretical observations, where such data were available, and further structural investigations are in progress.

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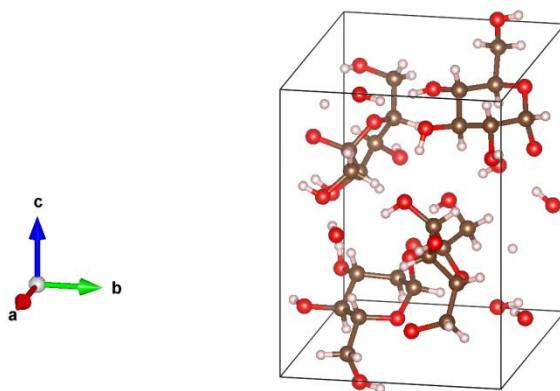
Figure 1. Visualization of the crystal structure of Sucrose (Placebo) showing monoclinic symmetry. Brown balls correspond to C atoms, red balls to O atoms, and white balls to H atoms, respectively.

O26 The cytotoxic effect of Achillea S., L., Rosmarinus officinalis L. and Juniperus communis L. on squamous and basal cell carcinomas cells

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INTRODUCTION: Squamous and basal cell carcinoma (SCC, BCC) are the most common cancers in the maxillofacial region. Both types of tumours remain a considerable medical challenge, despite important advances in the treatment that occurred during last decades, and finding new therapeutic modalities would be of substancial importance.

AIMS: To evaluate the effect essential oils using MTT assay on BCC and SCC cells in culture, to compare cell viability after 24h treatment, and to compare the effect of essential oils with 5-fluorouracil.

MATERIAL AND METHODS: SP-130 was used to dry plant material peppermint, rosemary and juniper fruits. For the production of essential oils, the technique of inverse distillation with water and water vapor without pressure was applied. Isolated cells from SCC and BCC were grown in DMEM supplemented with 10% FBS and antibiotic and seeded into T75 cell culture flasks. The cells were maintained at 37 °C in humidified atmosphere containing 5% CO_2. The medium was changed every 2-3 days and the cells were passaged prior to reaching 75-85% confluence. Ten thousand cells were seeded in a 96-well plate and incubated. After 24h they are treated with 100μl of 80, 50, 20 mg/ml 5-fluorouracil and 1%, 5% and 10% of all essential oils, previously supplemented with DMSO. After 24h/7 days, MTT was added to each well, incubated for 4 h, and the supernatant was discarded. Precipitates were dissolved in 150 μl DMSO by shaking. Optical density was measured at 540 nm using an ELISA reader. The assay was done on three different SCC and BCC in triplicate, repeated twice.

RESULTS: The SCCs and BCCs cell viability after the 24h treatment was significaly lower compared to 5-fluorouracil. The overall mean viabillity after essential oil treatment was 31 % and 17 % (Achillea S. L.), 37 % and 28 % (Rosmarinus officinalis L.), 33 % and 37 % (Juniperus communis L.), for SCC and BCC cells respectively.

CONCLUSIONS: These essential oils showed greater effect on cancer cell viability than chemoterapeutics. These results showed good starting point in future research of the effects of essential oils on SCC and BCC cells.

O27 Heart-brain interactions: infectious, congenital heart disease and heart transplant: Beyond embolic sources

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INTRODUCTION: We have presented papers at several International meetings, about stroke, neurological complications of cardiovascular interventions. In 2015, 2 young patients with non compaction cardiomiopathy (LVNC) in heart transplant protocol had TIA/Minor Stroke just prior to procedure. We did not find reports in PubMed search about TIA/Minor Stroke just prior to heart transplant and after transplanted. Recently a patient with past history of pulmonary atresia, severe PHT, depressive disorder, secondary polycythemia and mechanical hemolysis, asthma, headaches in childhood, with NCCT disclosing hyperdense vessels simulating a contrast imaging due severe polycythemia. In our endocarditis population we have found several factors beyond infectious embolus. Finally with patients in his 20´s and 30´s YO in the 1980´s now in theelderly and promiscuitythe HIV as a cause of stroke is appearing.

Objective: To share our experience from a 4th level Cardiovascular Center in Latin America with different pathologies in a Heart-Brain interaction.

Report: Two patients withL VNC and secondary heart failure were in heart transplant protocol, just in the period for it had TIA/MinorStroke with no possibility to perform MRI. They were evaluated with NCCT and clinical evaluation, base dont hem transplanted.

Case 1: A 21 YOM admitted for heart transplant after protocol approval, suddenly had left sidehemiparesis with blurred speech, NIHSS of 22, improving to 7 then 0. NCCT was normal. Carotid ultrasonography/TCD were normal. Following day possibility for heart transplant, no posible MRI due cardiovascular instability, NCCT no lession. He was undergone heart transplant, no complications. Brain MRI done after, right posterior subinsular and temporal areas with small enhancement, no aneurysm, no stenosis. He was discharged with no neurologicaldeficit and no new symptoms at subsequent evaluations.

Case 2:18 YOW was in heart transplant protocol with ICD, suddenly presented rightside hemiparesis with blurred speech, 2 hours duration. NCCT no lession. Next day new deficit, rigtht hemiparesis and hypoesthesia, less than 60 minutes, NCCT no lession. She was transplanted, acute rejection II and put on Metylprednisolone, post surgical biventricular dysfunction and UTI. She stabilizes, no neurological deficit and continues recovery from surgery. After the ICD removed MRI done disclosing small cerebellar ischemic lessions.

Congenital cardiophaties and Stroke: 24 YOM past history of pulmonary atresia, severe PHT, depression, secondary polycythemia and mechanical hemolysis, asthma, headache since childhood; at 15 YO on *Sildenafil,* starting occipital pulsatile HA with nausea/photophobia, exacerbated with effort. Previous 7 months daily HA, overusing analgesics. Neuroexam normal. NCCT showed engorgement/prominence of both MCA. Underdiagnosis of migraine without aura, chronic migraine and analgesi cover use HA treatment started; additionally HA associated with*Silfenafil* use. Great recovery with phlebotomy. 4 days after severe HA with leftside hypersthesia; neuroevaluation normal. NCCT with enhancement in vascular structures, Hb 24.6, Hct 74.6. Under vascular thrombosis diagnosis MRI done

disclosing chronic thrombosis, prominent colateral venous, suabacute ponslacunar infarct. OAC was initiated.

Endocarditis records: On past 4 years 9 patients with endocarditis had neurological complications, 7 of them men, 2 were in posterior circulation, 6 of them cardiovascular risk factors, 3 with comorbidities: one with SLE and CRF, one with HIV infection, one with hypothyroidism. The mechanism of CNS involment was catéter dyalisis infection, 4 patients native valve involment, 3 prosthetic valve, one in a IVC.

HIV in the elderly: 75 YOM consults for fluctuating motor deficit in his rightarm, in one week not recovery and also facial deviation appeared. Neuroexam: right central facial with right hemiparesis and hypoesthesia; NCCT left frontal subcortical hipodensity with small hyperdensity suggestive of luxury perfusion. Holter, Doppler US, TEE were normal. Undetermined TOAST stroke. One month after readmitted due progressive deterioration in right motor function, language and swallowing. Neuroexam: motor aphasia, right side hemiplegia, rigth facial paresis. NCCT left subcortical frontal hypodensity, a rigthparieto-occipital hypodensity both lesions with a digiti form edema. HIV test positive, suspicion of Toxoplasmosis vs Lymphoma Brain MRI performed, pathological changes in right occipital pole and leftfronto-parietal with extenive edema and irregular and incomplete enhacement suggesting *Toxaplasmosis.* No lesión was documented in MRA.

DISCUSSION: Stroke is the most common neurologic cause for patient admission to the emergency department and it risk increases with age. Acute decisions for neurologist in patients with Cerebrovascular Disease (CVD) going to surgery are a challenging as Endocarditis with acute embolism to CNS and need for immediately cardiac surgery and situations as presented with this two transplanted patients. Related to acute embolic endocarditis there are reports but in situations as the patients reported no information was found. There are reports of CVD as a complication after transplant. We want to emphasize the decision to perform the heart transplant in patients with acute CVD (TIA or small Stroke) based on clinical recovery and normal NCCT with acute Stroke symptoms and 24 hours after with complete recovery, with no possibility to perform MRI before heart transplantation and patient with a donor for transplanting.

Polycytemia symptoms include dyspnoea when lying down, dizziness, excessive bleeding, filling in the upper left part of the abdomen, headache, pruritus specially after warm bath, red face, phlebitis symptoms. A response to hipoxemia causing changes at microcirculatory level, alter ingstasis producing prothrombotic state, its correction by phlebotomy is used to improve symptoms, without any evidence. Severe polycytemia can produce abnormal hyperdensity of intracranial blood vessels on NCCT, which simúlates the appearance of a contrast enhanced CT scan and mimic dural venous sinus thrombosis.

In older patients, stroke-mimicking conditions can cause signs and symptoms indistinguishable from true stroke, representing 12.7% of elderly patients admitted to an ED. HIV infection can produce Stroke by opportunistic infection (TB, VZ, meningovascular syphilis) vasculopathy, cardioembolism and coagulopathy. There are stroke mimics: migraine, hypoglycemia, epilepsy, tumors, infections, functional disorder and wrong diagnosis.

CONCLUSION: Heart-brain interaction as etiology or pathophysiology in different disorders are implicated. Microcirculatory changes due inflammation, infectious diseases can produce thrombotic or embolic disorders. The insula when affected can produce cardiac manifestations.

O28 Pathogenesis of Parkinson's disease and microbiota - could we be wrong all the time?

Ilić TV

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There is growing awareness about the possible link of microbiota (gut bacteria) and early stages of neurodegeneration, as can be seen in Parkinson's disease. Current understanding of pathophysiological processes in Parkinson's disease is primarily associated with the accelerated loss of dopaminergic neurons in several brain regions, and in the first place in the substantia nigra. Several monogenic forms of a disease, linked to candidate genes as LRRK2, SNCA, VPS35, Parkin, PINK1, and DJ1 suggest an abnormal tendency of proteins to aggregate as a result of misfolding, specifically alpha-synuclein.

However, beside typical motor symptoms like bradykinesia, rigidity, tremor, postural instability (in advanced stage of disease) either so-called dopaminergic manifestations, there is also more and more non-motor symptoms involving olfactory, gastrointestinal, cardiovascular and urogenital systems, some of which may appear years before the motor symptoms arise.

In addition to these clinical observations, animal experiments show a clear dysregulation of the brain-gut-microbiota axis in model of Parkinson's disease. In this way, thoughts are open about microbiota as potential triggers of protein misfolding and sustained inflammation in the brain.

O29 Prognostic value of detrended fluctuation analysis in diferent disease states

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A number of new methods based on nonlinear system theory have been developed to quantify the complex HR dynamics and to complement the conventional measures of HRV. ECG signals are non-stationary and stochastic and exhibit self-affinity and self-similarity. While phenomena with characteristic scales are well defined by their mean and median, scale-free phenomena are better defined by their scaling exponent.

The detrended fluctuation analysis (DFA) method, introduced by Peng in 2000 is used to quantify the scaling behavior or fractal properties of physiological time series. In other words, it quantifies fractal correlation properties in non-stationary time series. DFA provides a distinction between intrinsic fluctuations generated by complex systems reflecting the intrinsic dynamics of the system and those caused by external stimuli. The DFA method has also proven useful in revealing the extent of long-range fractal correlations in time series which represent the intrinsic nature of the system.

DFA has been used to evaluate cardiovascular function in many disease states. Several studies have shown that a significantly reduced short-term scaling exponent $\alpha 1$ in patients with ischemic cardiomyopathy represents a strong predictor of cardiac death, sudden death and overall mortality. Decreased $\alpha 1$ was also the strongest predictor of risk for ventricular arrhythmia and subsequent mortality in patients with previous myocardial infarction. It has also been shown that patients with anterior wall ST segment elevation myocardial infarction had a significantly lower DFA$\alpha 2$ in the acute stage and lower DFA$\alpha 1$ at 3 months and at 12 months. In contrast, in patients with stress-induced cardiomyopathy both $\alpha 1$ and $\alpha 2$ scaling exponents are significantly increased and tend to normalize after administration of beta blockers. In patients with aldosterone producing adenoma DFA $\alpha 2$ scaling exponent was significantly decreased and normalized after adrenalectomy. In patients with end-stage renal disease, DFA is superior to linear parameters of heart rate variability in predicting mortality and the addition of $\alpha 1$ scaling exponent to the clinical risk factors significantly improves periction of outcome.

DFA in patients with Parkinson`s disease and multisystem atrophy reveals significantly increased $\alpha 2$ exponents during active wakefulness, NREM and REM sleep. In our group of 55 patients with amyotrophic lateral sclerosis DFA $\alpha 1$ was increased in bulbar onset disease on DFA performed on linear trend and in both spinal and bulbar onset disease on DFA performed on quadratic trend. Increased fractal scaling exponent $\alpha 1$ on both linear and quadratic trend was a significant univariate predictor of death in Cox regression analysis.

In conclusion, DFA carries additional prognostic information that is not provided by linear time and frequency domain measures. Reduced values of DFA scaling components, especially $\alpha 1$, seem to be characteristic of cardiac disease, indicating a greater degree of randomness and loss of correlation of heart rate fluctuation. In primarily nervous system disease states these exponents are increased, showing break down of fractal scaling with still preserved correlations.

O30 Cardiac involvement in dystrophinopathies

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Dystrophinopathies are due to mutations in the dystrophin gene on chromosome Xp21.1 and comprise the allelic entities Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD) and X-linked dilative cardiomyopathy (XLDCM). In all three entities, the heart is affected to various degrees, depending on the stage of the disease and the type of the mutation (cardiac involvement, CI). The pathoanatomic evidence of CI in dystrophinopathies is the replacement of myocardium by connective tissue or fat. DMD and BMD are responsible for over 80% of all muscular dystrophies. Cardiac disease is a common manifestation, not necessarily related to the degree of skeletal myopathy; it may be the predominant manifestation with or without any other evidence of muscular disease. Death is usually due to ventricular dysfunction, heart block or malignant arrhythmias. Not only DMD/BMD patients, but also female carriers may present cardiac involvement. Clinically overt heart failure in dystrophinopathies may be delayed or absent, due to relative physical inactivity. In DMD/BMD, the left ventricular posterobasal and lateral walls are most extensively affected, sparing the right ventricle and the atrium.

Degree and dynamics of CI vary among the three entities. In DMD/BMD, CI usually remains subclinical in the early stages of the disease. Typical initial manifestations of CI in DMD/BMD are sinus tachycardia, tall R1 in V1, prominent Q in I, aVL, V6 or in II, III, and aVF, increased QT dispersion and possibly autonomic dysfunction. Initially, echocardiography is normal or shows regional wall motion abnormalities in areas of fibrosis. With spreading of fibrosis, left ventricular dysfunction and ventricular arrhythmias additionally occur. In the final stages of the disease, systolic function may lead to heart failure and sudden death. Subclinical or clinical CI is present in about 90% of the DMD/BMD patients but is the cause of death in only 20% of the DMD and 50% of the BMD patients. XLDCM is a rapidly progressive, almost exclusively myocardial disorder, starting in teenage males as heart failure due to dilative cardiomyopathy (CMP), leading to death from intractable heart failure within 1-2 years after diagnosis. Therapy of arrhythmias and CMP in all three disorders follows the established cardiological recommendations. Due to its protective effect, ACE inhibitors are recommended already at the early stages of the disease. Beta-blockers may be an additional option if indicated.

Key words: Heart – Dystrophinopathies

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O31 Skin manifestations as independent predictors of stroke and total cardiopulmonal risk: a multidisciplinary study based on the Serbian national APS registry

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INTRODUCTION: Cutaneous manifestations has been described[1-4] as an integral part of antiphospholipid syndrome (APS) and the most of them have been found to be thrombotic on histopathology without evidence of perivascular inflammation.

AIM: The aim of this study was to investigate relationship between cerebrovascular, cardiopulmonal, and cutaneous manifestations in APS patients as well as their connection with type of antiphospholipid antibodies. This is the report of Serbian cohort of APS patients.

PATIENTS AND METHODS: Our study comprises a total of 508 patients: 360 PAPS patients and 148 SLE patients with secondary APS. Antiphospholipid antibody (aPL) analysis included detection of aCL (IgG/IgM), aß2GPI, and LA. Skin manifestations (livedo, skin ulcerations, pseudovasculitis lesions, superficial cutaneous necrosis and digital gangrene) were diagnosed by rheumatologist and dermatologist whereas the diagnoses of cerebrovascular manifestations (TIA or stroke) have been confirmed by neurologist.

RESULTS: The prevalence of skin manifestations in our cohort was 27.2% in PAPS and 76.4% in SAPS group (p=0.0001). In both groups, the most common manifestation was livedo. There was significant relationship between aCL IgG and digital gangrene in PAPS patients (p=0.026). The same aPL was significantly related to digital gangrene and pseudovasculitis lesions in SAPS patients (p=0.022, p=0.021 respectively). Double and triple aPL positivity were not related to skin manifestations in Serbian APS patients. The majority of cutaneous manifestations were significantly related to cerebrovascular events in SAPS and PAPS group, especially in PAPS patients where overall skin manifestations presence was highly statistically related to TIA and stroke occurrence (p=0.001, p=0.001 respectively). In PAPS patients the presence of LA was more common in PTE (p=0.005) and in pulmonary microthrombosis (p=0.003). We revealed statistical significance considering the presence of aCL IgM and pulmonary microthrombosis (p=0.05). Skin ulcerations correlated with positive titers aCL IgM and β_2 GPI IgM (p=0.03 and 0.04, respectively), while pseudovasculitis correlated with positive titers ß2 GPI IgM (p=0.02). PAPS patients were more more likely to develop pulmonary thromboembolisam if they had livedo reticularis (p=0.005),skin ulcerations (p=0.007), pseudovasculitic lesions (p=0.01) , superficial cutaneous necrosis (p=0.005), and digital gangrene (p=0.02). Patients were also more prone to pulmonary microthrombosis if they already had livedo reticularis (p=0.03),skin ulcerations (p=0.007), pseudovasculitic lesions (p=0.05) , superficial cutaneous necrosis (p=0.006), and digital gangrene (p=0.02).

CONCLUSION: In this cross-section analysis of a large cohort of Serbian APS patients, skin manifestations were strongly related to cerebrovascular and cardiopulmonal, suggesting more cautious approach regarding severe symptoms, especially in PAPS patients with skin manifestations.

Keywords: antiphospholipid syndrome, cerebrovascular, cardiopulmonal, and cutaneous manifestations., national cohort study.

Conflicts of interest: Authors declare no conflicts of interest.

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Table 1. Distribution of aPL in the patients with primary and secondary APS

	PAPS N=360	SAPS N=148	
	N (%)	N (%)	p
aCL IgG	107 (29.7%)	83 (56.1%)	**0.0001****
aCL IgM	172 (47.8%)	89 (60.1%)	**0.014***
ß₂GPI IgG	109 (30.3%)	60 (40.5%)	**0.038***
ß₂GPI IgM	147 (40.8%)	67 (45.3%)	0.489
LA	198 (55.0%)	79 (53.4%)	0.769

Legend: PAPS= primary antiphospholipid syndrome, SAPS= secondary antiphospholipid syndrome, aCL= anticardiolipin antibodies, β_2GPI=anti- β_2 glycoprotein 1 antibodies, LA= lupus anticoagulant, aPL= antiphospholipid antibodies

*statistically significant, **highly statistically significant

Table 2: Binary regression analysis for TIA occurrence in PAPS and SAPS patients

	PAPS			SAPS		
	OR	95% CI	p	OR	95%CI	p
Age	28.699	1.045-1.100	**0.0001****	9.705	1.018-1.082	**0.002****
Gender	1.878	0.816-3.158	0.171	0.424	0.144-2.644	0.515
aß2GPI IgG	8.484	0.149-0.689	**0.004****	0.115	0.375-1.997	0.734
Smoking habit	2.311	0.872-2.965	0.128	0.830	0.639-3.412	0.362
Hypertension	0.233	0.218-2.513	0.630	7.692	1.595-15.146	**0.006****
Cutaneous manifestations	10.256	1.472-4.989	**0.001****	0.295	0.494-3.474	0.587

* statistically significant difference, ** highly statistically significant difference

Table 3: Binary regression analysis for stroke occurrence in PAPS and SAPS patients

	PAPS			SAPS		
	OR	95% CI	p	OR	95%CI	p
Age	34.657	1.048-1.098	**0.0001****	5.329	1.005-1.064	**0.021***
Gender	0.166	0.599-2.183	0.684	4.737	1.144-13.128	**0.030***
aß2GPI IgG	2.588	0.316-1.120	0.108	3.079	0.920-4.491	0.079
Smoking habit	5.405	1.111-3.445	**0.020***	2.454	0.210-1.190	0.117
Hypertension	0.074	0.377-3.628	0.786	0.579	0.605-5.410	0.289
Cutaneous manifestations	2.416	0.886-2.845	0.120	2.104	0.772-5.647	0.147

* statistically significant difference, ** highly statistically significant difference

O32 Sneddon syndrome (SS) and antiphospholipid syndroma (APS)

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Background: SS is a combination of ischemic cerebrovascular disease (CVD) and widespread livedo reticularis (LR) in patients without evidences of connective tissue disease. The relationship of SS and APS is not completely clear.

The aim of present work was: 1) to analyze a whole spectrum of clinical manifestations of SS and study the following antiphospholipid antibodies (aPL): anticardiolipin antibodies (aCL), anti-ß2-glycoprotein I (aß2GPI), antibodies to prothrombin (aPT) and lupus anticoagulant (LA); 2) to compare clinical manifestations of aPL-positive SS pts and aPL-positive pts with CVD without LR.

Material and methods: One hundred twelve SS pts were examined (89 women, 80%, mean age 40.3±3.7 years). ACL (112 patients), aß2GPI (37 patients) and aPT (43 patients) were measured by ELISA. Lupus anticoagulant was detected by coagulation assays (101 patients). Control group consisted of 45 aPL-positive patients with CVD without LR (36 women, 80%, mean age 35.3±12.3years).

Results: In addition to CVD and LR there were other clinical manifestations of SS: fetal loss (69%), peripheral venous thrombosis (23%), ischemic heart disease (39%), thickening of heart valves on echocardiography (66%), arterial hypertension (67%), mild renal syndrome (49%), thrombocytopenia $<150 \times 10^{9}$/l (17%), anemia (26%), headache (77%), epilepsy (19%), chorea in the past history (19%). ACL (>25GPL) were found in 32% SS patients; aß2GPI (> 20 un/ml) in 35% (3% of them were aCL-negative); LA–positive - in 50% (27% of them were aCL-negative); aPT – in 58% (37% of them were aCL-negative, 21% - LA negative). 63% SS patients were positive to at least one type of studied aPL. Clinical manifestations of aPL-positives and aPL-negative SS did not differ. Comparison of aPL-positive SS patients and aPL-positive patients with CVD without LR showed that cortical dementia (46%), recurrent strokes (66%), cardiac valve thickening (68%) and renal syndrome (50%) were more frequently observed in the former than in the latters (17%, 39%, 14%, 17%, respectively), while peripheral venous thrombosis and pulmonary thromboembolism were more frequent in patients without LR (57% and 26%) than in aPL-positive SS (30% and 6%, respectively).

Conclusions. Clinical manifestations of SS are similar to those in APS. APL are found more than in a half of SS patients with LA and aPT being more frequent. An extension of the methods of aPL measurement increases the proportion of SS patients with positive APS biological markers. In the frame of APS SS is characterised by more severe brain damage and a greater tendency to development of arterial, but not venous thrombosis.

O33 Changing the concept of antinuclear autoantibodies screening: a new laboratory algorithm in the diagnosis of systemic autoimmune rheumatic diseases

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Background: Antinuclear antibodies (ANA) are fundamental in the diagnosis of systemic autoimmune rheumatic diseases (SARD). The indirect immunofluorescence (IIF) on HEp-2 cells is the gold standard method for ANA detection. In a recent study, the higher sensitivity for ANA detection of BioPlex ANA Screen than IIF on HEp-2 has been reported. Also, the early detection of autoantibodies by BioPlex predicts the development of autoimmune diseases before the clinical onset. The aim of the study is to elaborate a new laboratory algorithm for ANA screening in subjects with clinical suspicion of SARD.

Methods: The algorithm elaboration was based in a 3 years follow-up study on 411 subjects without clear diagnosis of SARD in whom autoantibodies were detected by BioPlex but not by IIF on HEp-2.

Results: After 3 years of follow-up, 76% of subjects were positive for autoantibodies by IIF and a diagnosis of autoimmune diseases was found in 87% of the patients. A new algorithm for ANA screening including the BioPlex ANA Screen in patients with clinical suspicion of autoimmune diseases was proposed.

Conclusions: BioPlex ANA Screen should be included as screening for autoantibodies in subjects with clinical suspicion of autoimmune diseases.

O34 Effects of training program on quality of life and fatigue in patients with systemic lupus erythematosus

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INTRODUCTION: Quality of life (**QOL**) measures have become a vital and often required part of health outcome appraisal in patients with SLE. Because lupus causes pain, inflammation and fatigue the very thought of exercising can be a challenge for patients.

AIM: To determine if supervised aerobic training or exercise improves fatigue and QOL in patients with lupus.

METHODS: 40 women with SLE (39.74 ± 10.58 year) in stady state (measured by SLEDAI score) were evaluated using Fatigue Severity Scale (**FSS**) and Short Form 36 **(SF36)** on baseline and after 6weeks. One randomly choosen group of 20 women had aerobic training on bicycle ergometer for 15 minutes, 3 times a week and other had exercise (same time of training).

RESULTS: Considering all 40 women, FSS values show significantly improvement in fatigue $43,78\pm5,75$ vs $19,08\pm7,84$ ($p<0,001$) during 6 weeks. But, there is no statistical difference in FSS values comparing two training groups ($19,23\pm7,86$ vs $18.37\pm7,66$; $p<0,005$). Statistical analysis of SF36 parameters shows significantly improvement of QOL in all parameters as in 2 general parameters: physical health ($46.30\pm7,01$ vs $60.0\pm7,05$; $p<0.001$) and mental health ($33,65\pm3,93$ vs $64.6\pm5,32$; $p<0.001$). But, there is no statistical difference in SF36 parameters between two training group at the end of 6 weeks. Training did not exacerbate disease measured by SLEDAI score.

CONCLUSION: This study showed significant improvement in fatigue and consequently quality of life after training in lupus patients.

O35 Impact of valvular changes on cerebrovascular manifestations in patients with primary and secondary antiphospholipid syndrome

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INTRODUCTION: Antiphospholipid syndrome (APS) may manifest itself as a primary (PAPS) or secondary disease, most commonly in the context of Systemic Lupus Erythemathosus (SLE) with various neurological and cardiac manifestations in its occurrence. This paper reports on the results from the Serbian National Cohort study, which was started in January 2000.

AIM: The aim of this study was to investigate relationship between cerebrovascular (stroke and transient ischemic attack (TIA) and valvular manifestations in APS patients as well as their connection with type of antiphospholipid antibodies.

PATIENTS AND METHODS: Our study comprises a total of 508 patients: 360 PAPS patients and 148 SLE patients with secondary APS. Antiphospholipid antibody (aPL) analysis included detection of aCL (IgG/IgM), ß2GPI, and LA. The diagnoses of valvular changes (valvular thickness and dysfunction and/or valvular vegetations) were established throughout transthoracic echocardiographic exam (presence of vegetatons were confirmed with transesophageal echocardiography). The diagnoses of cerebrovascular manifestations (TIA or stroke) have been confirmed by neurologist.

RESULTS: As expected, age was strong predictor for stroke and TIA occurrence in both groups as well as gender (stroke more likely at male SAPS and TIA in male PAPS patients) and well known standard atherosclerotic risk factors: hypertension, hyperlipidemia and smoking habits. Valvular manifestations overall were significantly related to TIA (not to stroke) occurrence in both groups of patients (p=0,045 for SAPS patients, p=0.001 for PAPS patients) and were independent predictors of TIA occurrence (OR 9.125 CI (95%) 0.003-0.617, p=0.003). Furthermore, presence of ß2GPI IgG was significantly related to stroke (p=0.018) and this aPL was significant independent predictor of TIA in PAPS patients.

CONCLUSION: Particular subpopulation of APS patients (smokers, hypertensive, male, ß2GPI IgG positive SAPS or PAPS patients with valvular changes present) should be under neurological observation and possible higher dose regime of antiplatelet or anticoagulant therapy.

Keywords: antiphospholipid antibodies type, valvular manifestations, stroke, national cohort study.

O36 Autonomic nervous system activity and chronic autoimmune thyroiditis – is there a missing link?

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Background & Aim: In spite of the thorough investigation of the relationship between thyroid and cardiovascular function, there are still many questions that have not been fully elucidated. It is well-known that cardiovascular morbidity and mortality has been increased in full-blown as well as subclinical hyper- and hypothyroidism. However, it seems that there is also a link between cardiovascular risk and thyroid autoimmunity, even in euthyroid patients. These observations have encouraged the authors to perform: (1) an investigation of the autonomic profile in patients with chronic autoimmune thyroiditis, according to thyroid function and (2) systematic search of the literature investigating the relationship between thyroid autoimmunity and the function of the autonomic nervous system.

Material and methods: Sixty-eight female patients with chronic autoimmune thyroiditis were studied. Among them, 42 patients (62%) were euthyroid and 26 patients (38%) hypothyroid, 15 with subclinical and 11 with clinically manifested hypothyroidism. In studied patients the simpathovagal balance was analyzed using cardiovascular reflex tests according to Ewing and/or autonomic nervous system acvtivity (ANSA) assessment. Statistical analysis was performed using SPSS for Windows, release 20.

Results and Discussion: There is substantial experimental and clinical evidence of autonomic nervous system involvement in both hypo- and hyperthyroid states, either manifested or subclinical. We have dealt with the autonomic nervous system activity in adult patients with autoimmune chronic thyroiditis. Among them orthostatic hypotension was demonstrated in 53%, without any difference between hypothyroid and those with preserved thyroid function. In most of the patients (96%) sympathovagal imbalance, with an increase in sympathetic and decrease in parasympathetic activity has been observed. Patients with the most severe autonomic neuropathy were highly positive for anti-thyroid antibodies. Quarter of these patients also expressed vitiligo or psoriatic changes. In significant number of them previous viral infections could be demonstrated. Kilic A et al have recently also demonstrated the association of autoimmune chronic thyroiditis with disturbed autonomic regulation of heart rate in eythyroid children proving that this association existed early in the evolution of chronic autoimmune thyroiditis.

Conclusion: Autonomic dysfunction among patients with autoimmune chronic thyroiditis is rather high and it does not depend on thyroid function. However, its association with previous (virus) infections and consequent systemic iflamation has been observed. It could be the reason for the increased cardiovascular risk in these patients, atherosclerotic as well as arrhythmogenic. Possibility of therapeutic modulation of this risk in these patients is still unproven and is open for future research.

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O37 Brain-reactive autoantibodies from patients with Neuropsyhiatric Systemic Lupusalter calcium homeostasis in cultured hippocampal neurons

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Objectives: The autoimmune disease systemic lupus erythematosus (SLE) is frequently accompanied bydiverse neurologic and psychiatric (NP) manifestations of unknown aetiology.Although pathogenic role of brain-reactive autoantibodies (BRA) has been proposed, cellular mechanisms of their action remain largely unknown.Since cytosolic calcium homeostasis reflects well the cellular events CSF and serum IgG fractionof NP SLE patients, as well as commercially-available BRA were tested for intracellular Ca^{2+} responses in rodent neuronal cultures.

Methods & Results: Calcium levels inthe primary culture of rodent hippocampal neurons weremonitored on 7 DIV cells loaded with a calcium-sensitive dye Fluo-4 AM (5 µM). Time-lapse images were obtained every second, before andafter the application of samples from four SLE CSF patients and one control NMO patient or commercially-available BRA. Set of blockers and inhibitors were used to elucidate specific receptor mechanisms. Compared to the control IgG, the amplitude of calcium transients was significantly larger in all SLE CSF IgG-treated neurons when external Ca^{2+}(2 mM) was present. This response was attenuated when solutions were Ca^{2+}- free, whereas no detectable response was observed with the control IgG. CSF from CNS SLE patients showed heterogeneity in the ability to induce intracellular calcium transients, and Ca^{2+}-free solution abolished the effect of CNS SLE CSF. CSF from the NMO patient did not have any effect on cytosolic calcium. Pharmacological dissection experiments indicated that voltage gated calcium channels and glutamate receptors have a role in the CNS SLE CSF-induced calcium transients with predominant role of NMDA receptors. Commercially-available BRAs failed to mimic the CSF- or IgG -induced calcium transients.

Conclusions: Our results suggest that neuronal responses to CNS SLE IgG canlargely beattributedto theinflux of extracellular Ca^{2+} through the plasma membrane, while the transients of smaller amplitude in Ca^{2+}-free external solutionreflectactivation of internal Ca^{2+} stores.The CSF samples from CNS SLE patients werediverse in their effect on intracellular Ca^{2+} and a GluN2-dependent Ca^{2+} pathway was revealed for one effective sample. Individual BRA samples however, elicited a smaller, but sustained $[Ca^{2+}]_i$ rise.The current findings support the hypothesis that BRAs fromCNS SLE patients are neuroactive.

O38 Coronary artery disease and clinical neurocardiology

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ABSTRACT

At the coronary artery disease (CAD) there was evaluation of diagnostic possibilities of high resolution heart rate variability (HRV) analysis in patients (pts) and definition of HRV predictors' complications by evaluation of sinoatrial heart node (SN) deregulations. The high-resolution RCG is enough adequate and informative method of the diagnosis regulative breaches in the heart.. At the coronary artery disease may be defined the nonspecific symptoms of breaches circulation in the heart tissues and the ischemic episodes at angina pectoris, functional classis of stenocardia and heart failure. Also HRV with extreme reduction of wave structure – stabilization of the heart rhythm testimonies about autonomic cardioneuropathy with high risk of lethal outcome. RCG with exact analysis of HRV is the excellent method in clinical pharmacology for studying autonomic action of the medicines, accessories affects and control of the treatment. RCG method may be used in arrhythmology for registration and analyses a number clinical forms of the heart arrhythmias, significant of every arrhythmic episode and its hemodynamic influence.

Key words: Rhythmocardiography, heart rate variability, coronary artery disease, cardiology, arrhythmology.

Purpose of this studying was evaluation of heart rhythm deregulations in diagnosis of cardiovascular pathology. Premises of this theme were known a number of the coronary artery disease (CAD) diagnostic negative forms, absence of the certain formalized signs of complications and lethal outcome in patients (pts) with CAD.

Materials and methods. During 5-9 years 3544 pts were under prospective observation in the neurocardiology laboratory of one Russian hospital. From them there were selected 534 pts with chronical CAD and stable angina pectoris (AP) of 1-4 functional classes (FC), 518 pts with the heart failure (HF) of 1-4 FC, 96 pts with acute myocardial infarction (AMI), 115 pts with acute coronary syndrome, 971 pts with the cardioarrhythmias (CA) of the background of the ischemic pathology. Criterions of exclusion were somatic diseases, which could distort HRV data. All pts were investigated by standard cardiological methods (ECG, EchoCG, Holter monitoring, and laboratory investigations) and by high-resolution rhythmocardiography (RCG) for the heart rate variability (HRV) analysis. 47 healthy men (control gr. -C) (Fig.1) were investigated too by the RCG and by hardware-software apparatus program complex CAP-RC-01-"Micor" (Reg. Certificate FS02262005/2447-06) -APC. Discretization of electrocardio-signal was 1000±3 Hz. There were determined middle HRV-indices in time-domain: RR-interval-RR, standard deviation of all HRV-waves- SDNN, middle quadratic indices in the sinoatrial node wave structure: σl- physiologically connected to humoral-metabolic influences, σm- sympathetic, σs-parasympathetic autonomic regulative factors. Here was spectral analysis with Fast Fourier Transformation and spectral windows Hamming and Parsen for evaluation of degree influences of three regulative factors in sinoatrial heart node in spectral correlation correspondingly to total spectrum (100%). These regulative influences produce fluctuations of R-R intervals: 0.033-0.04 Hz- humoral-metabolic very low frequency diapason –VLF%, sympathetic –more 0,04-0,12- LF% and parasympathetic high frequency diapason 0.12-0.24 Hz – HF%. RCG investigation created in four stimulant tests In tests there were evaluated maximal reaction of HRV to stimuli (ΔRR%), time reaction and restoration after stimuli (tAB, tr) At the mathematical analysis in researches was used program"STAT-6" with Student criterion-t and it analogue z for large volume material. Also there was used Spirman method with package SPSS 12.0. The obligatory conditions for clinical RCG are high resolution registration RR-intervals and correct program equipment.
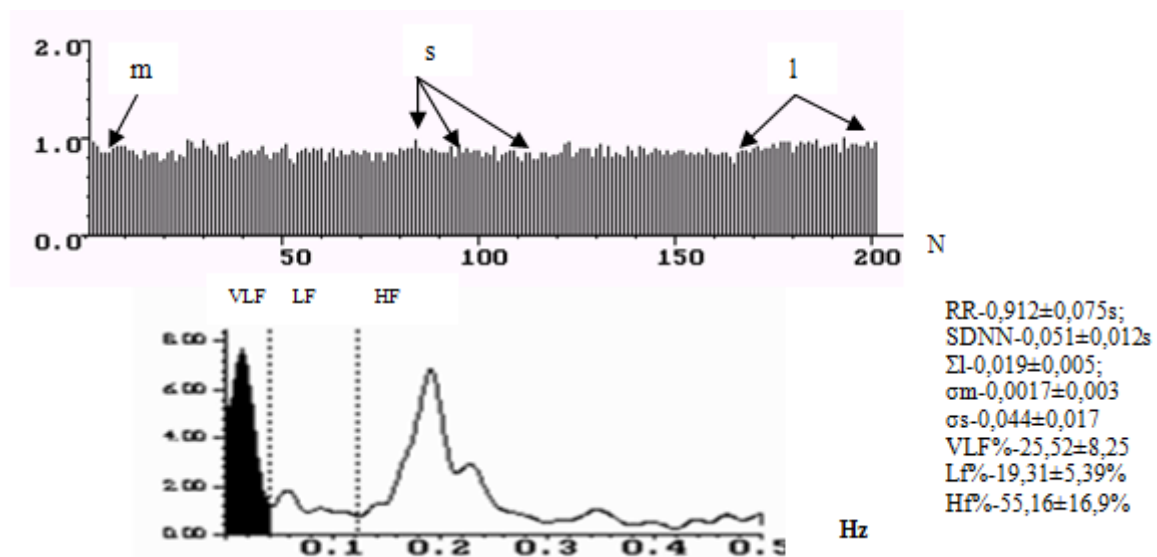
Fig. (1). Rhythmocardiogram, spectrogram and middle values of RCG-signs of healthy man. σl – middle quadratic deviation of the humoral HRV waves, **σm** - middle quadratic deviation of the sympathetic HRV waves, **σs**- middle quadratic deviation of the parasympathetic HRV waves. Spectral correlation of the autonomic and humoral-metabolic influences in sinoatrial heart node: **VLF%**- share of humoral-metabolic regulation, **LF%**- share of sympathetic regulation, **HF%**- share of the parasympathetic regulation in total spectrum (100%).

Results and its discussion. Received HRV data in seconds (s) and % were compared to standard data and clinical signs of the CAD. There were defined the common HRV symptoms of all forms of CAD. Its were caused by the chronic heart circulation breaches, because atherosclerosis plaques and others breaches. Results of researches showed, that expression, interaction of different spectral frequencies of HRV, and its reactions on stimulant tests correlated with clinical expression of CAD. Sometimes, its appeared before clinical and ECG data. (SDNN=0,018±0,004 s in pts CAD vs 0,032± 0,004 s in norm; z=5,6; n-278 and 47). Also spectral share of parasympathetic influences decreased (HF%=17,1±5,3% vs 41,5±4,52% in normal control; z-5,4 at n-278 and 47). Correspondingly the humoral-metabolic regulation, as ineffective and inadequate, increased in SN – (VLF% =56,5±16,7% vs. 28,08±11,27% in healthy man; z-7,12; n-278 и 47). At first, RCG signs of CAD were: decrease (σm=0.012±0.009 s; σs=0.013± 0.006 s in pts with CAD vs σm=0.025±0.007; σs=0.033±0.012 s in control gr.), HR reaction during passage in active orthostatic test (ΔRR=13.7±3.2% in pts, and 30.02±1.9% in healthy man), and also changed spectral interaction, (LF%=17.63±11.2%; HF%=25.86± 16.025 in pts vs 27.16±12.8; 44.7 ±15.04% in healthy man). Number and amplitude of the parasympathetic autonomic waves decreased and HR regulation changed in direction increase of the humoral influence. At second, there was stabilization of HRV wave structure, significant decrease middle statistic fast autonomic regulation - σm,σs and LF%, HF%. HRV autonomic regulation was transferred on low humoral level, at the same time any reactions absented at all stimulant tests. The most breaches were at the formatted autonomic cardioneuropathy (ACN). At the norm the parasympathetic influence in SN predominate over other regulative factors, because physiological peculiarities of the autonomic system. In pts with CAD this advantage reduced.

Periods of the significant HRV stabilization were registered during physical exercise in PWC test on Rcg in the pts with CAD and during ischemic episodes (Fig.2). Significant ischemic HRV stabilization was defined in 173 pts with AP by graphic cursor and consists difference between neighboring during ischemic episodes 3,55±1,02 millise- cond (Patent No. №2322942). On the modern monitor screen, on rhythmocardiogram (Rcg) these stabilizations seem as a direct line without any fluctuations. These Rcg stabilizations weakly correlated (r-0,305) to ST depression. HRV stabilization connected with heavy forms of CAD and risk of lethal outcome. RCG symptom of the angina pecto0ris with reduction of RR-intervals explicable by breaches of SN circulation and hibernation of it's pacemaker cells in the moment increase of the constriction coronary arteries, because endotelin-1 over the atherosclerosis plaque, when the artery occlusion increase till critical 70-80% level. At the 1-2 FC of AP such ischemic stabilization may be define by visually and graphic cursor. At the same time the reactions to stimuli in tests (ΔRR) decreased, and time of it and the time of the HRV restoration increased. But at the 3-4 FC CAD with AP, as well as at the FC of the HF, presented by significant reduction of the all registered HRV and reactions to stimuli were absent, as at the ACN syndrome (Fig. 3). Therefore HRV-record must be augment by the high resolution and correct program method.

RCG with statistic and spectral HRV analysis is enough sensitive method of the nonspecific, noninvasive

diagnosing of cardiovascular pathology, inclusively at the CAD. RCG adequately reflects degree breaches of autonomic SN regulation, which predicts to clinical CAD and consists certain criterions of disease heaviness and risk of complications. For example, the level of HRV reduction correlated to FC of the stable angina pectoris and FC of heart failure. Probably, also degree of RCG stabilization and decrease of reactions in tests indirectly connects with chronic ischemia, damaging tissue of the sinus node, myocardium and heart receptors. Besides, absence of any HRV fluctuations and reactions to stimulant tests at the RCG investigation, known as "rigid rhythm", is evidence of the prevalent humoral regulation, insufficient and inadequate, and with high risk of the lethal outcome.

There were made out researches in clinical pharmacology with value of nitroglycerine action on HRV regulation in SN in 44 pts with angina pectoris of 2FC. After introduction of one dose of nitroglycerine in the all patients was define the HRV reduction of the all autonomic indices –σl, σm, σs and also there was change of the spectral shares in HRV structure - humoral-metabolic –VLF% influence increased and sympathetic and parasympathetic indices (LF%, HF %) in the autonomic regulation decreased. The initial values were: σl=0,017±0,005 s; σm=0,018±0,004 s; σs= 0,015± 0,003s. And after 0,05 mg nitroglycerine these indices were σl= 0,008±0,002 s; σm= 0,011±0,002 s.; σs=0,009 ± 0,001 s., n-44, p<0,05-0,001. Spectral correlation was initially: VLF%=55,4±4,4%; LF%=22,5±2,8%; HF%= 21,1±4,3%. After 1 dose of nitroglycerine these indices were 65,4±3,2%; 18,7±1,7% and 15,9±2,3%.(Fig. 4). Thus, results were negative, because autonomic fast regulation was decreased and slow humoral-metabolic influence was increased. Here is question of a price treatment efficacy, therefore here supposition appears about more fast form of the heart failure. Thus, the high-resolution RCG is the adequate and perspective method of evaluation the regulation in actual cardiovascular status. Except, it may be used for evaluation of the medicine autonomic activity in clinical pharmacology at the selection of personalized treatment, dose of medicine and control efficacy of management in pts with angina pectoris. Also here is example of the necessary of evaluation autonomic pharmacodynamic of the some medici-nes. Some years ago there were studying of the autonomic action of β-adrenoblockers – obsidan, bisoprolol, nebivolol. Rcg registered before and after introduction 1 dose of these medicines. At the every case after every β-adrenoblocker introduction in HRV analysis increased parasympathetic signs –σs, HF% and correspondingly SDNN, that suppose the increase of frequency exit of acetylcholine quants in synaptic chink, but not blockade of β-adrenoreceptors.

Presented here some results of the studying of HRV investigation in pts with arrhythmias of the heart. HRV analysis in pts with cardioarrhythmias shows that the majority of clinical forms arrhythmias registered by RCG and may be fast diagnosed sometimes by visually on Rcg (Fig.5). The main preference of the RCG method in arrhythmology is possible to define an arrhythmogenic autonomic background and hemodynamic significance of the every arrhythmic episode.

Conclusion.
1. The high-resolution RCG is the enough adequate and informative method of the regulative breaches in cardiovascular system.
2. At the coronary artery disease may be defined the nonspecific symptoms of breaches circulation in the heart tissues and the ischemic episodes at angina pectoris, functional classis of stenocardia and heart failure.
3. Also HRV with extreme reduction of wave structure – stabilization of heart rhythm testimonies about autonomic cardioneuropathy with high risk of lethal outcome.
4. RCG with exact analysis of HRV is the excellent method in clinical pharmacology for studying autonomic action of the medicines, accessories affects and control of the treatment.
5. RCG method may be used in arrhythmology for registration and analyses a number clinical forms of the heart arrhythmias, significant of every arrhythmic episode and its hemodynamic influence.
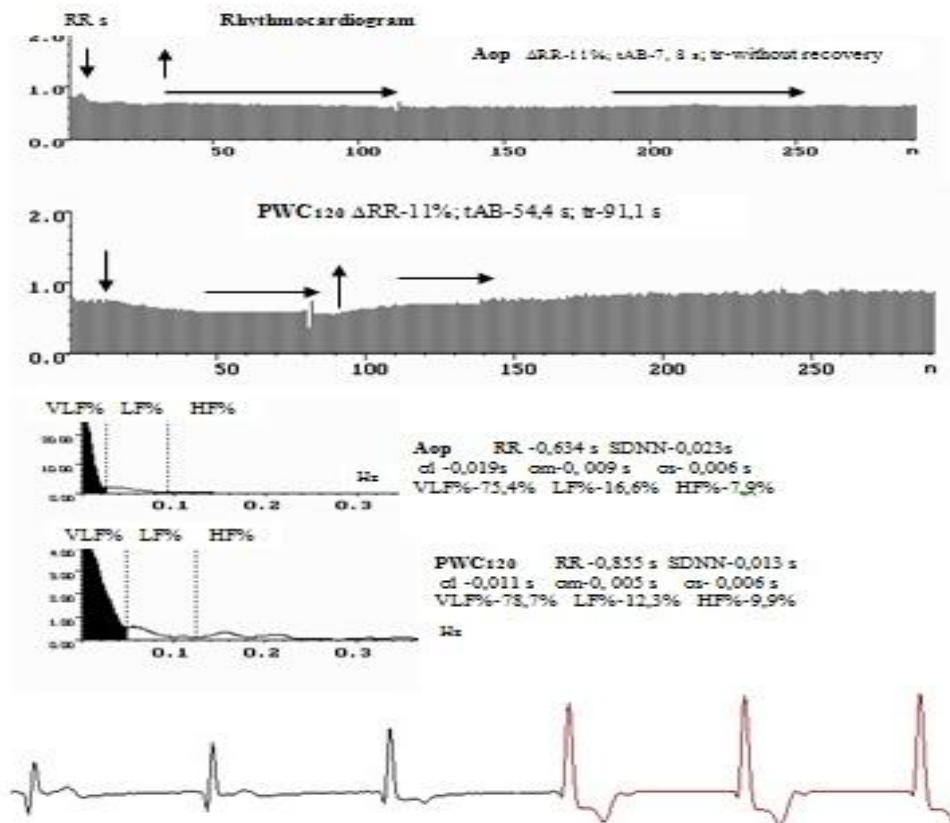
Fig (2). Rhythmocardiogram, spectrogram and HRV-indices patient with CAD and stable angina pectoris 2 FC in Aop and PWC120. The amplitudes of HRV waves are extremely reduced. Here are on spectrogram the spectral shares pathologically changed- influences of sympathetic and parasympathetic – LF%, HF%-oppressed of the regulation of the pacemaker SN activity and the humoral-metabolic influence significantly increased. Reaction to passage in Aop (ΔRR), the time of achievement this reaction and restoration time are increased (tAB, tr). The vertical arrows noted the beginning and end of stimuli action. Horizontal arrows show ischemic episodes.
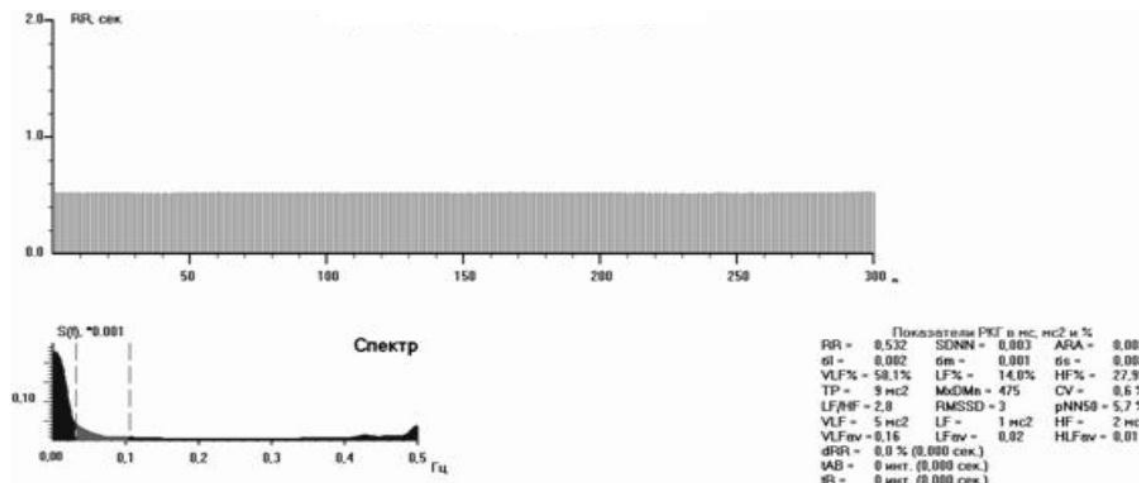
Fig.(3). Rcg, spectrogram and HRV-indices of patient with CAD and autonomic cardioneuropathy with HRV stabilization, values of σl, σm, σs in 2, 1, 2 milliseconds only and the most humoral influence in SN 58,1%. HRV- indices in sec., ms2, and %:RR-0,532, SDNN-0,003, ARA-0,003;σl-0,002 ; σm- 0,001 ; σs-0,002; VLF%-58,1%; LF% -14,0%; HF%- 27,9%; LF/HF- 2,8 ; RMSSD-2 ; pNN-5,7%; VLF-5 ms2; LF-1 ms2; HF-2ms2; ΔRR- 0,8%; tAB-0 s; tr-0s
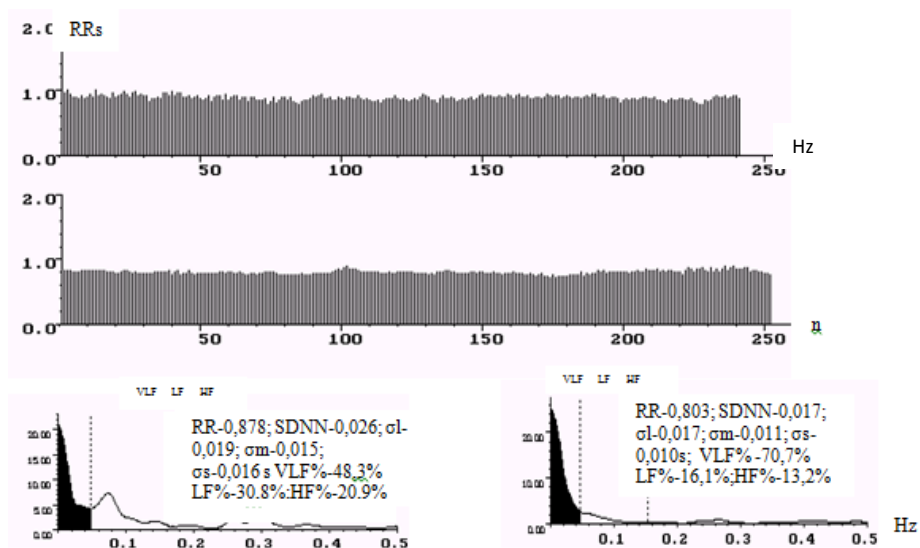
Fig. (4) Rhythmocardiograms, spectrograms and middle HRV –indices of wave structure of HRV before (1), and after of first one dose of nitroglycerine. On the Rcg1 here are reductions of all HRV-waves, but all fluctuations of sympathetic (σm), parasympathetic (σs) and humoral-metabolic (σl) regulative factors here presented. After the receiving 1 dose of nitroglycerine change the HRV- structure, amplitudes of all waves decreased (see spectrums and values of HRV-indices). The share of humoral –metabolic influence on activity of pacemaker cells in SN became the most large expense of the fast autonomic sympathetic and parasympathetic regulation. This supposes the negative action of nitroglycerine in treatment of angina pectoris, and over price of alternation pain at stenocardia. Frequent application of nitroglycerine accelerates form of the heart failure.
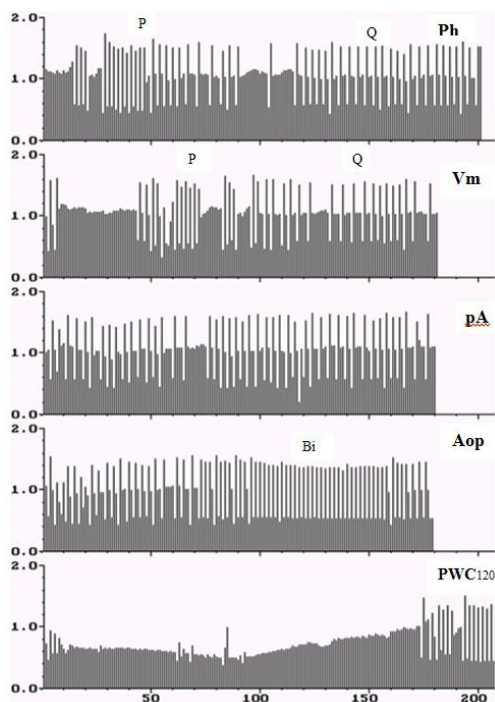
Fig.(5). Rhythmocardiograms of patient with polyfocal arrhythmias of complex form on the background of HRV reduction, bradycardia and absence of reactions to any stimulant tests – Valsalva maneuver (Vm), Ashner test (pA), active orthostatic test (Aop) and in exercise submaximal test PWC120. Here are allorhythmia – bigeminy (Bi), because preactopic intervals identical, quadrigeminy (Q) – here are extrasystoles through 2 normal intervals, parasystoly (P).
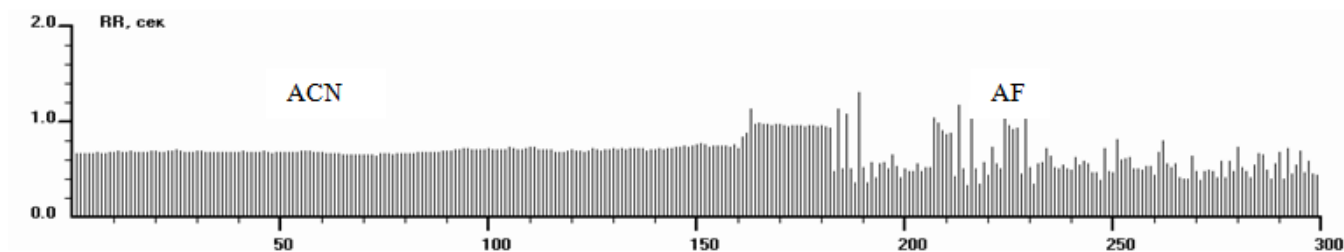
Fig. (6). Here is atrial fibrillation (AF) on the background of autonomic cardioneuropathy (ACN), without HRV waves, with stabilization of the heart rhythm and tachycardia.
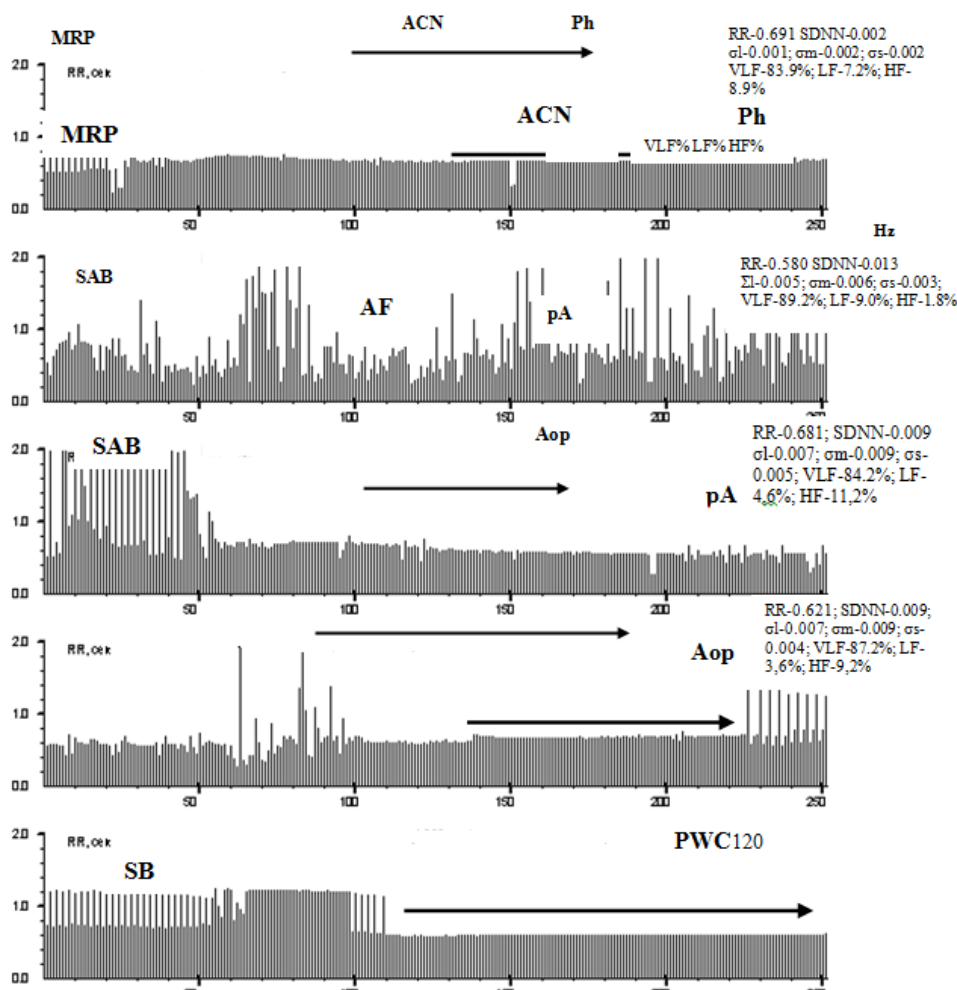
Fig.(7). Rhythmocardiograms, spectrograms and HRV middle meanings in the RCG indices of the patient D. before coronary artery bypass graft surgery. In Ph here is migration of the rhythm pacemaker (MRP)-(1-40i). On the background of autonomic cardioneuropathy -ACN (shown by horizontal arrow) here is the long ischemic episode with typical clinical syndrome of stenocardia. The middle deviations of SDNN, σl, σm, σs have calculations in units of milliseconds. At the spectral correlation of the regulative factors in the sinoatrial heart node here is significant predominance of the humoral-metabolic influence (VLF %) at the expense of reduction of the autonomic sympathetic and parasympathetic regulation (LF%, HF %). In Vm here is atrial fibrillation (AF). In pA here is sinoatrial blockade of 2-3 stage (SAB) on the background of the ACN. In the Aop (60-100 i) here is AF, then the ischemic episode with HRV stabilization (the difference between intervals 3.55± 1.02 millisecond). At the end of active orthostase here is supraventricular bigeminy (SB) with identical preectopic intervals. SB was also during PWC120, the here is the ischemic episode.

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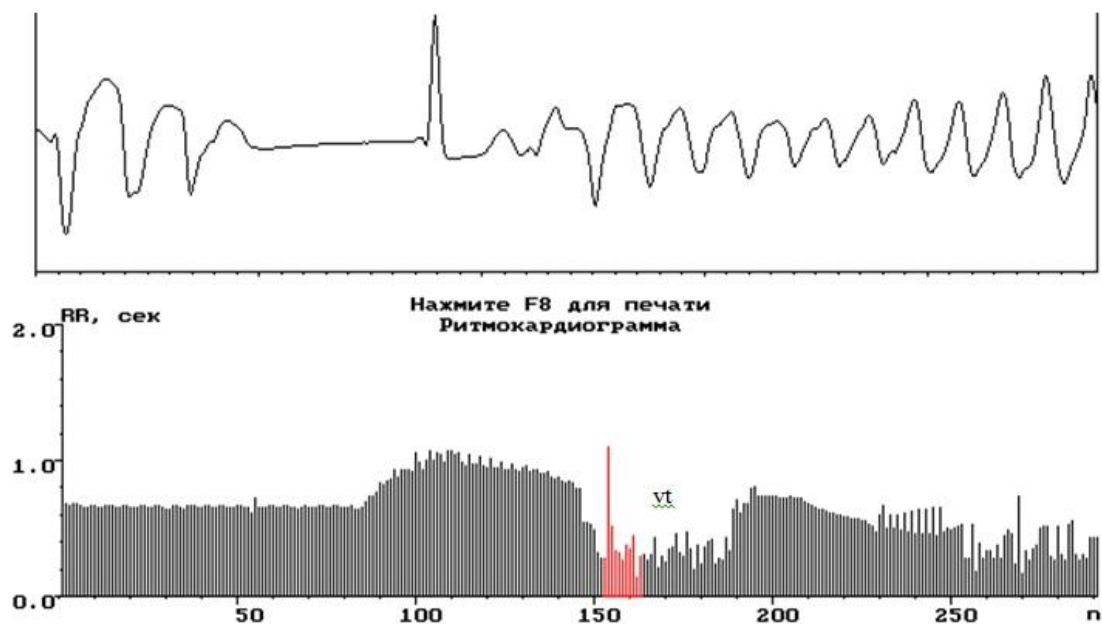
Fig. (8). Here are electrocardiogram and RCG of patient with CAD and ventricular tachycardia (VT).
Before 53 sec. the Rcg level increased and here was migration of rhythm pacemaker (MRP), which was predictor of VT and highest risk of lethal outcome. This case was in reanimation department, therefore this patient was saved. At this case level elevation of RCG and MRP was as predictors of the life danger.

O39 Analysis of body posture changing, painfulness, regulation of the heart and breath during night sleep in experiment with a 5-day dry immersion

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Space flights in the modern world have colossal strategic, technical and scientific significance. The model of "dry immersion" recreates the effects of deprived peripheral neuro-sensory systems of support afferentation and hypokinesia. It causes a sharp decrease in muscle tone and a violation of the regulation of cardiorespiratory and digestive systems, etc., characteristic for the first days of astronauts' stay in weightlessness. When a person is in "dry immersed" the main forced position of the body is the so-called "the position of embryos," in which the subject lying on his back, "hangs" on a thermoneutral water covered with an elastic waterproof fabric. In this case, prolonged exposure in this position causes pain syndromes in the lumbar spine. As recent studies (2015) have shown, the pains with spinal bifurcation on the background of weakening of long back muscles and an increase in the distance between the intervertebral discs. In addition, some volunteers complain of painfulness in the abdominal region, which is probably the result of prolonged compression of the abdominal cavity and dysfunction of organs.

At present, we couldn't find out studies shown the correspondence to the person's posture changes, the amount and intensity of motor activity during microgravity modeling. Probably, the total amount of position change (posture) and the preference for choosing a dream on the right or left side is an unconscious reaction of the body, compensating for the arising pains and discomfort from a long stay in an unfamiliar environment. The "BigData" analysis of the complaints of volunteers, hemodynamic and respiratory parameters will probably describe the relationship between pain intensity and adaptation to pain, autonomic regulation of the cardiorespiratory system, the effectiveness of night rest and the preferred position of the body of the subjects under conditions of "dry immersion".

The research involved volunteers, men aged 29 +/- 2, (height 177 +/- 1, weight 70.2 +/- 2.6). Of these, 6 people in the experimental group (age 24 +/- 1, height 178 +/- 1, weight 68.3 +/- 4.2) and 6 people in the control group (age 34 +/- 2, height 177+ / -1, weight 72.2 +/- 3.4). In the experimental group, the Penguin axial load suit was used. We used the Complex "Cosmocard" with portable digital Holter-like ECG amplifier "Anna Flash 3000-M" produced by the company "Medical Computer Systems" (Zelenograd) and Biometric T-shirt Hexoskin (Carré Technologies, Inc., Canada, Montreal).

The main conclusions: 1. During the first days there is an active adaptation to the "dry immersion" and to the emerging pain sensations, while the frequency of changing the posture and the general motor activity of a person directly correlates with pain in the back and abdominal pain. 2. A periodicity of the decrease / increase in the power of the spectrum of heart rate variability was detected at certain night hours, starting from the second day of stay in the "dry immersion". 3. The growth of HRV indicators reflecting sympathetic activity (Stress index and LF/HF) accompanies the moments of arousal, therefore, by the number of "episode stresses" one can assume about the quality of night sleep. 4. Some of the volunteers found the dependence of the obviously cyclicity of the phases of sleep with the days of immersion, namely: clear sleep phases disappearing at the beginning of the immersion, again begin to form again towards its end. 5. Using the costume Penguin potentiates the motor activity of the tester in the early days of immersion, and in half of the subjects reduces the pain effects. 6. On the basis of the «BigData» retrospective analysis, it is possible to create a system for predicting the tolerability of microgravity conditions and monitoring the efficacy of prevention measures.

Keywords: «Dry immersion», HRV, personal body posture change, sleep stage, painfulness, «BigData», countermeasures.

O40 Conventional and Complexity Analysis of RR Intervals Dynamics during Head-up Tilt Test

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Introduction: Head-up tilt testing (HUTT), a form of orthostatic stress used in the diagnosis of neurally mediated syncope, causes hemodynamic changes, which produce alterations in autonomic nervous activity. Time and frequency domain analyses of heart rate variability (HRV) are the most commonly used noninvasive methods to evaluate autonomic regulation. Also, nonlinear measures of HRV represent a powerful tool for understanding the complexity of heart rate dynamics. The aim of our study was to assess the autonomic mechanisms involved in the pathogenesis of neurally mediated syncope using conventional and nonlinear measures of HRV.

Methods: A group of 25 healthy subjects (13 men, 12 women, mean age 28 years) have been studied during HUTT. Heart rate was continuously recorded, and blood pressure was measured every 2 minutes, plus whenever symptoms ensued. The R-R interval series corresponding to supine and standing positions were recorded, before and during tilting. Spectral analysis was performed using fast Fourier transform (FFT) and autoregressive analysis (AR). The FFT and AR spectra were calculated from interpolated and detrended 512 seconds windows. Approximate sample entropy anddetrendedfluctuation analysis have been used for the study of heart rate dynamics. Baroreflex sensitivity (ms/mmHg), as a measure of complex mechanisms involved in the regulation of neurally mediated syncope, was also assessed in this study.

Results: The variation of spectral parameters revealed an important increase of sympathetic tone and a reduced vagal activity (LF, from 1343 ms^2/Hz to 1145 ms^2/Hz, p: 0.001). The autonomic imbalance was also reflected by the high low frequency/high frequency ratio (from 2.27 to 4.09, p: 0.0001), approximate entropy was significantly reduced after tilt at 70^0 (ApEn 1.26 to 1.09, p: 0.003).

Conclusion: Our study, **u**sing HRV analysis, conventional and nonlinear analysis demonstrates the cardiovascular autonomic changes related to HUTT. These have an important role in the pathogenesis of neurally mediated syncope.

Keywords: heart rate variability, healthy subjects, syncope, tilt testing

O41 Clinical, psychological characteristics and heart rate variability of persons with undifferentiated connective tissue dysplasia

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Summary

The article presents the results of the survey of persons with connective tissue dysplasia, and the results of MMPI and heart rate variability in the main and control groups of the study.

Key words: connective tissue disorders, pain, anxiety, depression, MMPI, heart rate variability.

Background

Connective tissue dysplasia (CTD) is a genetically determined condition caused by metabolic disorders of connective tissue, characterized by disruption of the structure of fibers and ground substance. The uniqueness of the structure and function of connective tissue creates the conditions for the emergence of a large number of anomalies and diseases caused by chromosomal and gene defects in the embryonic and postnatal periods and having a certain type of inheritance [7].

Depending on the characteristics of the etiological factor, it is advisable to allocate the hereditary disorders of connective tissue (differentiated or monogenic diseases) and the connective tissue dysplasia (undifferentiated forms – UCTD). The prevalence of hereditary forms is small. Thus, the frequency of Marfan syndrome in the population is 1:10000-1:15000. In contrast, UCTD is widespread in Russia: about 8.5 % in the sample of 400 people.

According to the literature, the prevalence of individual external signs is extremely high: single external signs are detected in 94% of persons of young age. Data on the frequency of occurrence of UCTD among young people are contradictory, according to some scholars, they range from 13.0% to 85.4% [2,7,14].

There are the following clinical syndromes of UCTD: a syndrome of neurological disorders, asthenic, valve, thoracolumbalis, vascular, arrhythmic, respiratory, visceral syndrome, immunological disorders, eye pathology, pathology of the foot, hypermobility of joints, and disorders of the mental sphere [1,3,4,5,11,12].

Widespread UCTD with progressive nature of the flow and multiple organ destruction make it an important medical and social problem. The aim of the study is to conduct a comprehensive evaluation of clinical, phenotypic characteristics and heart rate variability of persons with UCTD.

Methods

We studied 67 young adults aged 18 to 25 years. The research was conducted on the basis of the "5[th]Military Clinical Hospital of National Guard Troops of the Russian Federation" in Yekaterinburg.

The study based on a voluntary informed consent was attended by 67, students of the Ural State Medical University (USMU) with a median age of 22 (20÷23) years. Every patient had symptoms of CTD in the profile, based on the National Recommendations of the Russian Scientific Society of Internal Medicine, 2015 [7]. We took into account the following symptoms of UCTD: dolichostenomelia, arachnodactyly, Steinberg thumb sign and Walker-Murdoch wrist sign, protruding ears, "crumpled" ears, adherent ear lobe, high arched palate, dental crowding, malocclusions, diastema, lax joints, hyperextensibility of knees and elbows (Fig.1), hyperextensibility of thumbs (Fig.2) and fingers, genu varum, genu valgus, flat foot, clubfoot, pes planovalgus, wide gap between the first and second toes (Fig.3), syndactyly of toes 2 and 3 (Fig.4), short 1 toe, hallux valgus, degenerative disc disease, instability of the cervical spine, aesthenic, pectus excavatum or carinatum, scoliosis, winged scapula, straight back, hyperkyphosis, hyperlordosis, varicose veins, varicocele, hernia, strabismus, sclera blue, hypo/hypertelorism, hyperextensible skin (Fig.5), skin striae distensae, multiple moles, depigmentation. We diagnosed UCTD if there were 6 signs or more.

All subjects were surveyed in the study of mental and emotional status with the Hospital Anxiety and Depression Scale (HADS), a Multilateral Study of Personality (MSP) on the basis of Minnesota Multiphasic Personality Inventory (MMPI) in modification of F. B. Berezin et al. [10]. The severity of different pain syndromes was determined using a visual analog scale (VAS).

The second phase was a comparative study. In case of determining 6 signs and more, the examined were assigned to the main UCTD-group (n=43); if the signs were less than 6, the persons were assigned to the control group (n=24).

We studied the heart rate variability (HRV) by rhythmocardiography (RCG). The survey was carried out on a hardware-software complex (APC) - KAP-RC-01-"Micor" (registration certificate № FS 02262005/2447). (Fig.6). HRV

indicates statistical analysis: median (25%÷75%) of the duration of RR-interval in seconds to analyze the RCU, standard deviation of all the waves from the mean RR (SDNN), standard deviation of each fluctuation: humoral-metabolic (σl), sympathetic (σm), parasympathetic (σs) effects divisions of the autonomic system, and the average amplitude of respiratory arrhythmia (ARA). The ratio of the factors of regulation in the sinus node after the expansion wave structure of the HRV frequency components 3 in the program "Micor" presents the percentages of influence on the pacemaker: humoral-metabolic effects - in a very low frequency (VLF%), sympathetic - in a low frequency (LF%) and parasympathetic in a high frequency (HF%); in the frequency ranges relative to the total spectrum, taken as 100%. Recording was carried out in the supine position (initial background RCG record), modified Valsalva maneuver (Vm), Ashner-Dagnini test (Pa), active orthostasic test (Aop), loading test is a modified PWC120 test (Power Working Capaciti) [6,9]. Differences between the groups were assessed using nonparametric Mann-Whitney U-test, the differences in the frequency of symptom groups were assessed using χ^2 criterion, the significance of differences significant at $p < 0.05$.

Results

Signs of UCTD were detected among 100% of patients in different quantities. The frequency of detecting 6 UCTD-signs and more comprised 64.2% among young people. The results revealing the signs of UCTD are presented in Table1.

Table 1. The detection rate of connective tissue dysplasia signs among young people

Signs	Frequency of detection (n=67)	Group UCTD (n=43)	Control Group (n=24)	χ^2	p
Adherentearlobe	26 (38,8%)	16	10	0,09	0,76
Flat feet	**26** (38,8%)	**23**	3	8,49	**0,004**
Walker-Murdoch wrist sign	**24** (35,8%)	**23**	1	13,46	**0,000**
Scoliosis	23 (34,3%)	16	7	0,024	0,88
Aesthenic chest	**22** (32,8%)	**19**	3	5,21	**0,022**
Malocclusions	20 (29,9%)	17	3	3,48	0,063*
Hyperextensibility of thumbs	**20** (29,9%)	**19**	1	9,3	**0,002**
Steinberg thumb sign Hyperextensibility of	**19** (28,4%)	**17**	2	5,39	**0,02**
elbows	**18** (26,9%)	**18**	0	11,8	**0,000**
Hyperextensibility of fingers	**17** (25,4%)	**16**	1	6,7	**0,01**
Wide gap between the first and second toes	17 (25,4%)	12	5	0,093	0,76
Dental crowding	16 (23,9%)	13	3	1,36	0,24
Multiple moles	15 (22,4%)	13	2	3,45	0,063*
Hyperextensibility of knee joints	13 (19,4%)	12	1	3,77	0,052*
Arachnodactyly	12 (17,9%)	10	2	1,53	0,22
Skin striae distensae	11 (16,4%)	8	3	0,14	0,7
Protruding ears	10 (14,9%)	8	2	0,41	0,52
Theinstability ofthe cervical spine	10 (14,9%)	8	2	0,41	0,52
High archedpalate					
Jointlaxity	9 (13,4%)	9	0	3,86	0,05*
Syndactyly 2-3toes	9 (13,4%)	8	1	1,46	0,23
Winged scapula	9 (13,4%)	9	0	3,86	0,05*
Straight back	8 (11,9%)	7	1	1,04	0,31
Short first toe	8 (11,9%)	5	3	0,052	0,82
"Crumpled" ears	7 (10,5%)	5	2	0,006	0,94
Pes planovalgus	6 (9%)	6	0	2,04	0,15
Degenerative disc disease	6 (9%)	5	1	0,26	0,61
Pectus excavatum	6 (9%)	4	2	0,18	0,67
Hyperextensible skin	6 (9%)	6	0	2,04	0,15
Genu varum	6 (9%)	6	0	2,04	0,15
Hyperkyphosis	5 (7,5%)	5	0	1,43	0,23
	5 (7,5%)	4	1	0,056	0,81

People with UCTD are significantly more likely to have the following characteristics: flat feet, Walker-Murdoch wrist sign, aesthenic chest, hyperextensibility of thumbs, elbow joints and fingers, and Steinberg thumb sign (p<0.05). These signs can be considered the most important in the diagnosis of UCTD. With the high incidence of adherent ear lobe and scoliosis, these symptoms are often comparable in both groups. There is a tendency towards a higher frequency of high arched palate, syndactyly of 2-3 toes, malocclusion, hypermobility of knee joints and multiple moles in the group of UCTD. The results of the comparative study showed significant differences in the groups (Table 2).

Table 2. Characteristics of comparison groups

Signs	Group UCTD (n=43)	Control Group (n=24)	p
Age, years	22(20÷23)	22,5 (20÷25)	0,12
BMI, kg/m^2	**21,5 (19,3÷22,8)**	**22,8 (21,8÷24,4)**	**0,007**
Joint pain, score	**1 (0-5)**	**0 (0-0)**	**0,037**
Back pain, score	2 (0-5)	0 (0-3)	0,14
Heart pain, score	0 (0-2)	0 (0-3)	0,49
Headaches, score	1,5 (0-4)	1,5 (0-5)	0,7
The chest pain, score	0 (0-1)	0 (0-1)	0,83
Abdominal pain, score	0 (0-2)	0 (0-2)	0,71
L- scaleMMPI	4 (3-5)	3 (1-6)	0,23
F- scaleMMPI	9 (6-13)	8 (4-13)	0,31
K- scaleMMPI	12 (9-16)	13 (11-16)	0,33
1 – the scaleof hypochondria	17 (14-20)	14 (11-18)	0,10
2 – depression scale	18 (15-22)	19 (15-25)	0,49
3 –anxiety, hysteria	20 (18-25)	19 (14-24)	0,39
4 –the scale of psychopathy	18 (13,4-23)	21 (17,8-24)	0,07
5 –the scale of feminity	20 (15-24)	22 (19-26)	0,16
6 –paranoia scale	8 (6-11)	9 (7-12)	0,57
7 –psihastenia scale	23 (19-28)	27 (22-36)	0,24
8 –schizophrenia scale	24 (19-31)	28 (21-33)	0,46
9 –hypomania scale	17,4 (13,8-23)	21 (15,4-25)	0,16
10 – the scale of social introversion	**21 (16-30)**	**28 (22-32)**	**0,029**

The groups were comparable in age, but the UCTD group had a significantly lower body mass index BMI (p=0.007). This may be related to muscle hypotrophy and lower bone density in UCTD cases [13]. Patients with UCTD are more concerned about arthralgia (p=0.037). The frequency of pain at other sites in the main and control groups has no significant differences.
According to the results of MSP, patients with UCTD demonstrated significantly lower rates on a scale of social introversion (p=0,029): respondents with UCTD scored lower scoreson this scale. On scales of psychopathy and femininity, a tendency towards lower results was also noted, compared to the control group (p=0.07 and p=0.16, respectively), and towards higher performance on a scale of hypochondria (p=0.1). Thus, persons with UCTD proved to be less free and less prone to demonstrative reactions and conflicts; however, they tend to pay more attention to their symptoms.
According to RCG, the groups were compared according to the values misistries intervals (p=0.92), but no difference was determined. However, after the Valsalva maneuver the UCTD-group showed higher values of ARA (p=0.036) and σs (p=0.056). A similar trend was registered after the Ashner-Dagnini test as well (p=0.07; p=0.07). According to the test with the physical loading of a person, the main group had a tendency towards higher values of σs (p=0.073) and showed a shorter recovery period (p=0.001).

tests	Signs	Group UCTD(n=38)	Control Group (n=20)	p
ph	RR	0.831(0.767÷0.995)	0.846 (0.799÷0.947)	0.92
	SDNN	0.046 (0.039÷0.06)	0.043 (0.03÷0.05)	0.28
	ARA	0.081 (0.056÷0.114)	0.061 (0.042÷0.093)	0.14
	σs	0.03 (0.021÷0.044)	0.023 (0.015÷0.036)	0.18
	HF%	43.9 (27.8÷64.4)	41.5 (22.7÷34.1)	0.47
Vm	**ARA**	**0.067 (0.054÷0.087)**	**0.049 (0.036÷0.08)**	**0.036**
	σs	0.025 (0.02÷0.034)	0.018 (0.013÷0.031)	0.056
	HF%	40.35 (27.3÷54.5)	29.6 (18.8÷41.3)	0.12
Pa	ARA	0.074 (0.049÷0.097)	0.048 (0.033÷0.071)	0.07
	σs	0.028 (0.019÷0.039)	0.02 (0.012÷0.028)	0.07
	HF%	41.6 (29.1÷55.0)	32.65 (18.1÷49.9)	0.21
	tr, s	16.01 (13.49÷25.07)	22.14 (16.26÷28.62)	0.068
PWC	ARA	0.092 (0.06÷0.132)	0.08 (0.049÷0.103)	0.23
	σs	0.036(0.023÷0.052)	0.027 (0.017÷0.039)	0.073
	HF%	60.6 (41.7÷74.0)	56.2 (20.9÷69.5)	0.26
	tr, int	**116.5 (97.5÷128.5)**	**162 (122.5÷189)**	**0.001**
	tr,s	**84.5 (70.26÷102.28)**	**124.07 (92.9÷146.8)**	**0.001**

Insights

1. UCTD was detected in 64.2 % in the studied group.
2. The most important signs to diagnose UCTD are flat feet, Walker-Murdoch wrist sign, aesthenic chest, hypermobility of thumbs, elbow joints, fingers, and Steinberg thumb sign.
3. The UCTD-group has a significantly smaller body mass index.
4. Patients with UCTD are significantly more likely to have joint pains.
5. Personal characteristic of the examined with UCTD showed that they are more prone to introversion, they feature lesser propensity towards conflict and gender identity.
6.Vagal influence on the heart rate regulation is increased among students with multiple signs of UCTD.
7. The RCG method can identify the characteristics of heart rate regulation in UCTD patients more some other diagnostic methods.

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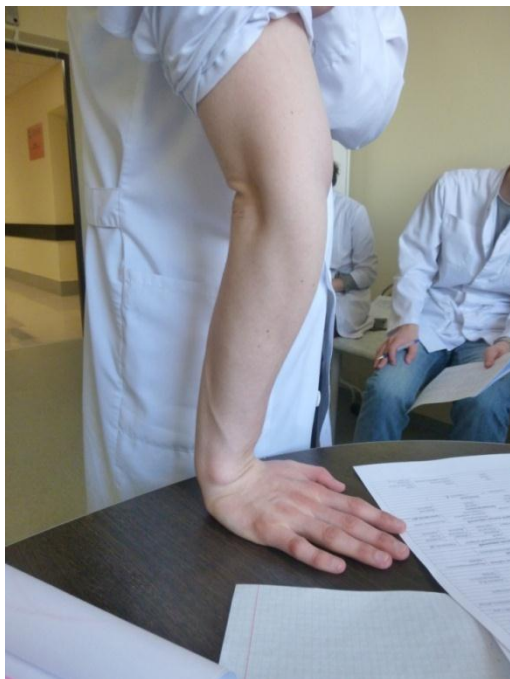
Fig.1. Hyperextensibility of elbow

Fig.2. Hyperextensibility of thumbs

Fig.3. Wide gap between the first and second toes

Fig.4. Syndactyly 2-3 toes and wide gap between the first and second toes

Fig.5. Hyperextensible skin
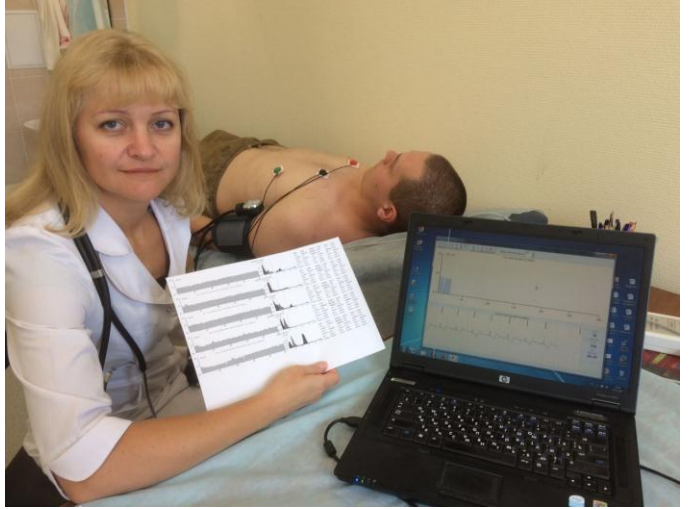
Fig.6. RCG recording

O42 The Chernobyl accident: 31 years later

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Tula oblast is one of the most affected regions from the Chernobyl accident on April 26, 1986 having 56.3% radioactive contaminated areas. The aim of the study was to examine health and autonomic status in the university students - contaminated area residents and compare with their counterparts living in 'clear areas' including Tula city.

Materials and methods. We have analyzed two group of medical students examined in 2014. Year 6 group examined in spring consisted of 68 females and 34 males, 38.2 and 29.4% of them lived in the affected areas. 114 medical university students (year 4; 82 females and 35 males) aged 21-22 yrs were studied in autumn 2014. 20 females and 11 males were contaminated area residents. Heart rate variability (5 min. ECG recording in sitting position with analysis in time and frequency domains) was used to determine the autonomic nervous system state. Also participants have completed some psychometric tests and questionnaires. Excel 7.0 was used for statistical analysis. Data presented as M±m.

Results. Students of the first group were born in 1990-91; 4-5 yrs later from Chernobyl accident and their parents have not been involved in "clean-up work". There were opposite findings regarding duration of RR interval: in females living affected areas it was longer (758±18 vs 715±15 ms, p=0.04), whereas in males – shorter (696±42 vs 808±32 ms; p=0.026). Sympatho-vagal balance only in males was tended to increase (3.86±0.76 and 2.61±0.38).

Systolic blood pressure (BP) only in males was significantly bigger (128.7±2.4 vs 120.2±2.8 mm Hg, p=0.018), no difference was found in females (114.3±2.3 vs 113.8±1.5 mm Hg. Diastolic BP was the same (72.7 and 73.0 mm Hg in females and 81.7 and 81.3 mm Hg in males. Males made fewer mistakes in Munsterberg test, while females spent more time for all completed tests. Students of the second group were born in 1992-93; 6-7 yrs later from accident. Heart rate variability analysis revealed some sympathetic predominance in students both males and females living contaminated territories: heart rate in females was greater (87.9+/-2.1 vs 84.4+/-1.4 bpm), SDNN and pNN50% were lesser. In males greater relative LF power (46.1+/-3.2 vs 36.7+/-3.2%; p=0.027) was found. Also males had tendency to decreasing of visual working memory.

In conclusion, no prominent health impairments were found in 21-23 yrs students living in radioactive contaminated areas of Tula region. Mild sympathetic predominance may be due to some behavioral reasons (daily trips to study or living in university hostel).

O43 Heart rate variability and circadian rhythmicity in modern students

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A lot of data exists that morning-types behave with more conscientiousness and less risk-taking than evening-type individuals and have better academic performance. It may be due to coincidence of exam time and activation of sympathetic nervous system.

The aim of our study was to examine autonomic state in students with different choronotype.

Materials and methods. 80 girls and 43 young men - year 4 medical students were examined in autumn 2016. All participants underwent 5-min. ECG recording in sitting in morning hours (9-11) for heart rate variability assessment in time and frequency domains. Also students were asked to determine their own chronotype. Statistical analysis was made by Excel 7.0. Data presented as M±m.

Results. Among girls there were 26 "larks" (32.5%), 30 – "pigeons" (37.5%) and 24 – "owls" (30%), among young men – 4 (9.4%), 17 (39.5%) and 22 (51.1%). Girls reported morning chronotype were more sympathetic activated: they had lower RR interval (710±19 ms) comparing to intermediate chronotype (766 ±18 ms; p=0.019) and evening chronotype (762±28 ms, p=0.06). They had also lower RMSSD and pNN50%. Despite the total power did not differ, morning-type girls demonstrated significantly greater LFn.u. (64.0±3.0), LF/HF, VLF% and lower HF% (20.8 ±2.5%) than evening-type ones (30.5±3.1%; p=0.01). Unlike girls morning-chronotype young men had lower AMo (29.8%) than evening-chronotype (36.8±1.5%, tendency) and significantly lower stress-index (34±10 units) comparing to intermediate (82±12 units) and evening chronotype (96 ±15 units; p=0.019). Thus, opposite results were obtained in our sample of medical students.

Conclusion. Gender differences exist between girls and young men reported different chronotype based on examination in morning hours: only girls-"larks" were more activated than "pigeons" and "owls". Opposite trend in autonomic state was seen in men.

O44 Heart rate variability and academic performance in medical school

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Academic performance plays an important role in medical education, but as usually some students stop training during their first or second year.

Aim. To examine the possible physiological reasons of poor or good academic performance in medical school.

Methods. 24 girls were studied in the first semester of training in 2011, 15 of them had good and 9 – poor performance. 70 girls and 23 young men (VI grade medical students) were examined in spring 2017. The mean academic rating during all yeas of education was obtained at the State exam was held June 26-27. Heart rate variability (HRV) was accessed by 5 min. ECG recording in sitting and standing position in the morning hours (9-11) in spring 2017. Excel 7.0 was used for statistical and Pearson's correlation analysis. Data presented as M±m.

Results. None of the students had any cardiovascular pathology. The casual blood pressure was 115.9/75.7 mm Hg in girls and 130.8/80.1 mm Hg in men, height 164.8±0.7 and 180.4±1.6 cm; weight – 58.3±1.0 and 80.8±2.7 kg, BMI – 21.4±0.4 and 24.8±0.7 cm.

The girls having stopped their classes in the 3-4 semester demonstrated lower total spectral power (TP, 3271±559 ms^2 vs 6040±1468 ms^2 (p=0.047), lower power of low frequency (LF) - 890±82 vs 1732±337 ms^2 (p=0.013) and high frequency (HF) band - 1061±300 vs 2126±479 ms^2 (p=0.036). The mean heart rate did not differ (85.8±6.7 vs 81.1±2.7 bpm). The tendency to hyperreactivity in ortostasis was seen in standing position.

Correlation analysis made in the VI grade students revealed some relations only in men: the performance increases with relative power of LF band augmentation (r=0.34; p<0.05) and decrease of RRNN (r=-0.34) and absolute and relative power of VLF band (r=0.39 and r=0.42; p<0.05). All students were divided into 3 groups: with performance between 3.5 and 4.0, under 4.5 and above 4.5 score. Girls having excellent score (n=23) had moderate sympathetic predominance: tendency to decreasing SDNN, significant increase of LFn.u. and relative power of VLF band. Relative power of HF band in this group was lower (21.1±2.5%) than in those with performance under 4.5 (n=29; 31.3±3.2; p=0.007) and with score under 4.0 (n=18; 28.6±3.7%, p=0.049). The total spectral power had no difference. The first group demonstrated tendency to greater relative VLF power in standing position. Despite TP did not differ in the men, those with greater performance (n=5) had lower both absolute and relative power of VLF band (p=0.009 and p=0.012) and tendency to increase LF% and HF% (26.2±4.6% vs 16.7±3.5%) comparing with performance under 4.5 (n=6). The sympathetic predominance was seen namely in this group (AMo 48.1 and 38.5%) than in those with score under 4.0 (n=12).

Conclusion. The success of training in medical students is related to autonomic status parameters lying within normal range. Sympathetic predominance in the first semester in girls with hyperreactivity to ortotest is disadvantageously for further study. The moderate activation of sympathetic drive obtained in the last semester is necessary for excellent performance in girls and for good – in young men.

O45 The relationship between subjective health evaluation and heart rate variability in students with different habitual physical activity

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OBJECTIVE: Heart rate variability (HRV) nowadays is served as a "gold standard" assessing autonomic nervous system state. However, there are limited data about functional relationship between autonomic nervous system state assessed by HRV and subjective evaluation of health level in students with different habitual physical activity. The aim of the current study was to examine the relationship between HRV and subjective assessment of health level in students with different habitual physical activity.

MATERIALS AND METHODS: 90 students (36 M, 54 W; mean age (M+/-m; 22.9+/-0.4 yrs; body mass index (BMI) 22.5+/-0.4 kg/m^2) were included during April 2016 – April 2017. Short-term HRV was assessed in the time and frequency domains using 5 min. ECG recording in the supine and standing position. Self-reported questionnaire to examine health level, habitual physical activity was completed in the same time. 100-points visual analogue scale (VAS) was also used for evaluation of health level.

RESULTS: Questionnaire results showed that low habitual physical activity had 42% of young people (13 M, 25 W), medium - 36% (13 M, 19 W) and high - 22% (10 M, 10 W). Association of habitual physical activity and BMI as well as average RR interval was not found. The mean VAS score was 63.9+/-1.9 points. Young men reported high habitual physical activity had higher VAS score (70.7+/-4.5 points) than those with medium (66.0+/-2.2 points, p<0.05) and low physical activity (58.7+/-2.7 points, p<0.05). The VAS score had negative correlations with heart rate in the supine (r=-0.21, p<0.05) and standing (r=-0.26, p<0.01) position. Also VAS score correlated with SDNN (r=0.17, p<0.05), total HRV power (TP, ms^2) (r=0.18, p<0.05) and stress-index (SI) (r=-0.20, p<0.05) in the supine position and with reactivity of hypothalamic-pituitary-adrenal axis (VLF, ms^2) (r=-0.17, p<0.05) and sympatho-vagal index (LF/HF ratio, %) (r=-0.21, p<0.05) in upright position. Complaints of headache correlated with absolute spectral power of LF band (r=0.18, p<0.05) and VLF band (r=0.20, p<0.05) in orthostasis and were significantly frequent in students with low habitual physical activity (26+/-7% vs 9+/-5% in medium physical activity, p<0.05, and 5+/-3% in high, p<0.05). Frequent exertional dyspnea was marked significantly more often in students with low habitual physical activity (30+/-3% vs 20+/-3% in medium physical activity, p<0.05, 8+/-2% in high, p<0.01) and observed in mild sympathetic predominance in the background (LF/HF ratio, r=0.24; p<0.01; TP,ms^2, r=-0.19; p<0.05) and upright position (CV%, r =-0.22; p<0.05; pNN50%, r =-0.21; p<0.05). Complaints of heart palpitation correlated with VLF% (r=0.17, p<0.05) and LF% (r=0.20, p<0.05) in supine and heart rate (r=0.22, p<0.05) in standing position and also were more frequently observed in students with low habitual physical activity (42+/-3% vs 33+/-3% in medium physical activity, p<0.05, 27+/-3% in high, p<0.05).

CONCLUSIONS: Subjective health evaluation and level of habitual physical activity are related to parameters of HRV. Self-assessment of health in students increases due to physical activity and may be used as additional method of functional state assessment in students during screening examination.

O46 Sleep Disordered Breathing and Autonomic Nervous System

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Sleep-disordered breathing (SDB) leads to elevated sympathetic tone and impaired vagal activity, promoting hypertension and cardiometabolic disease. A lot of data indicate strong modulatory effects on the autonomic nervous system at night through a number of mechanisms, including central respiratory-cardiac coupling in the brainstem, chemoreflex stimulation, baroreflexes, and reflexes relating to lung inflation. Arousals also contribute to the autonomic disturbance. There are a causal dependencies among respiration, blood pressure, heart rate variability, and peripheral vascular resistance. Although sleep is normally a time when parasympathetic modulation of the heart predominates and myocardial electrical stability is enhanced, SDB disturb this balance, creating an autonomic profile in which both profound vagal activity leading to bradyarrhythmias, and sympatho-excitation favoring ventricular ectopy. The resulting tendency toward cardiac arrhythmia may directly contribute to sudden cardiac death and premature mortality in patients with SDB.

O47 Heart Rate and Blood Pressure Dynamics in Hypertensive Patients

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Background: Hypertension represents an important condition that affects the adult population worldwide; it contributes significantly to morbidity and mortality from stroke, heart failure, coronary heart disease and renal failure. Heart rate (HR) is one of the most important physiological variables, and HR variability (HRV) reflects the dynamic interplay between ongoing perturbations of circulatory function and the compensatory response of short-term cardiovascular control systems.

A variety of linear, non-linear, periodical and nonperiodical oscillation patterns are present in heart rate fluctuations in healthy and hypertensive subjects. The main aim of this study was to demonstrate that even in the early stages, the autonomic tone is involved in the complex pathophysiology of hypertension with consequences in the outcome of patients.

Method: In 47 hypertensive patients (23 men, 24 women, mean age 54.2 years), ECG signal analysis and heart rate variability (HRV) measurements were performed for short time epochs (5 minutes epochs) using an ECG recorder. Also, a beat-to-beat finger photoplethysmographic waveform system, included in an ABPM system has been used for continuously recording blood pressure. Entropy analysis has been used for the study of heart rate dynamics.

Results: HRV in time domain showed reduced values independently of age, gender and severity of hypertension. Compared to the linear parameters of HRV, the nonlinear parameters, showed a much earlier impairment in hypertensive patients (parameter, mean ± SD, p value).

Conclusions: We have highlighted the complexityof heart rate modulation in hypertension and its relationship with the entropy of RR intervals in hypertensive and normotensive subjects.Even in the early stages of the disease, the autonomic tone is involved in the complex mechanisms of cardiovascular coupling regulation.

Keywords: Hypertension, heart rate variability, nonlinear analysis

O48 Autonomous nerve system changes during deep SCUBA dive

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Background: Influence of SCUBA diving on human physiology is well recognised and it can lead to severe health problems. Changes in autonomic nervous system (ANS) are of peculiar interest since they can be responsible for different medical conditions observed after a dive.Evaluation of ANS is challenging, but widely accepted method of heart rate variability (HRV) analysis which describes the cyclic variations in heart rate measured by ECG, offers acceptable non-invasive possibility for estimate of its function, especially in deep SCUBA diving conditions.

Objective: The aim of study was to evaluate influence of deep SCUBA dives with compressed air to a depth of 45 msw on ANS measured by HRV analysis of ECG signal. ECG signal was recorded from healthy volunteers, that were selected for recording (healthy, trained volunteers, non-smokers). Divers were carrying dry suits with ECG holters beneath. During SCUBA diving humans are influenced by environment that is not found in other activities.That include raised surrounding pressure, increased partial pressure of oxygen in breathing mixture, raised resistance during movement, additional weight and pressure from SCUBA equipment before the dive.Increased density of breathing mixture elevates breathing resistance and lower temperature of sea water on greater depth may trigger activation of sympathetic nervous system. Furthermore, serious consequence on nervous system may result from decompression sickness which can happen in inadequately prepared divers not following diving protocols. SCUBA diving can lead to raising of minute ventilation, lowering of heart frequency, increased risk of arrhythmia, lowering of peripheral circulation and rise of peripheral resistance. ANS is greatly involved in that adaptation, and HRV is method of choice for evaluation of changes.

Methods: Seven divers were equipped with ECG-holter devicesand performed a dive to a depth of 45 in accordance to diving protocol designed with V-planner. They were told not to swim on a bottom, where average temperature was 16°C. After surfacing they were told to keep ECG-holterfor 30 minutes, when it was removed, and data analysis performed.

Conclusions: Strenuous scuba dive to higher depths influence on both sympathetic and parasympathetic part of ANS.At specific time points (during rest, immersion, at the bottom, and during decompression) following changes were observed – higher heart rate during bottom time, significant lengthening of a QRS complex, lowering of all domain parameters (SDNN, RMSSD, PNN50), lowering of all spectral parameters (ULF, VLF, LF, HF, TP), predomination of vagal activity in sympathetic-vagal balance (raise of HF%, lowered Log LF/HF). Final conclusion is general lowering of function of ANS with vagal predomination, and rise of parameters during decompression.

Key Words: autonomous nervous system; heart rate variability

O49 The prevention of arrhythmias: HISPA program

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Introduction: Between 5 and 7% of general population experience syncope. Considering the possibility of injury, even one episode of syncope is a major clinical issue.

The aim: The aim at the paper is to show the HISPA approach to syncope and includes the noninvasive diagnostic tools for detection of cardiac causes.

Material and Method: In syncope with unknown cause the most important diagnostic tool is telemetric system, which provides 24 hours monitoring in period of 3 years, the first two implanted devices on Institute of Cardiovascular Disease Dedinje were on March 3, 2017 in two syncope patients.

Results: The female patient, age 66, was diagnosed the stroke of unknown etiology. Telemetric monitoring was conducted. During monitoring the asymptomatic episodes of atrial fibrillation were discovered, which in 90% are the reason of stroke which is present in 25% of all patients experience stroke.

Conclusion: Telemetric system enables the reliable diagnosis, follow up and treatment of syncope patients caused by a symptomatic or asymptomatic cardiac arrhythmias.

Key words: syncope, atrial fibrillation, HISPA approach

O50 Comorbidities associated with gender in patients with heart failure with preserved and mindrange ejection fraction

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Background: Heart failure complicates the cardiovascular disease, leading to disability and has remained a major cause of mortality from cardiovascular diseases for many years.A half of patients with chronic heart failure (CHF) has preserved or midrange left ventricular ejection fraction.

Methods: We included 153 patients with CHF I-IV New York Heart Association functional class and left ventricle ejection fraction (LVEF)≥40%.Participants were categorized according to LVEF as follows:HF with preserved LVEF (HFpEF; LVEF≥50%) (group I,n=110) and HF with midrange LVEF (HFmEF; LVEF=40-49% (group II, n=43). We analyzed comorbidities in the two groups and did a comparison between menand women. Differences between groups were tested with χ2 tests and Mann-Whitney test.

Results: Groups did not differ by functional classes of CHF. We compared women (n=72 in group with HFpEFand n=20 in group with HFmEF) and men (n=71 and n=23, respectively). Patients in both groups were similarin the frequency of comorbidities, such as diabetes, impaired glucose tolerance (IGT),smoking, kidney disease, obesity, chronic obstructive pulmonary disease (COPD), peripheral artery disease (PAD),cancer, gastric ulcer and gastritis, anemia and dementia.HFmEFwassignificantly associated with female sex (p=0.03), arterial hypertension (p<0.001), atrial fibrillation (p=0.04), other heart rhythm disturbances (p=0.09), whileHFpEFwassignificantly correlated with coronary heart disease(CHD) (p=0.04), myocardial infarction (p=0.04), cerebrovascular diseases (p=0.04), dyslipidemia (p=0.02).Opposed to women, men with HF weresignificantly younger (p=0.03), more often smoked (p=0.02), more frequently had HFmEF(p=0.03). Arterial hypertension, atrial fibrillation, diabetes, IGT, obesity, anemia to be more frequent in women compared with men CHF patients. Smoking, COPD, PAD, ulcer disease and CHD to be more common in male with CHF compared with female.

Conclusion: Comorbidities in CHF is significantly associated with gender.

Keywords: heart failure, ejection fraction, comorbidity.

O51 Data Preprocessing for ECG Signal Classification using Artificial Neural Networks

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Artificial neural networks (ANN) have been widely used for ECG signal classification problems. One of the main challanges for succesfull application of ANN in this domain is data preprocessing. The main problems related to creating high quality data sets include unbalanced data, extreme values, missing values and attribute selection. In addition to these, standardly used data normalization and dimensionality reducation techniques add a number of different choices that can be used when building data preprocessing pipeline. This study discusses some of the commonly used techniques for data preprocessing for ECG signal classification. A series of experiments with myocardial infarction ECG data showed that different combination of preprocessing techniques and settings have significant and sometimes unexpected impact on ability of the artificial neural network to learn and predict, and thus classifier perfromance.

Keywords: artificial neural networks, data preprocessing, ecg. classification

O52 Artificial neural networks for removing artifacts from heart rate variability signals

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In this research we are presenting an artificial neural network (ANN) based tool for artifact removal processing specialized for heart rate variability signals. It is a Matlab script with simple principle of dividing signal on short segments. ANN classifier is then trained to distinguish segments with and without artifact values. Afterwards, infected segments are corrected by simple mathematical operation and whole signal is then reconstructed by inverse function (desegmentation). The tool is fully automated. As an output it gives pure signal, cleaned from artifacts. The procedure of HRV artifact removal processing is comprised through next algorithm procedure:

- derivation of artificially infected HRV signal with artifacts;
- dividing HRV signal on 5-point segments;
- normalization of artificial HRV signal;
- importing of normalized segments of artificial HRV in Neuroph software;
- building ANN classifiers in Neuroph software;
- training and testing various configurations of ANN;
- evaluation of the results;
- choosing a configuration of ANN classifier with the best results of testing;
- exporting the code of ANN classification (classifier) to matlab script;
- importing real HRV signals with real artifacts in matlab script;
- dividing real HRV signals on 5-point segments;
- normalization(as previously mentioned for artificial HRV signal);
- testing it with ANN classifier;
- interpolation of detected (classified) artifact/removal of successive artifacts;
- inverse desegmentation (constructing signal from 5-point segments);
- renormalization (turning back to scale of HR values);
- plotting the processed signal and correlation with original signal.

Results. We trained and tested classification of correct from incorrect segments in artificial HRV signal. High accuracy of testing was achieved. Then we performed a processing procedure for 60 real signals with artifacts. We used RR intervals recorded and derived from Task force monitor (CNSystems, Austria; 1000 Hz sampling rate, ECG main leads). Accuracy close to 100 % in artifact recognition and removal in all 60 signals was achieved.

O53 Optimal screening of cardiovascular system in renal patients at the begining of the dialysis

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Cardiovascular disease (CVD) is major cause of death in ESRD pts, in more than 50%. It is established that a sucessful kidney transpant improves quality of life and reduces mortality when compared with maintenance dialisys. Despite that, kidney transplant recipients continue to have a higher mortality rate comapred to general population with CVD as the leading cause.

Pre-transplant cardiac screening test and procedures can be both labor- intensive and expensive, and must therefore be employed judiciously. It remains unclear which are most appropriate. Major cardiac event could be faster moving targer (hard to hit and prevent), due to uremia and other acceleratiors of CVD in CKD. There is a trade-off between the risks from a given procedures which are remote and a benefits from that procedure which for a given patient remain for the time being hypothetical.

Cardiac screening before kidney transplantation should start with anamnesis and physical examination. Resting ECG should be performed anually and 30days before transplantation.

Resting echocardiography should be performed in all pts after 3months on dialysis. Left ventricule size, systolic and diastolic function, wall motion abnormalities should be assessed.

Consideration about exercise stress testing in this population is: safety in pts with less than 4 METS; failure to achive target heart rate; problems in correlating ECG changes to territorial ischaemia.

Myocardial perfusion scintigraphy (MPS) is planned for those with HTA or arrhythmias; where it can be done using dipiridamol to rise endogen adenosine and to lead to vasodilatation. Limittions are: due to already higher resting blood flow due to higher basal adenosine level in ESRD pts; challenge induced to flow reserve is attenuated; medications decresing sensitivity of MPS; radiation dose equivalent to 750 chest Xrays examinations.

Cardiac NMR is useful in assesing: LVH, LA volume, nonischaemic cardiomyopathy (CMP), infiltrative and hypertrophic CMP. Examination is performed with no radiation, indipendent of the chambers volume, with no use of gadolinium (cave nephrogenic systemic fibrosis) but it is expensive, time consuming, and stil not in screening guidelines.

Use of cTnT in non-acute setting can point out on LVH, volume overload, or uncontroled HTA. Levels of cTnT in non acute setting correlates well with post-transplant cardiac events and overall survival.

While renal transplant candidates are on waiting list: cardiac stress testing should be repeted 1x anually, particulary in DM pts; and in non-DM pts 1x in two yrs. Patients should be kept on the waiting list while the screening is done. We should suspend the pts from the list only if: ACSy, CHF with EF less than 40%---until coronary angiography and PCI procedure or CABG or valve replacement are done.

Conclusion: Cardiovascular death still remains the leading cause of morbidity and mortality in stable post kidney transplanted pts. Due to limited avaliability of donor organs, careful cardiovascular risk stratification is paramount prior to listing for kidney transplantation not only to prevent adverse cardiac events in the perioperative period, but also to identify patients with lower risk of long-term major adverse cardiac events (MACE) to optimaze functioning graft longevity.

O54 Analysis of 24-hour blood pressure and arterial stiffness in patients before and after renal transplantation.

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Cardiovascular diseases is the main cause of death in patients with chronic renal failure. 24-hour analysis of arterial stiffness (AS) similar to ambulatory blood pressure monitoring (ABPM) helps to detection the target organ damage in these patients in time.

The aim of our study was to research specific features the daily changes of the vascular stiffness (VS) and the central aortic pressure (SBPao) in patients with chronic renal failure who receiving different types of renal replacement therapy (RRT).

Methods. 158 people were examined and they divided into 4 comparable age groups: receiving program hemodialysis (PGD), patients after renal transplantation (RT), patients with essential arterial hypertension (AH) and healthy volunteers. All of them underwent 24-hour blood pressure monitoring with a daily evaluation of VS indices and SBPao.

Results. Patients who receiving RRT had elevated pulse wave velocity (PWVao), night central aortic pressure and decrease pulse time index of norm (PTIN - percentage of 24-hour period, during which the PWVao is not more than 10 m/s). PTIN changes was the most significant.

Conclusion. In patients receiving replacement therapy, compared to patients with essential hypertension, recorded a marked increase in the daily VS and the night SBPao. The most significant changes in the VS index reflects the daily PTIN.

O55 Assotiation between HRV parameters and mortality in HD patients

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After beginning chronic kidney disease patients on hemodialysis, depressed heart rate variability (HRV) has been proven to be a powerful independent predictor of a poor outcome. Although patients with end stage renal disease (ESRD) have also markedly impaired HRV, the prognostic value of HRV analysis in these patients remains unknown. The aim of this study was to investigate whether HRV parameters could predict survival in 24 ESRD patients on hemodialysis.

Twenty four dialysis patients were investigated group. Hemodialysis patients had been on regular hemodialysis treatment and were selected from our unit. The exclusion criteria was diabetes mellitus. The mean time spent on hemodialysis was 34 ± 26 month. Blood concentrations of urea, creatinine, lipids parameters, C-reactive protein (CRP), protein, albumin and phosphorous were examined of laboratory parameters and the adequacy of hemodialysis by Kt/V, as an index of fractional urea clearance was investigated.

In the prognostic analysis Cox proportional-hazards model, the following factors were investigated: age, protein, albumin, phosphorus and HRV measures derived from 24-hour electrocardiography monitoring, calculated in the frequency domain-total power (TP), power within low-frequency band (LF), and power within high-frequency band (HF) and ratio LF/HF. During follow-up of 3 years, 7 patients (29%) died and 5 patients (71%) died from cardiovascular disease. Cox's univariate analysis identified the following factors to be predictors of death: age (p 0=0.02), serum albumin ((p = 0.004), phosphorus ((p = 0.02), HF (p = 0.003) and ratio LF/HF (p = 0.05).

We conclude that depressed HRV on 24-hour ambulatory electrocardiography monitoring is an independent risk factor for a poor prognosis in patients with CHF. Whether analysis of HRV could be recommended in the risk stratification for better management of patients with CHF needs further investigation

Key words: HRV parameters, hemodialysis, mortality

O56 Association of Diabetes Related Complications with Heart Rate Variability in Type 2 diabetic patients

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Objective: Microvascular, macrovascular and neurological complications are the key causes of morbidity and mortality among Type 2 diabetic patients (T2DM). The aim of our study was to investigate the alterations of cardiac autonomic function, or presence of cardiac autonomic neuropathy (CAN) in diabetic patients, in relation to three types of diabetes-related complications.

Materials and Methods: ECG recordings were collected and analyzed from 119 T2DM patients in supine position who were diagnosed with nephropathy (n = 25), peripheral neuropathy (n = 64) and retinopathy (n = 56) at our University Clinic.

Results: Comparison between combinations of patients with complications and a control diabetic group (CONT) with no complication (n = 34) was performed using time, and frequency measures of heart rate variability (HRV). OR of low frequency power to high frequency power ratio (LF/HF) showed a higher association with these diabetic-related complications compared to CONT, especially for the patient group combining all complications (OR: 4.92). This study confirms that the type of microvascular or peripheral neuropathy complication present in T2DM patients implying disorders of multi-organ connectivity are directly associated with autonomic nervous system dysfunction. Clinical practice may benefit from screening methods for CAN in patients with diabetic complications to ensure better preventive and treatment outcomes in T2DM.

O57 Totally Connected Healthcare with TV White Spaces

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Recent technological advances in electronics, wireless communications and low cost medical sensors generated a plethora of Wearable Medical Devices (WMDs), which are capable of generating considerably large amounts of new, unstructured real-time data. This contribution outlines how this data can be propagated to a healthcare system through the internet, using long distance Radio Access Networks (RANs) and proposes a novel communication system architecture employing White Space Devices (WSD) to provide seamless connectivity to its users. Initial findings indicate that the proposed communication system can facilitate broadband services over a large geographical area taking advantage of the freely available TV White Spaces (TVWS).

O58 Visualization of multivariate dependency structures via copula tomography

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Copula is a power mathematical tool that estimates a coupling level of multivariate time series. Its majorbenefit is a possibility to visualize the dependency structures. Figure 1 (left panel) presents an empirical copula density of systolic blood pressure (SBP) and pulse interval (PI) signals of a rat exposed to high temperature (34^0C). Right panel of the same figure presents the structure of dependency levels transformed back to the original SBP-PI plane.

Dependency visualization could be messy in multivariate time series, so we propose "copula tomography", where dependency structure of two chosen signals is presented in "slices" that correspond to subsets of the remaining observed signals. In mathematical terms, copula tomography would correspond to a conditional bivariate copula density. Figure 2 shows an example of tomographic dependency structures corresponding to five levels of body temperature of the rat in Fig. 1. It may be seen that the dependency is decreasing if the body temperature increase.It is envisaged that tomographic copula analysis would become a useful tool for understanding the bindings of different biomedical processes.
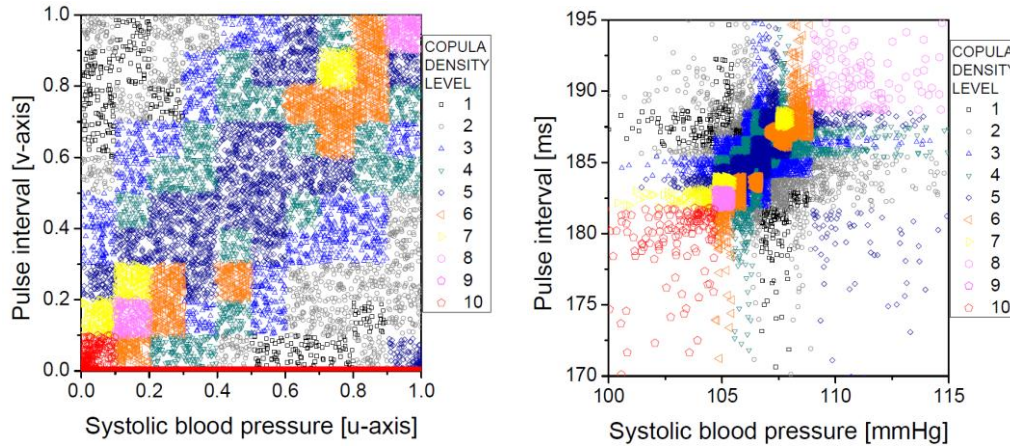
Figure 1. Copula density of rat exposed to high temperature (left) and dependency level transformed to
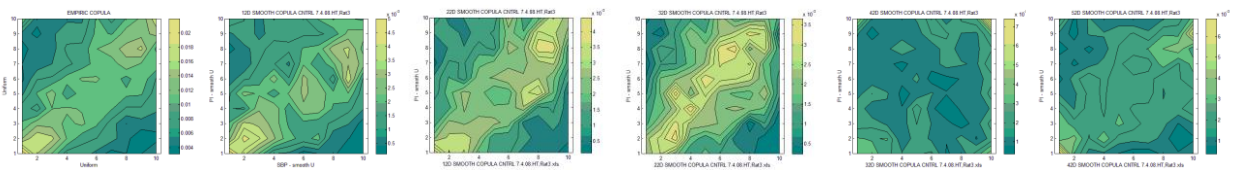
Figure 2. Copula tomography; from left to right: copula density of the complete signal followed by tomographic slices for decreasing temperature levels

O59 Cross-approximate entropy of PI-transformed signals

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Probability integral (PI) transform implements a distribution function of a random variable (r.v.) for its transformation, thus obtaining a new transformed r.v. with uniform probability density function. It is illustrated, together with a simple proof of PI transform, inFigure 1: if x is an observed random variable with probability density function f(x) and with distribution function F(x), then density u(y)=F(f(x)) of r.v. y is uniform. PI transform in its inverse form was important in early computer era, to generate r.v. with arbitrary distribution, and it regained its popularity in copula studies. Joint probability density function of PI-transformed signals (copula density) showsa pure dependency structure, excluding the influences of marginal densities. Such a transform can be beneficial for cross-approximate entropy (*XApEn*) that quantifies the relationship of simultaneously recorded signals: a) if one of the signals has large skewness, this property might blur a level of their association; b) for statistically independent z-normalized uniform signals it is easy to calculate a referent value, Eq. (1) where N is a time series length and m, $r$and $\cdot$are parameters required for *XApEn*estimation; c) an exact value of estimation error for a particular sequence pairis easily evaluated using Eq. (2), where z are samples of the master signal (and logarithm of zero cases processed). It should be noted that this method is not related to copula entropy that usescopula density histogram bins to evaluate Shannon entropy.

$$XApEn\ (m,r,N,\tau=1) = -\ln((r\cdot(4\cdot a - r)/(4\cdot a\cdot a)),\quad a=\sqrt{3}. \tag{1}$$

$$XApEn\ (m,r,N,\tau) = \frac{\sum\limits_{i=0}^{N-(m-1)\cdot\tau}\ln(p_i^m(r))}{N-(m-1)\cdot\tau+1} - \frac{\sum\limits_{i=0}^{N-m\cdot\tau}\ln(p_i^{m+1}(r))}{N-m\cdot\tau+1},\text{where}$$

$$p_i^m(r) = \begin{cases} \dfrac{\prod\limits_{k=0}^{m-1}\big(\min(a,z_{i+k}+r)-\max(-a,z_{i+k}-r)\big)}{(2\cdot a)^m}, & |z_{i+k}|-r < a \\ 0, & |z_{i+k}|-r \ge a \end{cases}. \tag{2}$$

$$\Pr\{F(x)\le y\} =$$
$$= \Pr\{x \le F^{-1}(y)\} =$$
$$= F(F^{-1}(y)) =$$
$$= y,\quad \text{a property of}$$
$$\text{uniform distribution}$$
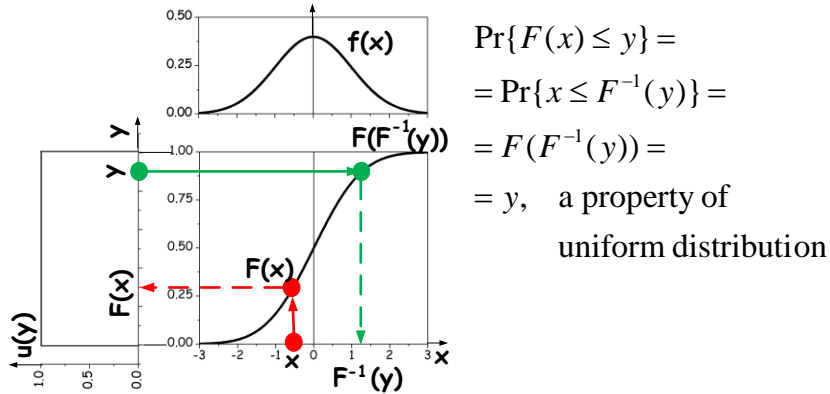
Figure 1. Probability integral transform

O60 Copula as a quantifier of SBP and R-R dependency measure in diabetes mellitus patients

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One of the serious complications in diabetes mellitus patients is dysfunctionality of cardiovascular system autonomic regulation. In this study a level of possible baroreflex impairment in diabetes mellitus patients was analyzed using a statistical copula method.

Beat-to-beat time series of systolic blood pressure (SBP) and R-R intervals were recorded in 15 diabetes mellitus patients ofUniversity Clinical Center, Zemun, and in 15 healthy controls, using Task Force Monitor at Laboratory for neurocardiology, KBC BezanijskaKosa. The pre-processing included artifact and slow signal component (trend) elimination, as well as linear interpolation of input signals and window sliding procedure. Then the copula method was used to determine level of SBP and R-R interval statistical dependence, as well as time lag for which the observed signals exhibit the maximal interaction. Copula also provided an insight into SBP and R-R dependency structures, expressed as copula density and as tail concentration function. An optimal copula family was selected applying a goodness of fit methods.

Considering the time lag necessary for signal transmission and integration by the autonomic nervous system (ANS), and considering the level of synchronization/similarity between SBP and RR time series expressed by copula parameter, the patients could be classified into 3 groups: 1) time lag remains the same, level of synchronization unchanged; 2) time lag longer than in healthy controls, level of synchronization unchanged, 3) time lag longer than in healthy controls, level of synchronization lower than in healthy control. Dependency parameter (level of synchronization) as a function of time lag(delay in ANS response) is shown in Figure 1, for averaged control group and for three patients, each one from a particular group. Further analysis indicated differences in dependency structures, especially in taiil regions.
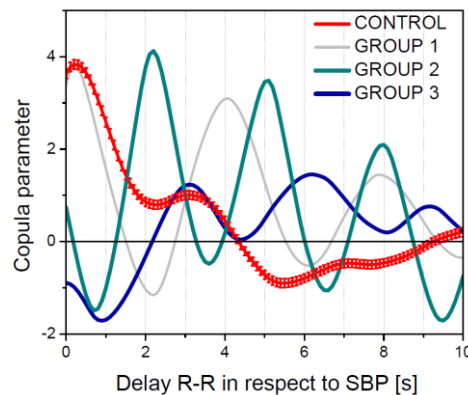
Figure 1.Level of synchronization/similarity between SBP and R-R(copula parameter) as a function of delay in ANS response

O61 Effects of ranolazine on ultra low frequency heart rate fluctuations assessed from very shortterm recordings

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The aim of research presented in this paper is twofold, to emphasize a mathematical method which allows the assessment of very low and ultra low frequency components of heart rate variability (HRV) from short-term recordings of electrocardiography (ECG), as well as explore the effects of drug ranolazine on the heart rate fluctuations. ECG signals were taken from a former study [1], available on PhysioNet [2]. After R peak extraction and interpolation, uniformely sampled RR interval signals were derived (14 to 18 samples in length with sampling frequency equal to 2 Hz). Such short signals are expected to provide insight almost entirely into high frequency (HF) and low frequency (LF) range. However, this paper shows that filter diagonalization method [3] can be successfully utilized on RR sequences, thus producing very low frequency (VLF) and ultra low frequency (ULF) data. Several important parameters of the method have been discussed. Spectral powers integrated over ULF, VLF, LF, and HF bands, i.e. over all spectral components which emerged in these bands, exhibited several effects of ranolazine. Statistical analysis presented significant decreases of HF ($p=0.0494$) and normalized HF power ($p=0.0045$) due to administration of ranolazine, and a significant increase of the normalized ULF power ($p=0.0092$). These results have been discussed in the context of known physiological mechanisms assossiated with ranolazine, and HRV analysis. The decrease of HF power is explained by indications of the drug's ability to inhibit parasympathetic nerve activity [4]. Regulatory mechanisms of ULF fluctuations of heart rate are vaguely determined in literature. However, this paper provides several hypotheses connecting ULF power and ranolazine, which incorporate glycemic control, physical activity and blocking of voltage-gated sodium channels. The accordance of these hypotheses with the previous research [5] justifies the utilization of filter diagonalization as a method of accessing ULF data in short-term recordings.

Index Terms: autonomic nervous system, filter diagonalization, heart rate variability, long-term fluctuations, ranolazine

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O62 Task Force® signals in patients with Lyme disease

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Task Force®monitor possesses a unique property of non-invasive simultaneously recording of blood pressure (BP) waveforms and ECG waveforms, with sampling frequency that is equal to 1000 Hz. The corresponding cardiac parameters are, therefore, extracted from two independently acquired sources. Figure 1 presents heart rate (HR) signal, obtained as an inverse of R-R interval extracted from ECG waveforms with resolution of 1ms, and systolic blood pressure (SBP) signal extracted from BP waveforms. Although the signals are recoded in ambulatory patients (thus minimizing the movement artifacts) and with professionally attached electrodes and finger cuffs, artifacts are inevitable. Possible artifacts in HR are detected by ADA filter designed specifically for HR, while suspicious occurrences in BP waveforms are marked by setting the SBP values to zero. Within this paper the correct parts of both signals are identified and the statistics of erroneous recording outlined. From the correct parts of the signals the cardiac parameters are evaluated. The statistics is done for signals recorded from 45 patients with lyme disease. From the parts of signal where both HR (R-R) and SBP are correct the statistics of cardiac parameters is evaluated and compared to the mean values calculated automatically.
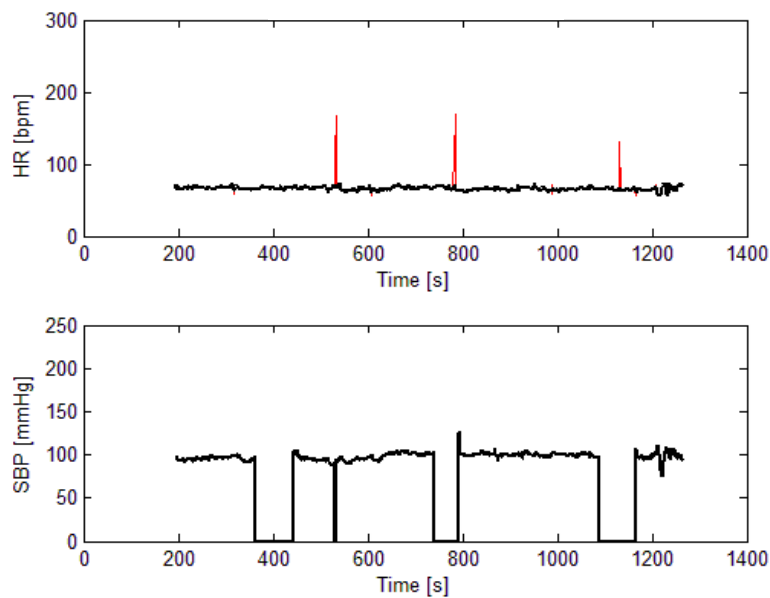
Figure 1. HR and SBP signals extracted from ECG and BP waveforms; (possible) HR artifacts are detected by ADA filter (red lines in upper panel); the suspicious parts of BP

O63 On error statistics in Portapres ® signals

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Continuous non-invasive recording of blood pressure (BP) waveforms is a challenging task even in ambulatory patients. Portapres® is a device that solves even a harder problem, managing to record BP in freely moving subjects. Embedded software (Beatscope®) extracts cardiac parameters, including systolic and diastolic blood pressure (SBP and DBP) and pulse interval (PI). Sampling frequency of BP waveforms is equal to 100Hz, yielding a PI signal resolution of 10ms. An importantPortapres feature is blood pressure correction, necessary due to increasing and decreasing elevation of finger cuffs.

The signals acquired in such a complex way are inevitably accompanied by artifacts. The aim of this paper is to analyze errors in BP waveforms and their impact on SBP and PI statistics.

It is shown that dominant errors are tracking errors that occur when the monitoring start (Fig. 1) and short interrupts that occur sporadically during the monitoring (Fig. 2). While the first ones are eliminated removing the first part of signal, the second ones influence the SBP and PI signals, as shown in Fig. 3 and
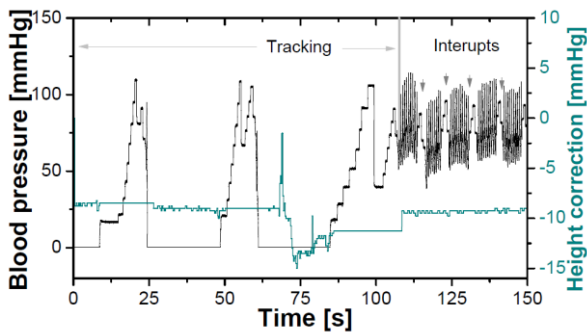
Fig. 1: Artifacts in BP waveforms
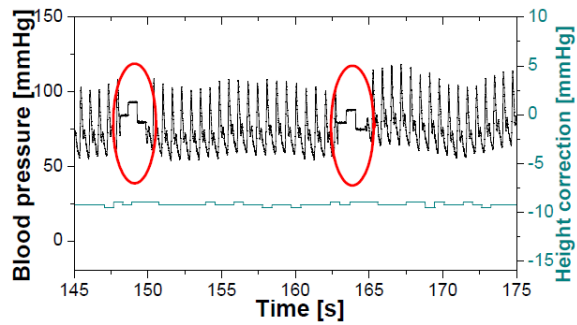
Fig. 2: Signal interrupts (encircled)
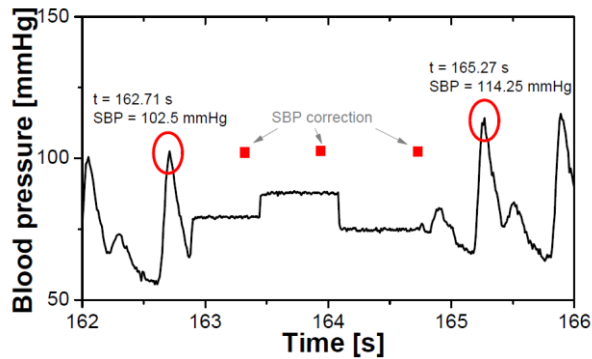
Fig. 3: Position and amplitude of SBPs in BP waveforms prior and after the interrupt

Time [s]	SBP [mmHg]	HR [bpm]	Comment
162.66	101	92	Slightly different from raw BP signal in Fig. 3
163.31	101	95	Assumed values
163.94	101	80	Assumed values
164.69	101	113	Last RR interval happened to be too short
165.22	113	95	Slightly different from raw BP signal in Fig. 3

Table 1: SBP and HR parameterscorresponding to Fig. 3

O64 Benefits and Risks of Artificial Intelligence in Complex Biomedical Systems analysis: a review

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Over the last several decades have become commonplace in our lives. With the evolution of digital capacity, more and more data is produced and stored in the digital space. The growth of the effectiveness and ubiquity of artificial intelligence methods has also stimulated thinking about the potential benefits and risks associated with advances of artificial intelligence.

The most obvious application of artificial intelligence in healthcare is data management. Collection, storage, preprocessing, analysis and reproduction are the first step in revolutionizing the existing healthcare systems. Speeding this up and making more cost-effective would have an enormous effect on today's healthcare and how innovations reach everyday medicine.

Because artificial intelligence has the potential to become more intelligent than any human, we have no surefire way of predicting how it will behave, which opens many questions about its safety. We can't use past technological developments as much of a basis because we've never created anything that has the ability to, wittingly or unwittingly, outsmart us.

One technical challenge is to guarantee that systems built automatically via statistical "machine learning" methods behave properly. Another challenge is to ensure good behavior when an artificial intelligence system encounters unforeseen situations.

Artificial intelligence algorithms are no different from other software in terms of their vulnerability to cyber attack. With the development of high secure softwares malware can be prevented. The another concern is that artificial intelligence will become so sophisticated that it will work better than the human brain and after a while, it will aim to take control over our lives.

If the medical community understands how artificial intelligence could be beneficial in improving healthcare, these systems can be implemented in every day practice.

POSTER PRESENTATIONS

P01 Heart from the perspective of Neurocardiology

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Abstract: Neurocardiology may provide a broader definition of heart than biomedicine oriented on neural research. Heart of neurocardiology is not just a pump or a muscle, but a complex multifunctional organ. To confirm such a concept we have reviewed modern information about biophysical properties of the heart. Through this cardiocentric context we represent our results of neurocardiological research. In general it is pointing on integrative biomedical approach to heart and *with heart*, as well.

Index terms: Neurocardiology, heart, brain, autonomic nervous system, organic coherence

Introduction. On the last year *Neurocard* conference we gave an introduction to Neurocardiology and determined it as a multidisciplinary biomedical science that combines insights from cardiology and neurology with information and engineering techniques. Our presentation highlighted integrative potentials of Neurocardiology in personal medical approach, systematic diagnostics, optimisation of therapy, and research of brain-ANS-heart interconnections. It has also pointed to fruitful affinity of Neurocardiology toward linkage with nanotechnologies, pharmacology, other branches of medicine andTraditional Chinese Medicine (TCM) [1]. In meanwhile we have located one more definition: "*Neurocardiology can be defined as the field that studies the heart as a neurohormonal organ or the study of the heart as a neurological, endocrine and immune organ*" [2].

Neurocardiology defined like this might be used for overcoming the over-emphasizing of the brain through the modern research of neurosciences. On the other hand, biomedical handbooks [3] and even formalism of everyday life briefly defines heart as a pump or a muscle. These insights have obviously made *encephalocentric* view of man [4] predominant in our modern era.Yet, in earlier human civilization *cardiocentric* approach was general basis of understanding. An ancient man was mostly relying on heart, considering it as a center of organism, means of cognition and perception of reality. Recent neurocardiological research might rehabilitee this view and even overcome the opposition between encephalocentric and cardiocentric approaches.

Heart in the light of Neurocardiology. As mentioned, Neurocardiology is offering much wider definition of heart. From neurocardiological research we can generalize that heart is equipped for dignified communication with brain and ANS. Heart rate variability (HRV) is reflection of that communication and it might be even main signal for systematic regulation of organism[5], homeodynamics[1] and organic coherence[2].Thus, heart is not just a muscle: only one third of total cardiac cells are ordinary muscle cells [8]; heart possesses more then 40 000 neurons capable to form cardiac neural networks which is the informational base for local processing and memory[9]; heart produces hormones and neurotransmitters [2], sound waves, heat, mechanical pressure, EM fields measurable not only in all parts of the body but also outside of it [9, pp. 125-140]. Sound echoes and micromechanical oscillations from the heart could travel through the vessels and tissues. The mechanoreceptor and magnetoreceptor cells are receiving these impulses, which was demonstrated experimentally [10]. It might also mean that HRV and related cardiac features are giving sensitive biorhythmic tact for proper functioning of organism.The question is why we cannot use HRV parameters for recognition of diseases like physicians in TCM do with pulse palpation? Maybe TCM practitioners are sensitive for more subtle patterns, since it was shown that diseases are followed by loss of HR fractality and complexity [11].

After summarizing this information we can get image of heart as multi-emitting, multi-functioning and sensor organ. Thus, it can invite us to focus more on heart like ancients have done.

Heart-brain synergy. Heart influences the brain as well. Beside selectivity of heart's reaction on external stimuli, there have been noticed that „afferent inputs to the brain from heart can either inhibit or facilitate the brain's activity, which, in turn, can affect perception and motor activity" [12]. Clinical trials are showing that after solving

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[1]Homeodynamics is referred on dynamic nature of regulatory processes in which variability in physiological functions is fundamental feature, especially the fractal dynamics [6].

[2]Organic coherence is optimal, consistent, orderly physiological functioning that is result of properly tuned organs dependent on each other [7].

cardiac issue some neural problem disapears as well [13]. Thus, both brain and heart are important for organic coherence. Oposite to modern encefalocentric view great scientists like Claude Bernard and Charles Darvin were agreeing and insisted on primacy of heart [14]. In Neurocardiology we also should not interpret HRV indices just as brain regulating patterns in heart rythm. Our research shows that state of ANS *per se* could be essential for the organic coherence [1]. Instead of overemphasis of one organ, it is better to speak about synergy of brain and heart with ANS as mediator of it.

Neurocardiovascular system. Heart is the first functional organ to develop in embryogenesis [15]. First assimetry-the breake of symmetry in embryo occures when heart beat is established and heart's looping in circulatory system is formed [16]. Since that moment, heart has to operate continuously until the end of life. Left-right asymmetry is fundamental for organic coherence. It was indicated in cases of functional organic problems as a consequence of defected asymmetry during prenatal period. It is still speculative how asymmetry is established. Also, the origin of bilateral symmetry is not fully understood. There are assumptions that it is governed by magnetic field or/and by gene expressions [17]. However, some regulation system is still needed to direct it. Integrative medicine research is pointing to the acupuncture system. In the context of our research it might be related to neurocardiac informational, energetic and functional inter-conections whose manifestation is qi (vital force). In favor of it, synchronous and synergetic interacions of sympathetic and parasympathetic ANS (balancing or excessing/deficiting) are having patterns as same as yin and yang shifting [1]. Hence, in our presentation for *Neurocard 2017* we are going to ilustrate a block diagram of qi regulation established on neurocardiovascular system. Based on it, as we showed earlier [1], Neurocardiology and TCM might give a promising integral approach of personalized medicine.

Conclusion. In our approach information about heart is gathered aiming to highlight the mutual cardio-neural interactions and their significance for unity of human organism. However this is not a systematic review. Such gathered information could serve to indicate a possibility of a balanced approach. In other words, it is a pointing to a bridge for all of us living in modern world to overcome a gap between heart and mind.

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P02 HEART RATE VARIABILITY IN YOUNG MEN WITH AUTONOMIC DYSFUNCTION SYNDROME

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Background: Autonomic dysfunction syndrome (ADS) is a pathological disturbance of the autonomic regulation of internal organs, blood vessels, and metabolic processes as a result of primary or secondary morphological and/or functional changes in the autonomic nervous system (ANS).

Methods: We examined 40 men aged 18-25 years who didn't indicate the presence of diseases. Autonomic status was assessed by special questionnaire (A.Vein., 2003). Heart rate variability (HRV) was determined by the rhythmocardiography (RCG). Conducted initial background RCG record, modified Valsalva maneuver, Ashner-Dagnini test, active orthostasic test, loading test. HRV indicators: median($25\%\div75\%$) of the duration of RR-intervals, standard deviation of all the waves on the average value of RR (SDNN), standard deviation of each fluctuation: humoral-metabolic (σl), sympathetic (σm), parasympathetic (σs) effects divisions of the ANS, the average amplitude of respiratory arrhythmia. The ratio of regulatory factors in the sinus node: humoral-metabolic influence in the very low frequency (VLF%), sympathetic - in the low-frequency (LF%) and parasympathetic high-frequency (HF%) ranges in relation to the total spectrum (100%).

Results: ADS was diagnosed in 23 young men of studied group (57.5%) by questionnaire of A.Vein. We compared the ADS-group (n=23) and healthy men (n=17). Groups did not differ by age. Patients in both groups were comparable by RR-interval. The ADS-group has obtained lower VLF% (p=0.003) in the background sample. The increase in $\sigma m\%$(LF%) correlates with the release of norepinephrine in the synaptic cleft. In the ADS-group revealed a longer period of vagal stimulation (p=0.04) in the Valsalva maneur. The trend is to shorter period of achievement of the maximum response (tAB) in the active ortostatic test (p=0,066) in ADS-patients can be explained by higher capabilities of interaction of norepinephrine with postsynaptic membrane receptors.

Conclusion: Assessment of HRV by RCG-method showed the presence of long-lasting increase of the sympathetic tone in patients with ADS.

Keywords: heart rate variability, autonomic dysfunction syndrome.

P03 Changes in Raman spectra of programmed placebo samples

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Abstract. Raman spectroscopy as rapid, sensitive and non-destructive tool, has been method of choice for many investigation in solid state physics and chemistry. It is based on analysis of inelastic scattered light and due to its large possibility of application in medicine, biomedical issues, clinical implementation, food industry and pharmacy, it has attracted significant attention. By Raman spectroscopy it is possible to 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 changes on nano level between placebo forms obtained from sucrose and industrially produced gutron. We have used samples of sucrose with different informations programed for cancer treatment. All samples have been investigated by micro-Raman spectroscopy on 532 nm laser line in spectral range from 185 to 3800 cm^{-1} with TriVista TR557 Raman spectrometer which is more appropriate for organic samples. Significant changes in Raman spectra of all samples are noticed. Influence of information on samples is visible in change of peak intensity.

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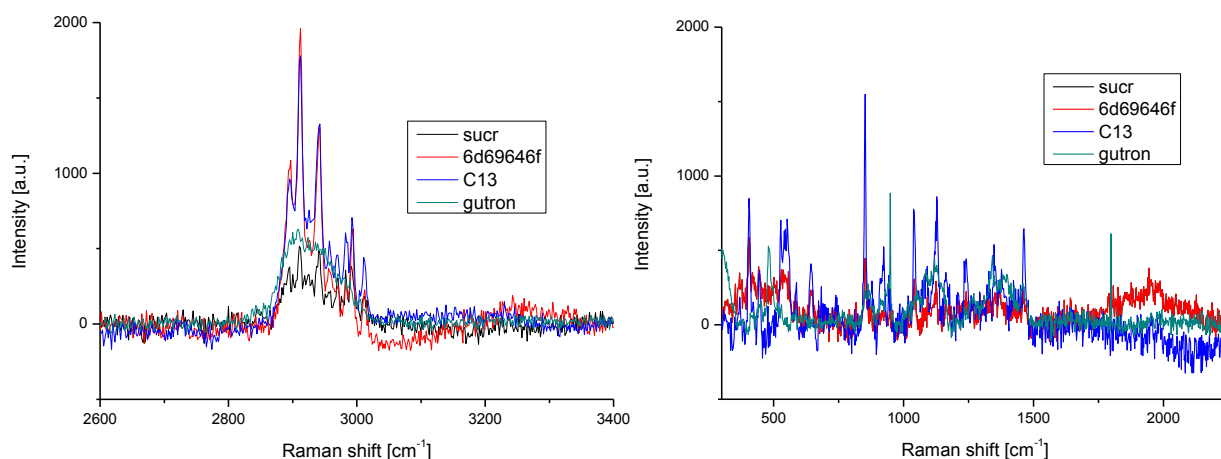
P04 The response of the cardiovascular system to short-term and long-term methods to improve the performance of trained athletes

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Abstract
Increasing the efficiency of trained athletes with non-pharmacological methods and special training is one of the priorities of modern sports of higher achievements. It is known that intensive training of different directions affects the vegetative regulation of blood circulation and changes in systemic arterial pressure. So endurance training, mainly has a hypotonic effect, reducing blood pressure (BP). Strength training, on the contrary, provokes the growth of blood pressure. If the training regime is incorrectly chosen, cardiovascular disorders are observed.

A homogeneous group of healthy young men actively engaged in specific physical activities (boxing, wrestling, martial arts) was selected for the study, in the number of 7 people aged 21-36 years (age 27.5 ± 1.1 years, height 176.3 ± 1.2 cm, body weight 76.4 ± 1.3 kg). The study was conducted in a training camp under the conditions of a special designed 4-week cycle consisting of microcycles in each of which loads and special training were selected to develop complex coordination skills without reducing endurance. Techniques to improve performance based on the short-term electrostimulation of biologically active zones (MC-6) with «AVR-051» (LLC «Inferum», Yekaterinburg) and the use of the method of interval breathing of a specially prepared hypoxic-hyperoxic air mixture in which nitrogen was replaced by helium (long-term) were applied. In this study, an attempt is made to evaluate the influence on the character of the physiological response of trained athletes whose vegetative tone is formed under the influence of many years of training on functional tests that cause an increase in blood pressure and pulse rate and the effects of short and long action "before" and "after" the training fee.

The effect of a single electrostimulation was manifested by a less pronounced "pressor" reflex (a smaller increment in SBP) in response to the activation of mechanoreceptors of working muscles under static loading. According to HRV, electrostimulation affects the reduction of sympathetic "control" in rest and stabilization of vegetative reactivity in response to performance of functional loading tests, and also causes activation of subcortical regulatory structures in athletes with predominantly normotonic type of vegetative regulation. The use of electroneurostimulation is most likely useful for athletes with hypertensive response to physical exertion. The long-term effect of increasing working capacity without reducing strength and achieved endurance values according to VO2 max indices was observed a month after the interval breathing course of the hypoxic-hyperoxic air mixture.

Keywords:
Electroneurostimulation, biologically active zones, "pressor" reflex, vegetative Kerdo index, performance.

P05 Theoretical and experimental investigation of pure water and aqueous solutions as placebo, and water based biological samples

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Water and aqueous solutions are often used as placebo. The results of the theoretical research at the *ab initio* level provide information of metastable and stable modifications of the examined structures. XRD measurement provides information of the solid state structure. The aim of this study was to investigate water structure before and after programming as a placebo, and possible influence to the structure of patient's biological samples after the application of placebo. We investigated the structure of water in solid state at *ab initio* level, and made a comparison of water in solid ice forms with experimental data from the ICSD database. Theoretical analysis has been performed using CRYSTAL 14 software, and later with VESTA and Kplot visualization programs. In the experimental conditions, we have investigated aqueous solutions with different informations programmed, in solid state at temperatures below -40 $^{\circ}$C and at atmospheric pressure, and performed XRD measurements in order to determine the unit cell parameters. We have performed similar procedure for extracted extracellular fluid as for aqueous samples in order to obtain cell parameters. We compared all results, the theoretical and experimental, whose values of the unit cell parameters differ and give us the basis for further researches on the programmed placebo.

Keywords: water, aqueous solutions, placebo, biological samples, *ab initio*, XRD

P06 Exposure of chronically stressed rats to treadmill running induces potentially positive adaptations of the catecholaminergic turnover in stellate ganglia

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Abstract: Sympathetic nerves innervating the heart originate from stellate ganglia and influence the catecholamine levels in the heart. Our earlier studies showed that reduction of catecholamine synthesis in stellate ganglia may be linked to the beneficial effects of treadmill exercise on cardiovascular system in stressed animals. To confirm whether the exposure of chronically stressed rats to daily treadmill running induces potentially positive adaptations of the catecholaminergic turnover in stellate ganglia, this study discusses the effects of additional acute immobilization stress. Immobilization (IMM) is a standardized procedure frequently used as an additional acute stressor and is considered as one of the most intensive stressors that significantly changes gene expression. This study aimed to investigate the impact of the additional acute immobilization stress on the gene expression of vesicular monoamine transporter 2 (VMAT2), which mediates transmitter uptake into neurosecretory vesicles in stellate ganglia of chronically stressed rats exposed to daily exercise. In this experiment the individually housed rats were exposed to daily treadmill running during 12 weeks and, after this animals were exposed to additional acute stress for 2 hours. The rat training program consisted of 12 weeks running on a treadmill (20 m/min, 20min/day). The animals were sacrificed 3 hours after the acute immobilization. We found that additional acute IMM increased mRNA levels of VMAT2 by 300% in stellate ganglia of chronically stressed rats exposed to daily exercise. Significantly high VMAT2 transcript levels confirm that the additional acute immobilization reveals high readiness of chronically stressed animals exposed to daily exercise for the accumulation of catecholamine in stellate ganglia. This could mean that exercise may condition physiological systems to "expect" a problem and therefore, be more ready to respond to a novel additional acute stressor by increased accumulation of catecholamine. It can be concluded that the exercise can be beneficial because it induces an adaptive response to possibly other stressor, that may be encountered later.

P07 Changing the concept of antinuclear autoantibodies screening: a new laboratory algorithm in the diagnosis of systemic autoimmune rheumatic diseases

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Abstract

Background: Antinuclear antibodies (ANA) are fundamental in the diagnosis of systemic autoimmune rheumatic diseases (SARD). The indirect immunofluorescence (IIF) on HEp-2 cells is the gold standard method for ANA detection. In a recent study, the higher sensitivity for ANA detection of BioPlex ANA Screen than IIF on HEp-2 has been reported. Also, the early detection of autoantibodies by BioPlex predicts the develop of autoimmune diseases before the clinical onset. The aim of the study is to elaborate a new laboratory algorithm for ANA screening in subjects with clinical suspicion of SARD.

Methods: The algorithm elaboration was based in a 3 years follow-up study on 411 subjects without clear diagnosis of SARD in whom autoantibodies were detected by BioPlex but not by IIF on HEp-2.

Results: After 3 years of follow-up, 76% of subjects were positive for autoantibodies by IIF and a diagnosis of autoimmune diseases was found in 87% of the patients. A new algorithm for ANA screening including the BioPlex ANA Screen in patients with clinical suspicion of autoimmune diseases was proposed.

Conclusions: BioPlex ANA Screen should be included as screening for autoantibodies in subjects with clinical suspicion of autoimmune diseases.

P08 Direct oral anticoagulants in atrial fibrillation in elderly patients – time for the new challenges

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Elderly population include people over 65 years of age. In the world, they make up 8.5% (617 million) of the world's global population with a tendency to rise to 17% by 2050. Demographic expectations are that in the period ahead, the number of "oldest" (older than 80) will triple, and in some countries it will increase four times.[1] As in the rest of the world, in the Republic of Serbia is also notable the trend in aging. For example, in 2015, elderly people made up 18.73% of the population, while in 2030, it is expected that as much as 22% of the population will be older than 65 years.[2] The aging process is specific, inevitable and associated with polymorbidities, and therefore by polypharmacy. Therefore, prevention and adequate treatment of the disease are considered very important in order to prevent the complications of the disease, and consequently functional dependence.

When it comes to atrial fibrillation (hereinafter: AF), as one of the most common arrhythmias, in this context it implies both its treatment, and the prevention and treatment of its complications - stroke and troboembolization. In 2010, it was estimated that 20.9 million men and 12.6 million women had AF.[3] The prevalence of AF in elderly patients is rising rapidly, so in patients with 65 years of age and over it is 5%, while in those over 80 it is as high as 10%.[4] It must be taken into account a large number of patients with 'silent' AF or paroxysms of very short duration that are difficult to record electrocardiographically.

To assess the risk of ischemic stroke in AF, the most commonly used is the CHA2DS2-VASc score. Most of the parameters involved in calculating the score (heart failure, hypertension, embolization data in the past, blood vessel disease, diabetes) are more common in older age, as well as years of age. All together contributes to age increasing the risk of ischemic stroke 1.5 times for every 10 years.[5] Flamingam studies have shown that 23.5% of strokes in people over 80 years are the result of atrial fibrillation.[6] Patients who had a stroke due to AF have a worse prognosis than patients who do not have AF.[7]

In the treatment of AF and the prevention of complications in addition to therapy for controlling frequency and rhythm, oral anticoagulant therapy (OAKT) is also important. According to the latest recommendations from 2016, the value of the CHA2DS2-VASc score that is indicated for the introduction of OAKT in men is 1, while in women this value is 2.

Vitamin K antagonist- warfarin, as the first anticoagulant used in the treatment of AF, has been widely used since 1950. In patients with adequately dosed warfarin, the incidence of ischemic stroke decreased to 1.4% per year compared to 4.5% per year in patients not on anticoagulant therapy.[8] However, its use is associated with more frequent complications in the form of bleeding. To assess the risk of bleeding in wide use is HAS-BLED score. The risk of bleeding associated with anticoagulant therapy increases with age, approximately 40% at every 10 years of age.[9]

Bleeding in the elderly is more comon, independetly from use of OAKT, due to multiple comorbidities - anemia, hypertension, decreased renal function, diabetes, increased risk of falls, neuropsychiatric diagnosis (dementia), and polypharmacy (e.g. use of antithrombotic therapy, NSAIL, antibiotics, etc.), as well as reduced BMI and amount of fatty tissue. The fact is that the factors listed above are the reason why only 50 to 60% of patients who are indicated for OAKT are estimeted to recive it.[10] It is also noticeable that with the age of patients the number of patients taking anticoagulant therapy decreases: 75% of patients aged 65-69, 59% of patients Aged 70-79, 45% of patients aged 80-89, 24% of patients ≥ 90 years, even though the risc of stroke rises with age.[11] It should also be noted that patients who use warfarin spend 30-50% of the time out of the therapeutic range, which additionally increases the risk of both bleeding and stroke and embolization.[12]

Since 2008, direct oral anticoagulants (DOAC) have been used successively, as a more modern therapy associated with fewer complications and greater comfort. According to the activities of the DOAC, they are divided into: direct thrombin inhibitors - dabigatran and factor Xa inhibitors - apixaban, rivaroxaban. The advantage of therapy is reflected in a fixed dose, with fewer interactions with food and medicine, without the need to monitor INR (International Normalized Ratio), which is also stated as a primary advantage. Each of the DOACs was examined in the atrial fibrillation in phase III of the controlled randomized studies.[13,15,17] Their success in preventing stroke was examined in AF patients, as well as its safety, i.e. the occurrence of bleeding, all in relation to warfarin.

ARISTOTLE Study[13] (Apixaban for Reduction of Stroke and Other Thromboembolic Events in Atrial Fibrillation) controlled randomized double blind study, the third phase of the apixaban testing. Study envolved patients with non-valvular AF or flutter in presens, or a minimum of two episodes in a span of two weeks in the

past year. In addition, included patients hade to have   one of the risk factors for the development of stroke (75 years of age, previous stroke or TIA, previous screening, manifest cardiac failure 3 months before inclusion or systolic function <40%, diabetes, hypertension). A total of 18201 patients are randomized into two groups, those who took apixaban at a dose of 5/2.5mg * twice a day and those taking warfarin at an adequate dose depending on the INR. The median age of the patients involved was 70 years and CHADS2 score was 2.1. The primary effect monitored is the incidence of stroke (ischemic, hemorrhagic and undefined) and embolization, and as a secondary effect monitored, is the fatal outcome of any cause. In addition to monitoring the safety of the drug, the major bleeding event (defined by the ISTH criterion) was primarily monitored.

It was observed that the risk of stroke (predominantly hemorrhagic) and embolization, using apixaban decreased by 21%, large bleeding by 31%, and fatal outcome by 11% compared to warfarin. The result is maintained in various subgroups including elderly population.[14]

ROCKET AF Study[15] (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for the Prevention of Stroke and Embolism Trial in Atrial Fibrillation) is a phase III of testing, a randomized double-blind, controlled study. Patients who had non-valvular AF and who had a moderate or high risk of stroke were involved. Risk of stroke is estimated based on: previous stroke, transient ischemic attack, embolization or at least two of the following risk factors: systolic function <35%, hypertension, over 75 years, diabetes, or $CHADS_2 \geq 2$. A total of 14264 patients are included those taking rivaroxaban at a dose of 20 / 15mg ** once a day and those taking warfarin at an adequate dose depending on the INR. Median age was 73 years and $CHADS_2$ score 3.

Based on the results of the study, rivaroxaban was shown to be not inferior at one dose per day in relation to warfarin at an adequate dose, in the prevention of stroke and embolization. There was no significant difference in the occurrence of large haemorrhage and clinically significant minor bleeding in these two groups, although less intracranial and fatal haemorrhage was observed in the rivaroxaban group. In subgroups of the elderly population (≥75 years) it was noticed that the results were consistent with the results from the overall study. [16]

RELY Study[17] (Randomized Evaluation of Long Term Anticoagulant Therapy) is phase III of the dabigatran examination and represents a randomized controlled study. Patients who have been involved in the study have an AF registered on the electrocardiogram at the moment of entering the study or within the past 6 months with one of the additional criteria (had a stroke or transient ischemic attack, systolic function <40%, to be at least NYHA II for the last 6 months, older than 75 years or between 65 and 74 years old with diabetes, hypertension or coorrhynic syndrome). There are 18113 patients classified into 3 groups: those taking dabigatran at a dose of 110 mg twice daily, dose of 150 mg twice daily or warfarin at an adequate dose depending on the INR. The average age of the patients involved was 71 years with average $CHADS_2$ 2,1.

Both doses of dabigatran did not show inferiority compared to warfarin in primary outcome - stroke and embolization. A dose of 150mg showed superiority over warfarin in the primary outcome, but also increased the risk of large extracranial bleeding, while a 110mg dose showed superiority compared to warfarin against the risk of the occurrence of large extracranial bleeding. Both doses of dabigatran showed a lower risk of occurrence of intracranial haemorrhage compared to warfarin.There is no proven difference in the risk of stroke in the elderly population between dabigatran and an adequate dose of warfarin. [18] Both doses of dabigatran compared to warfarin have a lower risk of major bleeding in patients under 75 years of age and the same or greater risk in patients over 75 years of age. In other words, the risk of extracranial, but not intracranial bleeding in patients on dabigatran increase with years. [19]

Based on the data obtained from the above studies (ARISTOTLE, ROCKET AF, RE-LY) and several meta-analyzes of the studies[20,21], it has been shown that DOAC reduces the risk of stroke and embolization in a patient with AF compared to warfarin. Decreasing of relative risk by using DOAC is 30% on average[22]. There was also no increased risk of major bleeding in comparison to warfarin, except for a more frequent gastrointestinal bleeding associated with dabigatran at a dose of 150 mg. It is significant that in patients with DOAC in AF, the risk of intracranial haemorrhage is reduced by 30-70%.[22] An analysis of the older population (≥75 years) in all three studies has shown that the absolute risk of thrombotic events and bleeding increases with age, however, the increased risk is similar for both patients using DOAC and patients using warfarin. This means that the results obtained in these three studies can also be applied in the older population.[23]

Elderly patients themselves have an increased risk of bleeding due to multiple comorbidities, as well as the physiological conditions that the aging process carries. On the basis of this and the data presented, it can be concluded that the use of DOAC reduces the risk of stroke and embolization, and at the same time does not increase the risk of bleeding compared to the risk that years above 75 are already carrying on their own. Based on the analysis of the risks (consequences) and benefits of using DOAC, it can be said that patients who have an increased risk also have the highest profit from using DOAC. Scores can greatly assist in assessing the need for the introduction of DOAC, but an individual approach to the patient plays the most important role in the decision.

*over 80 years of age, body weight ≤60kg, creatinine value ≥ 133μmol / L
** In patients with ClCr 30-49ml / min

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P09 STENT LOSS DURING PCI AND SUCCESSFUL RECOVERY USING NEW APPROACH

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A 68 year old female with earlier history of CVD, and previous MI (20 yrs. ago), was admitted to ICU with ongoing and persistent chest pain, lasting for less than 2 hours. ECG showed ST elevation in inferior leads and ST depression in D1, aVL, and V1 to V3. Physical examination showed no signs of LV dysfunction, with unremarkable findings on heart and lungs.Preliminary laboratory findings were within reference values, with exception to leukocytosis (Le 16.710^9/L). On arrival patient was transported in to Cath-lab. for PPCI, preliminary angiography showed significant stenosis with thrombus in medio-distal segment of RCA, successful PPCI RCA was performed with implantation of one BMS (Multi Link Vision 2.75x12mm), in the further course two more BMS were implanted proximal to the first stent. During implantation the last stent was dislodgedand was lost in ostium of RCA, this was due to heavy calcification and difficult angulations of ostial and proximal segment of culprit vessel.

WHAT TO DO?
Try to recapture lost stent and to pull it out of the patient body.
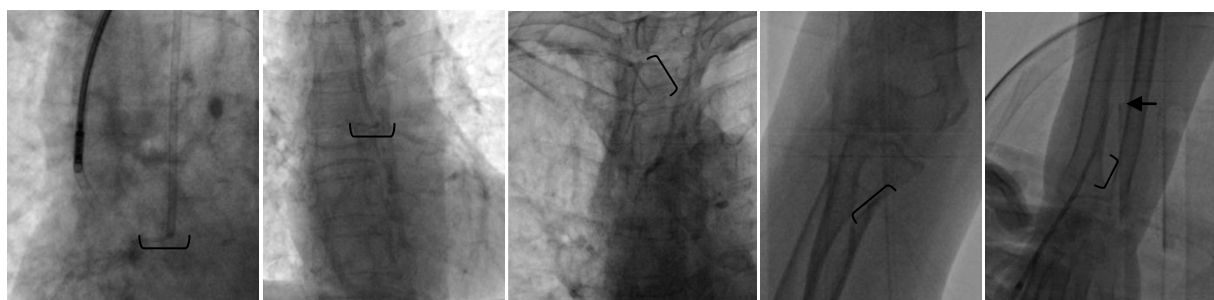
Fig. 1a: device stent capture attempt (marker is outlining the dislodged stent).**Fig. 1b:**pulling dislodged stent by guiding catheter (marker is outlining the dislodged stent). **Fig. 1c:** pulling dislodged stent into right subclavial artery (marker is outlining the dislodged stent).**Fig. 1d:** passing the elbow (marker is outlining the dislodged stent). **Fig. 1e:** pulling dislodged stent by guiding catheter into introducer (arrow pointing at the distal tip of introducer and marker is outlining the dislodged stent).

In further course operator tried several techniques of stent capture using various devices. First approach was by second small balloon catheter, and a second wire, but with no success. Snare loop was also used but with no success in recapturing dislodged stent. As it was obvious that conventional methods did not give expected results, operator opted to try jamming dislodged stent into the guiding catheter. This was accomplished by advancing guiding catheter trough the ostium of RCA and compressing dislodged stent by the tip of guiding catheter against struts of previously expanded stent i proximal segment of RCA. As seen on pictures stent was successfully jammed into the tip of guiding catheter, and slowly pulled to the introducer, and out of the patients body. Patient was transported to the ICU.

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P10 CEREBROLYSIN IN THE TREATMENT OF ACUTE ISCHEMIC STROKE

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Abstract:
Stroke is the second cause of death and the leading cause of disability among patients. Cerebrolysin is a neuropeptide preparation with neuroprotective and neurorestorative properties.These pharmacologic effects are of relevance in cerebrovascular and neurodegenerative diseases.
This research was conducted as a prospective study at the Clinic of Neurology, University Clinical Centre Banja Luka. It included 40 patients who were treated for stroke at the Clinic of Neurology. The aims of this research were to confirm that patients with acute ischaemic stroke randomized to administration of Cerebrolysin for 10 days show better outcome on motor and functional recovery compared to patients randomized to placebo.
We notice a significant drop in NIHSS score in the Cerebrolysin group (from 9.90, over 4.50 to 1.20 after three months) than in the control group (from 9.05 over 6.65 to 4.35). We also notice a significant decline in RANKIN score in the group of patients who were on Cerebrolysin (from 3.65, over 2.05 to 0.55 after three months) than in the control group (from 3.65 to 2.90 to 2.20).
Based on this, it can be concluded that patients who received cerebrolysin had far better recovery than patients who did not receive cerebrolysin, and when looking at only a neurological finding on discharge and after three months and when looking at the functional recovery.

Key words: Stroke, Cerebrolysin, Outcome

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. 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. . 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 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.

Cerebrolysin
Cerebrolysin is a neuropeptide preparation with neuroprotective and neurorestorative properties similar to endogenous neurotrophic factors as shown in vitro and also in several animal models.
These pharmacologic effects are of relevance in cerebrovascular and neurodegenerative diseases as these generate immediate or over time a pathological environment, which is deleterious for neurons, cause their degeneration, dysfunction and cell death.
Cerebrolysin is indicated for the treatment of:
 · Organic, metabolic and neurodegenerative disorders of the brain, especially senile dementia of Alzheimer's type

- Post-apoplectic complications
- Craniocerebral trauma; post-operative trauma, cerebral contusion or concussion

First reports on clinical efficacy in neurological disorders date back several decades covering different and also less specified etiologies. Findings from experimental studies and smaller clinical trials set the stage for the clinical development of Cerebrolysin with focus on dementia, stroke and traumatic brain injury.

Clinical trials in stroke have focused on ischemia; considering the possibility of wrong diagnosis or hemorrhagic transformation of ischemic stroke efficacy and safety of Cerebrolysin have been investigated in hemorrhagic stroke as well.

The clinical development program for Cerebrolysin in ischemic stroke completed to date includes:

Fifteen randomized, double-blind, placebo-controlled trials (Herrschaft 1998, Hong 1999, Haffner 2000, Ladurner 2000, Wege 2000, Skvortsova 2004, Skvortsova 2008, Lang 2009, Hong 2011, Muresanu 2011, Qaragozli 2011, Stan et al. 2013, Aminianfar et al. 2013, Amiri-Nikpour et al. 2014, Guekht 2015)

Three dose-response trials (Skvortsova 2004, Gusev et al. 1994, Gusev et al. 2007)

Three comparative trials with actovegin (Vilensky 1998, Ershov et al. 2011), citicoline (Ershov et al. 2011) and kinesiatrics/TMS (Khabirov et al. 2011)

One long-term trial over one year (Vilensky 2007)

Population subset: acute (Lang 2009, Haffner 2000, Skvortsova 2004, Skvortsova 2008, Hong 2011, Vilensky 1998, Vilensky et al. 2000, Skvortsova 2006, Vilensky 2007, Ladurner 2000, Gusev et al. 1994, Muresanu 1999, Ershov et al. 2011, Herrschaft 1998, Hong 2004, Muresanu 2011, Domzal & Zaleska 1995, Qaragozli 2011, Stan et al. 2013, Aminianfar et al. 2013, Amiri-Nikpour et al. 2014, Guekht 2015), sub-acute (Barolin et al. 1996, Gusev et al. 2007, Hong 1999, Wege 2000) and rehabilitation phase (Volc et al. 1998); NIHSS >12 (Hong 2011)

Clinical trials with Cerebrolysin have been performed mainly in the Caucasian and Asian population. Cerebrolysin showed a wide therapeutic dose range and due to its mode of administration Cerebrolysin is subject to minimal metabolism. Furthermore, no potential for drug-drug interactions is known for Cerebrolysin;

For treatment of stroke daily dosages of 20-50 ml Cerebrolysin were most effective, administered over a period of 10-21 days. Long-term use of Cerebrolysin over one year (three treatment courses) had positive effects on stroke recovery

Study objective:

To confirm that patients with acute ischaemic stroke randomized to administration of Cerebrolysin for 10 days show better outcome on motor and functional recovery measured by NIHSS scale and Rankin scale on admission on discharge day and after 3 months compared to patients randomized to placebo.

Methodology:

The study is designed as a prospective, randomized, double- blind, placebo-controlled, parallel-group study.

Patients with ischaemic stroke and moderate to severe motor function impairment hospitalized at the Clinic of Neurology, University Clinical Centre Banja Luka were included. We included 40 patients in total, 20 were on Cerebrolysin (they recieved 30 mg cerebrolysin per day during 10 days) and 20 of patients were in placebo group (classic therapy for ischaemic stroke but without cerebrolysin). All patients were scored on admission on dissmison day and after 3 months (NIHSS scale and Rankin scale).

Results:

NIHSS – cerebrolysin

NIHSS cerebrolizin

NIHSS - control group

Rankin – cerebrolysin

Rankin – control group
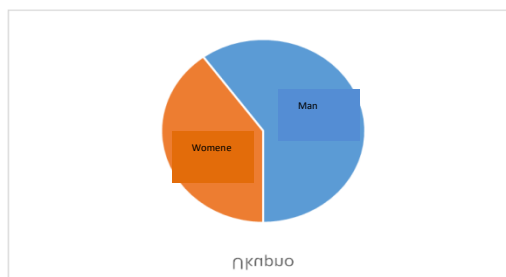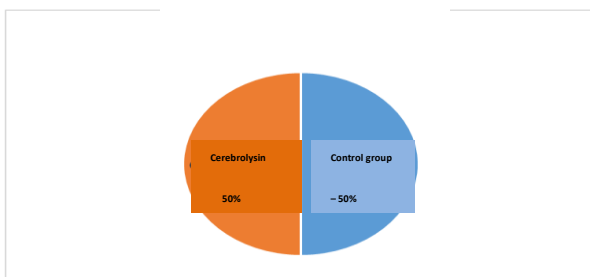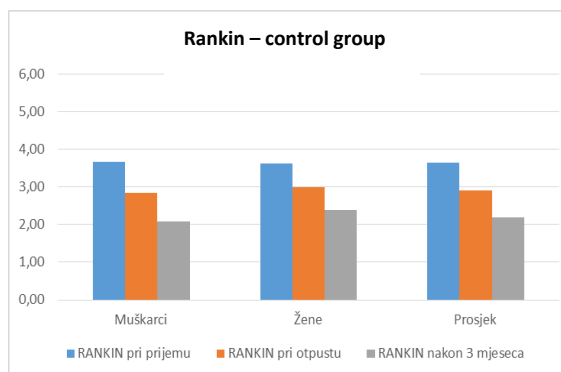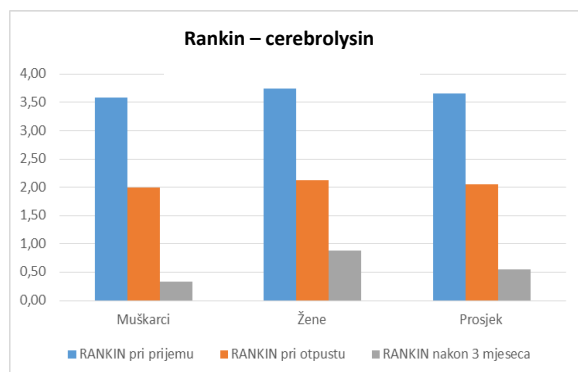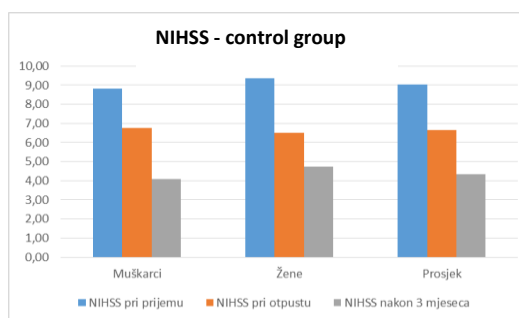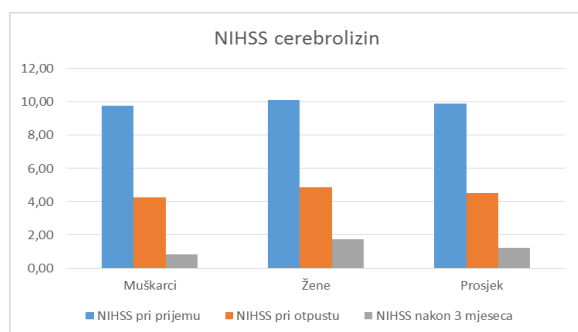
40 patients were included in our study. 20 of them recieved Cerebrolysin and 20 of the did not. In both group we had 60% of mail and 40% of female patients. Average old was 66,45 year in group with Cerebrolysin and 64,4 in group without cerebrolysin. Average NIHSS score on admission in group with Cerebrolysin was 9,9 and 9,05 in group without cerebrolysin. At day of admission NIHSS score was 4,5 in group with Cerebrolysin and 6,65 in group without Cerebrolysin. After 3 months NIHSS score was 1,2 in group with Cerebrolysin and 4,35 in group without Cerebrolysin. Average Rankin score on admission in group with Cerebrolysin was 3,65 and 3,67 in group without cerebrolysin. At day of admission Rankin score was 2,05 in group with Cerebrolysin and 2,83 in group without Cerebrolysin. After 3 months NIHSS score was 0,55 in group with Cerebrolysin and 2,08 in group without Cerebrolysin.

Conclusiones:

In our study were two groups of patients with iscaemic stroke. In one group patient secieved Cerebrolysin (20 patients) and in one groupe they did not recieved Cerebrolysin (20 patients also). Both group has the same percentage od male and female (60% of male and 40% of female) and the both group were about the same age.
On admission both group were with simillar NIHSS and Rankin score which means that patients had approximately equal stroke in both group. But on the day of release, we have a situation that the NIHSS and Rankin score in the cerebrolysin group are significantly lower than the control group. After three months, the situation is even more apparent, and there is a far greater difference when we look at NIHSS and Rankin's scores in favor of the group that received cerebrolisin. Based on this, it can be concluded that patients who received cerebrolysin had far better recovery than patients who did not receive cerebrolysin, and when looking at only a neurological finding on discharge and after three months and when looking at the functional recovery. Further testing is required on a larger number of patients in order to confirm our results. Previous studies conducted with cerebrolysin were also encouraging and the results are similar to our.

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P11 CASE WITH LETHAL OUTCOME AT AUTONOMIC CARDIONEUROPATHY

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Abstract:
Presented here one case with lethal outcome after coronary artery bypass (CABGS) for myocardial revascularization in patient D. with coronary artery disease (CAD), heart failure 3-4 functional classis (FC), paroxysms of stenocardia 4 FC and arrhythmias of the heart. This status wasn't becoming to life and this patient can die in the whichever moment. Intervention surgical operation was the last hope and patient insisted on CABGS, notwithstanding on the high risk of the death. The patient was investigated by the high-resolution rhythmocardiography some times, except standard cardiological methods. Analysis of this case data presented here.

Key words: rhythmocardiography, heart rate variability, coronary artery disease, shunting, autonomic cardioneuropathy, case of death after coronary artery bypass graft surgery

Introduction. Actuality of this theme connects to deficiencies of the patients (pts) selection for intervention surgical treatment of the coronary artery disease [1, 5, 7], which may be reason of the inadequate its efficacy. For that purpose one insufficiency case was analyzed by high-resolution rhythmocardiography (RCG) [2]. At the earlier articles about clinical heart rate variability (HRV) analysis in pts with coronary artery disease (CAD) were presented the results of the pts investigation by the RCG. HRV data were compared between standard data of the cardiological investigations and RCG-indices. In these researches were investigated 123 pts with CAD and 47 healthy men for control (Fig.1). There were conclusions, that RCG is the adequate and perspective method of evaluation of the actual cardiovascular status before and during making out of the cardiosurgical myocardial revascularization in pts with angina pectoris. HRV analyzed in time- and frequency domains consists the supplementary symptoms for the intranosological diagnose at the selection of pts for the cardiosurgical treatment of the angina pectoris [2, 4, 7]. There were used high resolution RCG (discretization of cardiosignal 1000±3 Hz) and HRV indices: average RR, standard deviation all RR –SDNN, average quadratic deviation of sympathetic, parasympathetic and humoral-metabolic waves –σm, σs, σl and their spectral shares LF%, HF%, VLF%. Also maximal reaction in 4 stimulant tests, time of reaction achievement and time recovering after stimuli [5]. The receiving data about multitude variants of deregulations of the sinus node pacemaker activity of the heart, physiologically adequate to stages of the cardiosurgical operation. Degree of CAD was corresponding to ischemic breaches of the coronary arteries. Also there was proved, that coronary artery disease obligatory accompanied by the deregulations of the pacemaker activity of the sinus heart node in a number variants. Its dynamics corresponded to actual cardiovascular status of pts and may be used in a number cardiological diseases and at their cardiosurgical treatment [2]. Except that HRV consists symptoms of the high risk of complications during CABGS, including the life-dangerous cardioarrhythmias, as soon as breaches of the heart rhythm, caused by the cardiosurgical manipulations during CABGS. The most dangerous for life the syndrome of autonomic cardioneuropathy (ACN). The pts with ACN had the clinically heaviest CAD form. These pts differed from pts without CAD [2].

Table 1. Results of HRV comparison in patients with autonomic cardioneuropathy (ACN) (n-56, first line) and in patients without ACN (n-67, second line) before CABGS

HRV indices ($M \pm \sigma$) in sec. (s) and %	Ph, Initial posture	Vm, Manoeuvre	pA, Ashner test	Aop, Active ortos-tatic test.	PWC_{120} Exercise test
RR s, average interval	0,522±0,081 0,768±0,114 **t= 14.05 *****	0, 542±0,072 0,770±0, 102 **t= 14.61*****	0,546±0,082 0,777±0,107 **t=13.83****	0,698±0,095 0,810±0, 087 **t= 7.25****	0,783±0,124 0, 730±0,074 **t=2.83***
SDNN s, average dispersion of all HRV waves	0,011±0,002 0,017±0,006 **t=2.0***	0,011±0,005 0,016±0,005 **t= 5.98****	0,011±0,006 0,017±0,004 **t= 7.79****	0,009±0,004 0,017±0,006 **t=8.88*****	0,010±0,005 0,018±0,004 **t= 10.3*****
σl, s average quadratic dispersion of humoral waves	0,002±0,001 0,008±0,004 **t= 10,0*****	0,008±0,004 0,011±0,005 **t= 4.28***	0,008±0,004 0,012±0,005 **t= 5.19****	0,007±0,003 0,012±0,004 **t= 8.33*****	0,008±0,003 0,015±0,004 **t= 11.6*****
σm, s average quadratic of sympathetic HRV waves	0,001±0,001 0,006±0,002 **t= 6.02****	0,004±0,002 0,008±0,002 **t=4.0****	0,004±0,002 0,009±0,003 **t= 3.57***	0,003±0,002 0,009±0,002 **t= 5.45****	0,005±0,003 0,012±0,002 **t= 8.49*****
σs, s average quadratic dispersion of parasympathe-tic HRVwaves	0,002±0,001 0,007±0,004 **t= 7.93****	0,006±0,003 0,011±0,003 **t= 4.54****	0,006±0,004 0,010±0,001 **t= 6.34****	0,004±0,003 0,012±0,001 **t= 16.0*****	0,007±0,005 0,014±0,003 **t= 5.38****
VLF% spectral share of humo-ral HRVwaves	78,8±8,42 56,39±14,89 **t= 10.47*****	74,64±8,34 60,26±16,30 **t=6.3****	76,19±9,98 55,31±16,42 **t=8.66*****	77,20±19,64 59,36±16,23 **t=5.42****	78,46±24,39 57,87±19,35 **t= 5.11***
LF% spectral share of sym-pathetic HRVwaves.	12,33±7,03 17,84±10,83 **t=3.39***	13,77±8,99 16,60±5,82 **t=2.02***	13,98±8,88 17,75± 10,0 **t=2.21***	12,89±7,32 18,91±14,22 **t= 3.02***	14,87±6,98 16,64±7,79 t=1.33
HF% spectral share of para-sympathetic HRVwaves.	15,7±4,78 25,76±12,53 **t=6.03****	16,58±7,84 21,12±16,18 **t=2.028***	16,88±7,61 20,93±12,7 **t=2.19***	17,9±6,31 22,72±11,24 **t=2.88***	22,66±7,11 37,48±19,12 **t= 5.87****
Δ RR % maximal reac-tions in tests.		6,48±6,13 11,59± 9,96 **t= 3.48***	4,12±3,60 7,95± 6,87 **t= 3.95***	12,31±6,78 21,69±8,07 **t = 6.91****	9,62±7,21 19,23±11,26 **t = 5.72****
t_{AB}, s time of maximal reac-tions in tests.		9,92 ± 2,56 7,78±2,58 **t =4.6****	9,38±2,47 5, 55±2,38 **t = 8.71*****	18,61± 6,39 11,99±3,82 **t =6.8****	43,85 ±12,96 20,0±12,16 **t =10.45*****
t_r, s s time of restoration after tests.		12,73± 8,61 7,48±4,71 **t =4.07***	24,61±7,85 14,47±4,98 **t = 8.36*****	20,03±6,26 15,05±5,74 **t = 4.56****	102,06±32,21 75,06±27,71 **t = 4.92****

*p<0,05; ** p<0,01; ***p<0,001

Here are HRV data before CABGS of patients with and without ACN were compared. Initial HRV indices had authentic and considerable differences between groups. In table you can see, that in pts with ACN (56 pts) the HRV indices were with high authentic less, than in remaining 67 other pts, except of the spectral share of the humoral-metabolic influence in SN and time of achievement of the maximal reactions in tests and time restorative after stimuli. One of key role in the development of the cardioarrhythmias was the ischemic dysfunction of the myocardium at the surgical myocardial revascularization in the operated pts. Frequency of the cardioarrhythmias in

pts with ACN significantly negatively differed in average degree correlated to the background of the myocardial contraction ability reduction (r=0,584-0,638). At the subsequent continuous registration of Rcg the stages of preparation and carrying out of narcosis and other stages of shunting. Here are in table presented results of the comparison HRV indices in pts with and without ACN. There was received very reliable difference at the all positions.
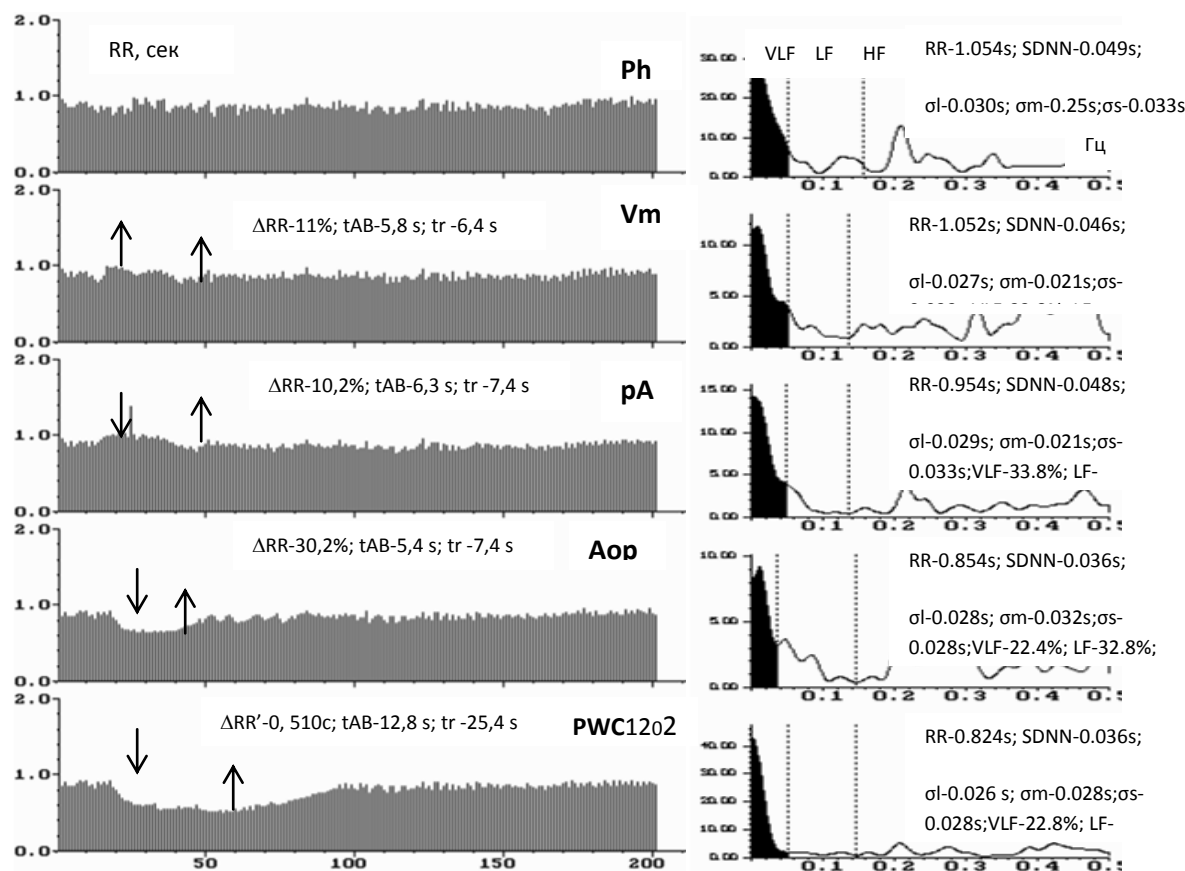
[Fig.1] Here are example of rhythmocardiogram (Rcg), spectrogram and HRV indices of a healthy man in rest (Ph), in parasympathetic Valsalva maneuver(Vm), in the humoral Ashner test (pA), in sympathetic active orthostatic test (Aop), in test with exercise (PWC120). On the all Rcgs here is predominance of the high frequency waves, characteristic to parasympathetic influence in SN. The vertical arrows show of stimulant periods in tests. σl, σm and σs –are the average quadratic dispersion of the humoral-metabolic, sympathetic and parasympathetic HRV –waves, correspondingly; ΔRR-is maximal reactions to stimuli; tAB-time of achievement of this reaction; tr-time of HRV restoration after stimuli. VLF%, LF%, HF% - spectral shares of the humoral-metabolic, sympathetic and parasympathetic influences on the pacemaker cells of the sinoatrial heart node.

These results of HRV researches testimonies about the possibilities of exposition increase of the risk of life-dangerous arrhythmias [3, 4, 5, 6, 7] and also lethal outcome at the CABGS and after it. The loss of peripheral autonomic sympathetic and parasympathetic control in the sinoatrial heart node, as syndrome of the autonomic cardioneuropathy (ACN), is the predictor of complications at the CABGS. Presented here in table 1 analysis HRV data in pts with ACN and without ACN. Here show that risk of the complication and lethal outcome adequate to the reduction of HRV indices. In 123 pts with CAD and angina pectoris of 2-4 FC was made out surgical myocardial revascularisation by CABGS. Except standard cardiological and laboratorial method (ECG with load, EchoCG, ECG-monitoring Holter and BP, CAG). Also every pt was investigated by RCG before, during and after CABGS. Results were satisfactory in the early period after shunting, but one pt was dead. The RCG data this pt D. presented here in Fig. 2-4 RCG. His data essentially differed from data of other pts.

The most important result, that the ACN is the unspecific predictor of the complications and high risk of the death [5]. Such ACN may be possible to observe in the heavy pts with hypertension disease 3st., heart failure 4 FC, with cerebral tumor, diabetes, lupus erithematosis, and etc [2, 3, 5, 6]. ACN with HRV stabilization without any rhythm fluctuations, without any reaction to stimuli in tests is the predictor of the life-dangerous complications at the surgical operation. At this notification, as example here will be presented case in HRV figures 2-4, demonstrated the ACN and complex rhythm breaches in operated pt D. during 4 days before death. Initially before CABGS in pt D. there were exposed a number of intensive poststernal pains some times a day. Its were

without any symptoms of the acute ECG breaches. At the extra angiography there were exposed breaches of many coronary vessel with occlusion 70-80% of left and right coronary arteries. Initial RCG presented on the Fig.2. SDNN was 0,002±0,001 sec. vs normal 0,052±0,006 sec. This corresponded to the ACN.
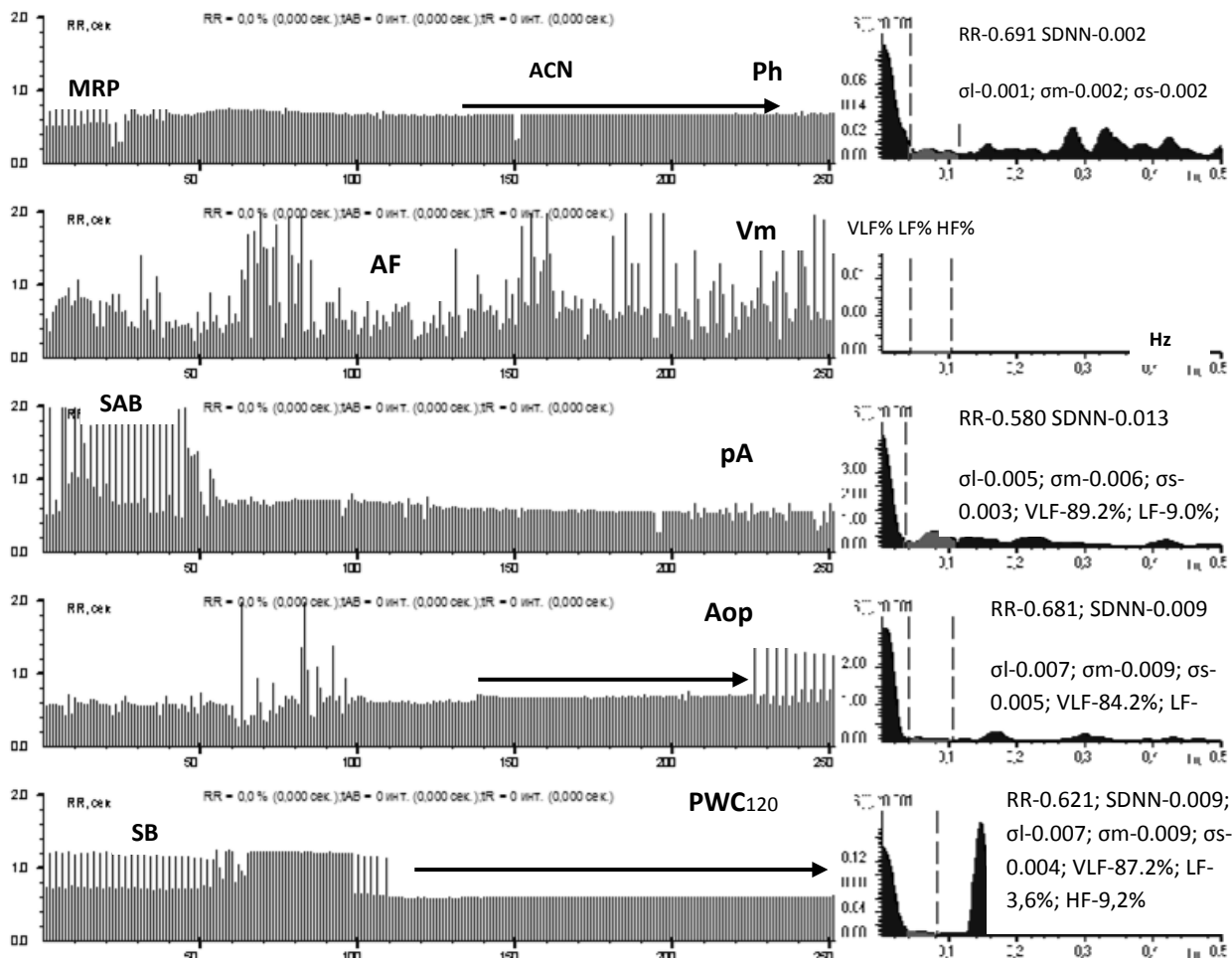
[Fig. 2]. Initial Rcgs, spectrograms and HRV middle meanings in the Rcg indices of the patient D. before CABGS. In Ph here are the rhythm migration of SN pacemaker (MRP)-(1-40i). On the background of ACN (shown by horizontal arrow) here is the long ischemic episode with typical clinical syndrome of angina pectoris. The middle deviations of SDNN presents in units of milliseconds vs normal 0,052±0,012 s. At the spectral correlation of the regulative factors in the sinoatrial heart node here is significant predominance of the humoral-metabolic influence (VLF%) at the expense of reduction of the autonomic sympathetic and parasympathetic regulation (LF%, HF% vs normal). In Vm here is atrial fibrillation (AF). In pA here is sinoatrial blockade of 2-3 stage (SAB) on the background of the ACN. In the Aop (60-100 i) here is AF, then the ischemic episode with HRV stabilization (the difference between intervals 3.55±1.02 millisecond).At the end of active orthostase here is supraventricular bigeminy (SB) with identical preectopic intervals. SB was also during PWC120, here is the ischemic episode.
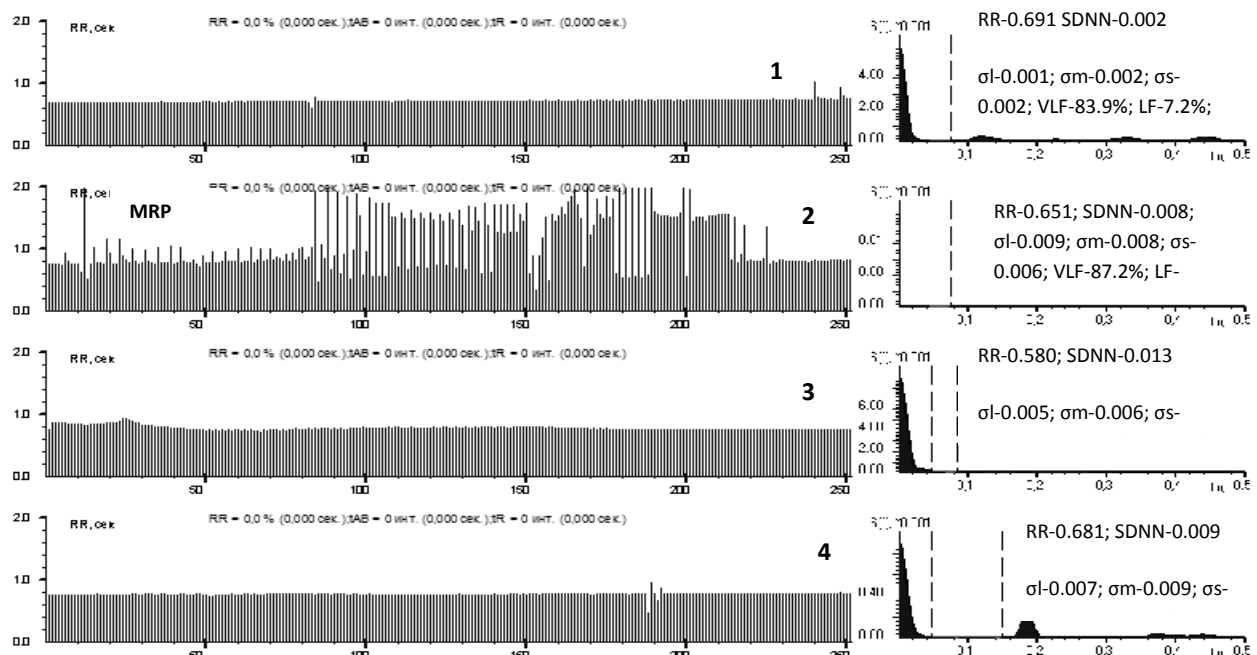
[Fig.3] On the background of intubation narcosis during CABS the significant rhythm stabilization was registered, sinoatrial conducting breaches (end RCG1 and RCG 2 between 1-84 interval), then sinoatrial blockade (84-225 interval) and bradycardia till 45/min during cannulation of the left atrial veins on the predominance of the humoral-metabolic influence (VLF%) and extremely oppression of the autonomic regulation (LF% and HF%) in the sinoatrial heart node at the all positions.
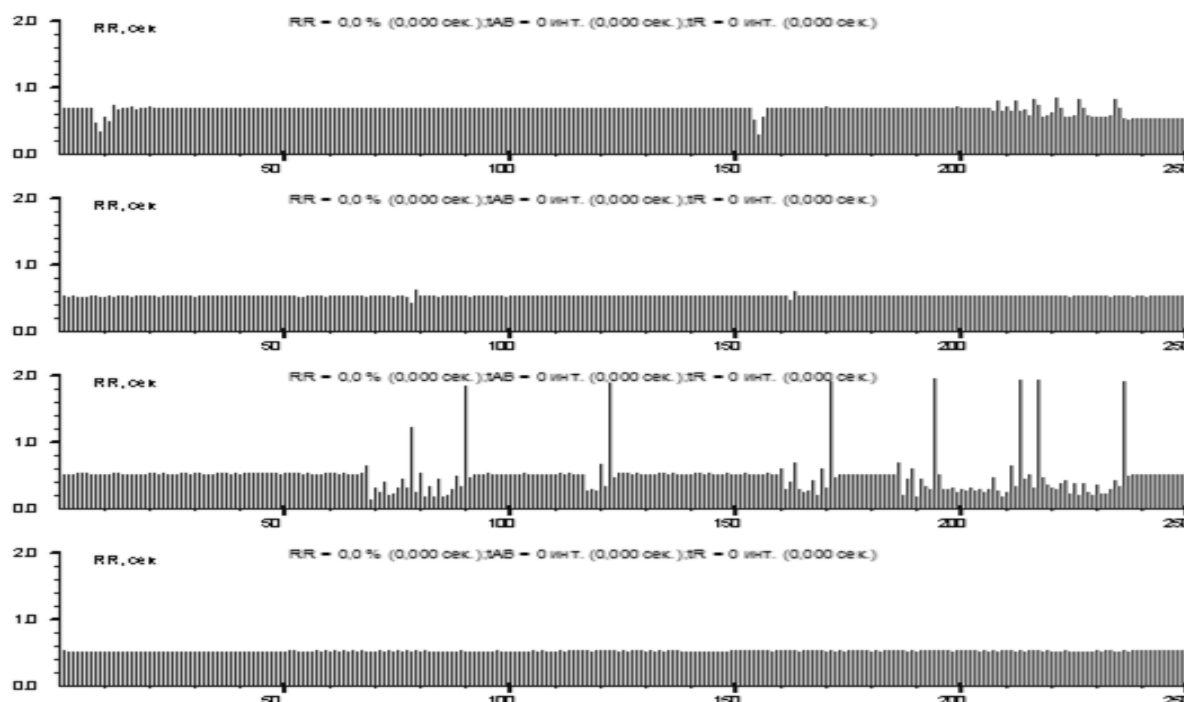
(Fig.4) Rcg of pt D. Here are significant HRV stabilization on the background of the tachycardia (120/min and >) and absent of any reactions to stimuli in tests after CABGS. The predominant share in the regulation of the sinoatrial heart node is the humoral-metabolic factor- VLF%, nonsufficient and inadequate. In the end Ph (205-235 int.) registered RCG –signs of the sinoatrial blockade of 2 type, 2 degree. In Ashner test here are 6 episodes of the heart rhythm migration. Active orthostatic test was unpossible cause heavy status of pt D.

After CABGS through 4 days pt D. dead from acute heart failure. At the pathological anatomic in pt was exposed myocardial infarct in the most acute stage, which was not registered during intraoperative ECG and accorded by non stable hemodynamic, on RCG by extremely low HRV, by syndrome of sick sinus, syndrome of tachy-brady. Pathological anatomic diagnosis: Repeated acute myocardial infarct in the anterior wall of the left heart ventricle

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(circulation breaches 20%). Atherosclerosis of the coronary arteries 3 st. 3 degree. Subocclusion of middle third right coronary artery, subocclusion of the beginning coronary artery of partition between ventricles, subocclusion of the anterior artery between heart ventricles from mouth of third septal branch, t the angina of effort. Hypertension disease 3 stage, risk 4, myocardium mass 550 gr, hypertrophy of the left ventricle (thickness of the wall till 2 sm), system arteriologialinosis. Here is progressive heart failure, the pulmonal swelling. Here was rhythm of the electric stimulator. There was the prolonged (4 days) artificial circulation. There was installated of the intraortal balloon for contrapulsation. The direct reason of death is the heart failure. Initially in pt D. at the RCG-investigation was registered extremely low HRV on the background of the acute coronary syndrome. Because of absent any efficacy from medicinal treatment there was decision about the myocardial revascularization by operative intervention, which was ended of pt death. Intraoperatively there was the sick sinus syndrome with episodes of the bradycardia (heart rhythm in Ashner test was 30 beat/ min), also there were paroxysms of atrial flutter and atrial fibrillation on the background of absent any autonomic control, which was direct reason of lethal outcome.

And what is situation in the sinoatrial heart node? We succeeded to receive the autopsy material of the sinus node in healthy man (Fig.5.1) and patient with ACN in life (Fig.5.2). Here we presented data of the electronic histology of the pacemaker cells without ACN and with this syndrome.

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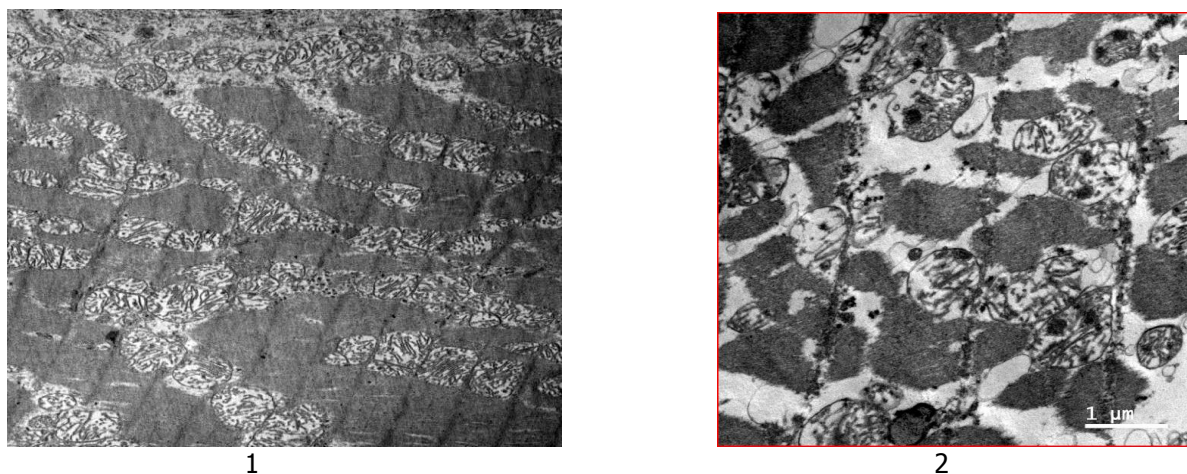
[**Fig.5**.] Here are electronic histological structures of the pacemaker cells in the sinoatrial heart node in healthy man, which perished from non cardiological cause (left picture) and in patient with autonomic cardioneuropathy in life (right picture) on the background of the coronary artery disease and with the arrhythmias of the heart and the sinoatrial blockade of 2 type 2-3 degree.

5.1. Here are the histology of P-cells in sinus node of the healthy man. Here are normal tissue structure with good expressive mitochondries and crists.

5.2. Here are histology of autopsied tissues patient after lethal outcome from coronary artery disease with heart failure 3-4 FC and angina pectoris 4FC, sequels of the acute myocardial infarct. At the clinical status here was ACN. Here are structure breaches in destruction of crists and mitochondries, fccomulations of fucsin, potassium, vacuoles – these are dystrophy.

Conclusion.

1.The loss of the autonomic sympathetic and parasympathetic control of the heart rhythm is the serious deterioration of the patient status. It is syndrome of the autonomic cardioneuropathy, which testimonies about high risk of death.

2. Recently ACN may be defined by high-resolution RCG with very exact HRV analysis. It signs: HRV stabilization and absent of any reactions to stimuli.

3. The pathogenesis of ACN is by result of morphological and functionl breaches of the P-cells of sinoatrial heart node or the result of circulation breaches and dystrophy in SN.

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P12 HYPERTENSION DISEASE, HEART RATE VARIABILITY, SOME CLINICAL POSSIBILITIES

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Abstract.
Presented here the results of observation and investigation of patients with the hypertension disease (HD). By high resolution rhythmocardiography for the heart rate variability analysis at stages of HD. At the HD 1 stage were defined prevalence of the sympathetic wave structure and the symptom of the beginning of remodeling of heart. At the 2 stage of HD were registered decrease of the HRV waves and prevalence of the humoral-metabolic influence on the sinus node pacemaker cells. At the HD of 3 stage was registered the most heavy disease and autonomic cardioneuropathy. Also there was defined the possibilities of the HRV analysis for evaluation of the autonomic activity of drugs in the clinical pharmacology.

Key words; Heart rate variability, hypertension disease

The purpose of this part of the clinical neurocardiological researches was evaluation of the heart rate variability (HRV) in 1281 patients (pts) with hypertension disease of 1, 2 and 3 stages and autonomic changes at these stages. Actual of these researches was connected to disparity between stages and the level of pressure blood, peculiarity at the beginning of the hypertension disease (HD) [1-5]. At the HD HRV analysis also was useful for intranosological diagnosis between stages (st) of HD. During 3-4 years named pts were at the prospective observation. All pts were studying by RCG a number times. There were selected by special criterions 54 pts with HD 1st., 61 pts with HD st. and 63 with HD 3 st. 48 healthy men (Fig.1) were control group (gr.C). The main criterion of the exclusion of pts were the noncardiological diseases, because its can change the results of HRV researches. RCG was the high resolution method and any pathology may have reflection in HRV analysis [2, 4]. HD 1 st. was characterized as wave structure with predominant sympathetic fluctuations (Fig. 2). On the Rcg HD1 there were high-amplitude m-waves (σm=0,023±0,01 sec. vs 0,025±0,01 in gr.C.sec.) and the most spectral density in low frequency diapason (LF%=50,72± 16,14% vs 19,584±10,1% in gr.C, p<0,001). Also the time of the maximal reaction achievement increased. The beginning of the left heart ventricle breach was as increase of the time reaction in stimulant orthostatic test (tAB=21,1±4,2 sec. vs 15,2±2,2 sec. in gr.C, p<0,01). This testimonies about some weakness of the myocardium and this HRV-symptom may be registered earlier clinical and ECG symptoms. In the subsequently the amplitude of m-waves decreased and at the HD 2 st. (Fig. 3) σm=0,011±0,005 sec. vs 0,025±0,01 sec in gr.C, p<0,01). Also other HRV indices decreased too. The amplitudes of parasympathetic and humoral-metabolic HRV waves were: σs=0,008±0,003 sec. and σl=0,015±0,006 sec. vs σs=0,046±0,017 and σl=0,028±0,011sec. in gr.C, p<0,05-0,01). In this case these breaches connected to myocardial morphological and functional changes, so far as HRV waves have different physiology. HD 3 st. (Fig. 4) characterized as HRV decrease and even the stabilization. Also reactions in stimulant tests absent and it correspond to the autonomic cardioneuropathy (ACN) and more heavier HD. In this cases HRV signs calculate in units milliseconds. For example, SDNN, σl, σm, σs at the pt with HD 3 st with breaches of the heart and other organs and systems, may be 0,009±0,001, 0,005±0,002, 0,007±0,002, 0,009±0,002 millise-conds, correspondingly. In the such pts there are predominant regulative influence- humoral-metabolic environment, reactions to stimuli in tests are absent. Except this, in some cases HRV breaches allow to surmise the symptomatic genesis of HD. Besides were made out researches on evaluation of autonomic action of antihypertensive medicines - β-adrenoblockers, inhibitors of angiotensin receptors and calcium antagonists. It was proved, that the β-adrenoblockers aren't blocked β-adrenoreceptors of the presynaptic membranes. Its increase the number of quantums of acetylcholine to the synaptic chink and this throw out decrease blood pressure. For example, before and after one dose of β-adrenoblocker anape HRV sympathetic and parasympathetic data were: before σs=0,005±0,002 sec. and after 0,013±0,001sec., p<0,05, σm=0,015±0,001 sec. and 0,009±0,001 sec, p < 0,05, correspond-dingly). Also, spectral shares were HF%=11,06±5,1% before and after 22,85±10,9%, p<0,05; and spectral sympathetic share were 27,46±8,7% and 21,21±4,1% before and after anape. But on the whole HRV allows to chose

antihypertensive medicines and value it's effectiveness for personal therapy. Thus, the high-resolution RCG with exact analysis of HRV is useful for researches of the autonomic action of the every medicine, for the evaluation of the negative effects. Without such researches the medicines, specially the new medicines, cannot applicable for the treatment.

Conclusion.
1. In these researches were exposed HRV peculiarities at the stages of hypertension disease in increase of HRV- signs of the sympathetic regulative influence on the pacemaker activity of the heart rhythm at the 1 stage, in decrease of amplitudes of all HRV waves at the 2 stage and autonomic cardioneuropathy at the 3 stage of this disease.
2. By HRV analysis in the stimulant tests there were exposed the early symptome of the hypertrophy of the left heart ventricle in aspect of the prolongation of time HRV recovery after stimulant active orthostatic test, connecting with braches in the heart myocardium.
3. Rhytmocardiography is the adequate and high sensitive diagnostic method of evaluation of the autonomic status in patients with hypertention disease and on the background HRV data it possible to expose the clinical form, stage of this disease in intranosological diagnosis. In a same cases complex autonomic symptoms may be define the diagnostic direction.
4. High resolution rhythmocardiography is adequate and informative method for researches of the autonomic activity of the medicines.

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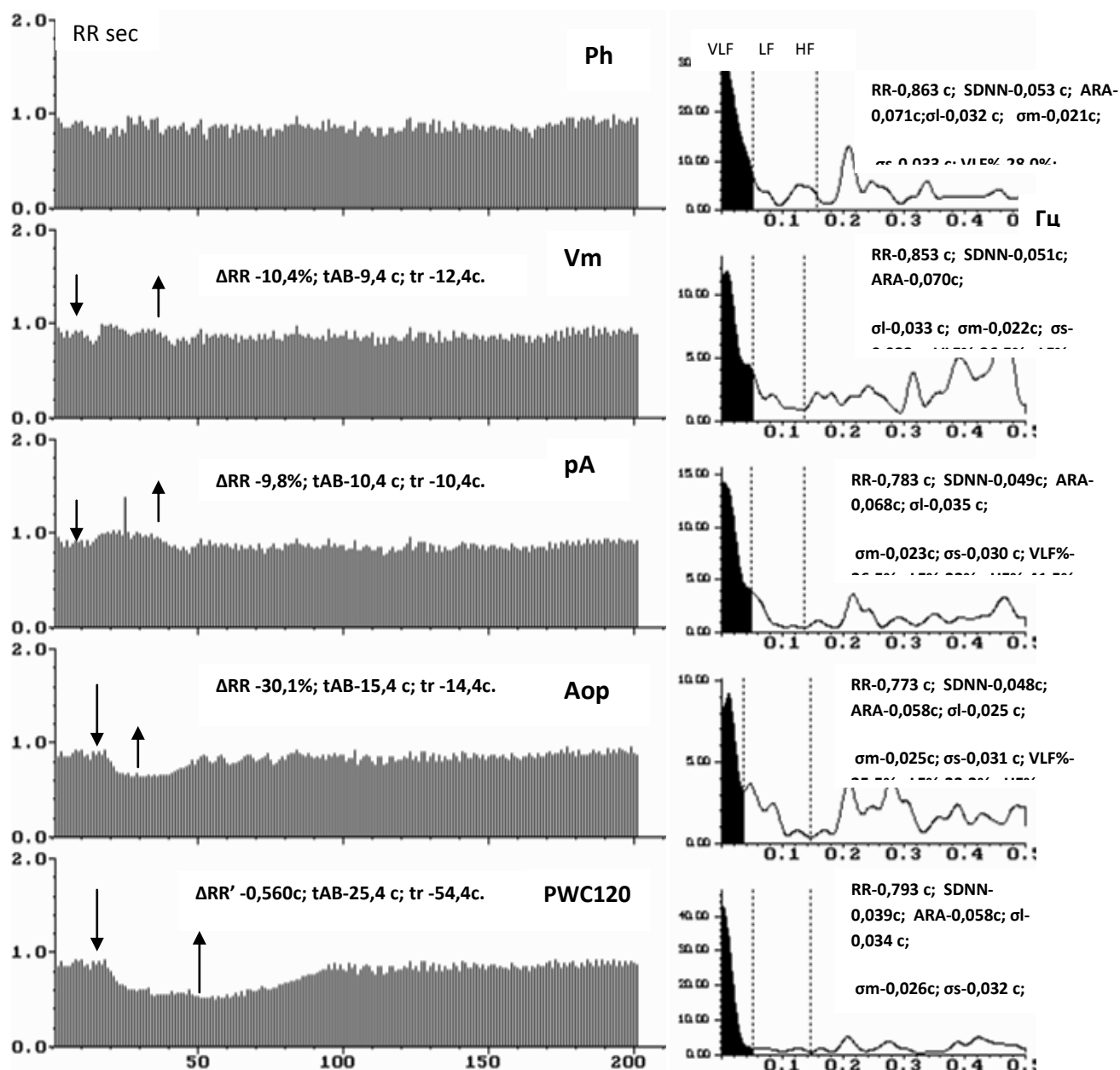
Fig.1. Rcgs and spectrograms, average indices of HRV in healthy man in lay posture (Ph), Valsalva-Burcer maneouver (Vm), in Ashner test (pA), Active orthostatic test (Aop), in test with load (PWC120). Statistic HRV indices: RR- average interval; SDNN- standard deviation of all HRV waves; σl- humoral-metabolic waves; σm-sympathetic waves ; σs- parasympathetic waves. Spectral indices of the influences correlation regulative factors in the sinus node: VLF% -share of humoral-metabolic influence in the sinus node; LF%- share of sympathetic regulation in the sinus node; HF%- share of sympathetic regulation in the sinus node correspondingly to Total spectrum. Vertical needles show beginning and end of the period of stimuli in tests. Indices of the stimulant period: ΔRR- maximal reaction; tab- time of achivemnt this reaction; tr – time of recovery after stimuli in tests.
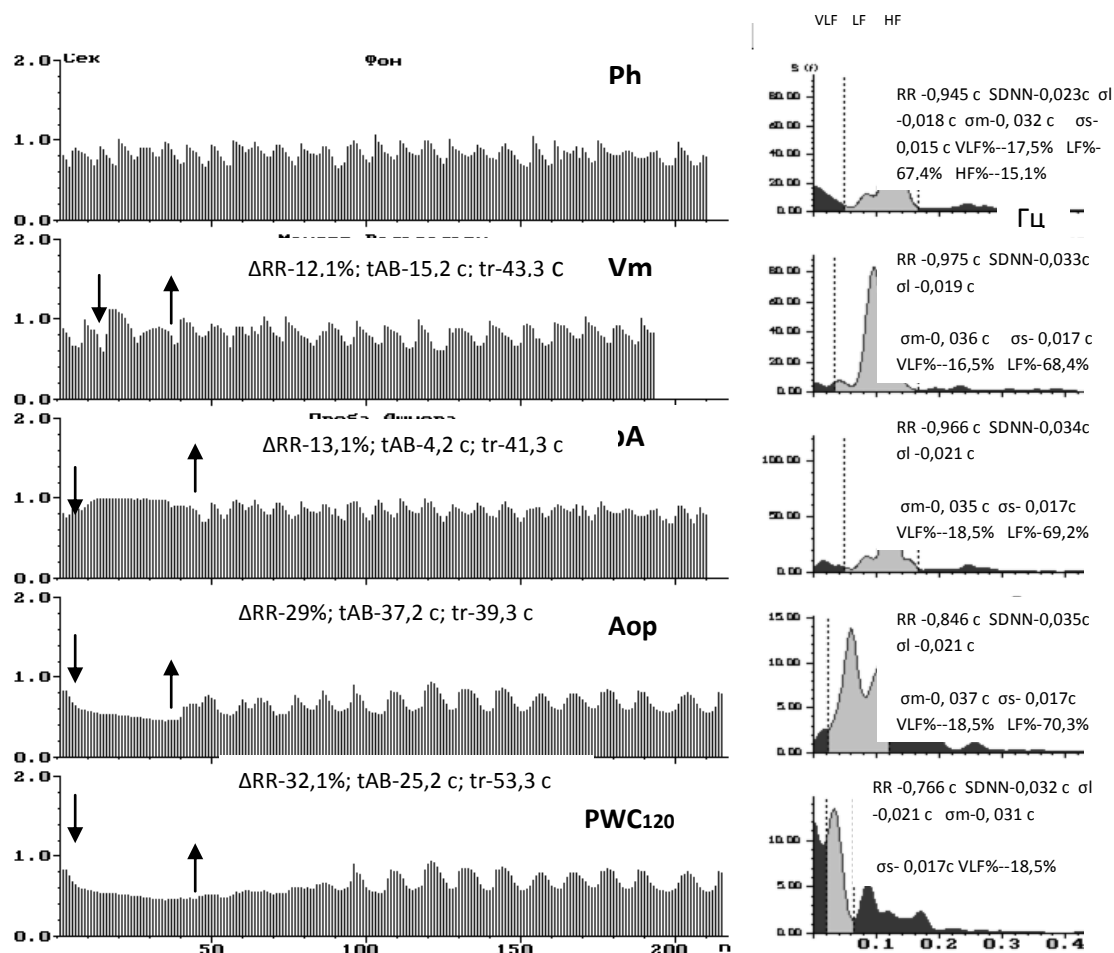
(Fig.2) Rhythmocardiograms, spectrograms and HRV- indices in patient with hypertension disease 1 st. Here is the predominant sympathetic waves of the most amplitude (σm) and most sympathetic share in spectral analysis (LF%) in diapason 0,11-0, 14 Hz. Here are normal reactions in tests, but in Aop in passage period the time of the postural reaction is prolonged – more 37,2 secondss correspondingly to normal 15seconds, because here is beginning of the hypertrophy of the left heart ventricle.
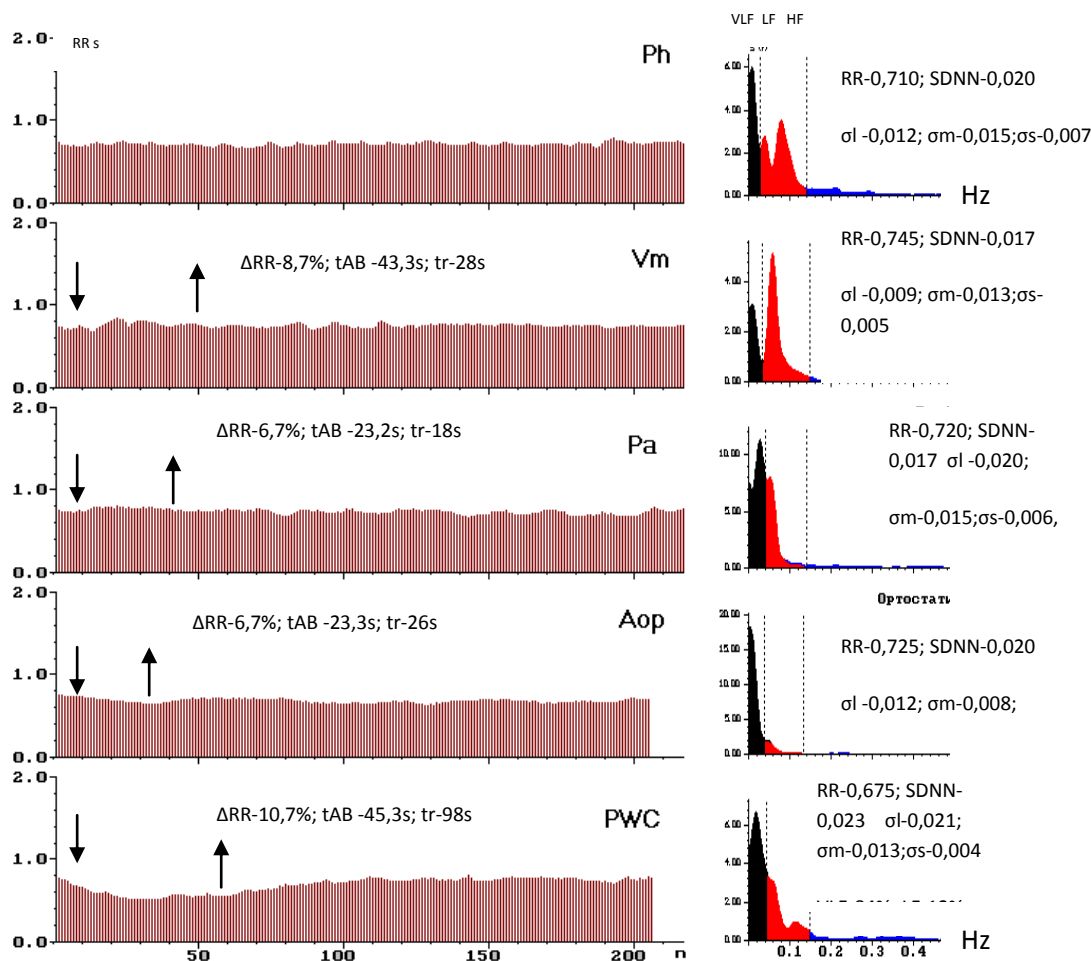
Ph

RR-0,710; SDNN-0,020

σl -0,012; σm-0,015;σs-0,007

Hz

ΔRR-8,7%; tAB -43,3s; tr-28s

Vm

RR-0,745; SDNN-0,017

σl -0,009; σm-0,013;σs-0,005

ΔRR-6,7%; tAB -23,2s; tr-18s

Pa

RR-0,720; SDNN-0,017 σl -0,020;

σm-0,015;σs-0,006,

ΔRR-6,7%; tAB -23,3s; tr-26s

Aop

Ортостат.

RR-0,725; SDNN-0,020

σl -0,012; σm-0,008;

ΔRR-10,7%; tAB -45,3s; tr-98s

PWC

RR-0,675; SDNN-0,023 σl-0,021;

σm-0,013;σs-0,004

VLF LF HF

Hz

(Fig.3) Rhythmocardiograms, spectrograms and HRV-indices of patient with hypertension disease of 2 st. Here are the decrease of the RCG at all. But spectral correlation shows the maximal share of the humoral-metabolic influence in rhythm regulation, but amplitudes of all HRV waves and at the all positions here is minimal. All reactions to stimuli in tests (ΔRR) decreased too, enlarged the time of re3action and recovery after stimuli. Complex of these symptoms testimonies, that there is the remodeling of the left ventricle in myocardium and other heart tissues.
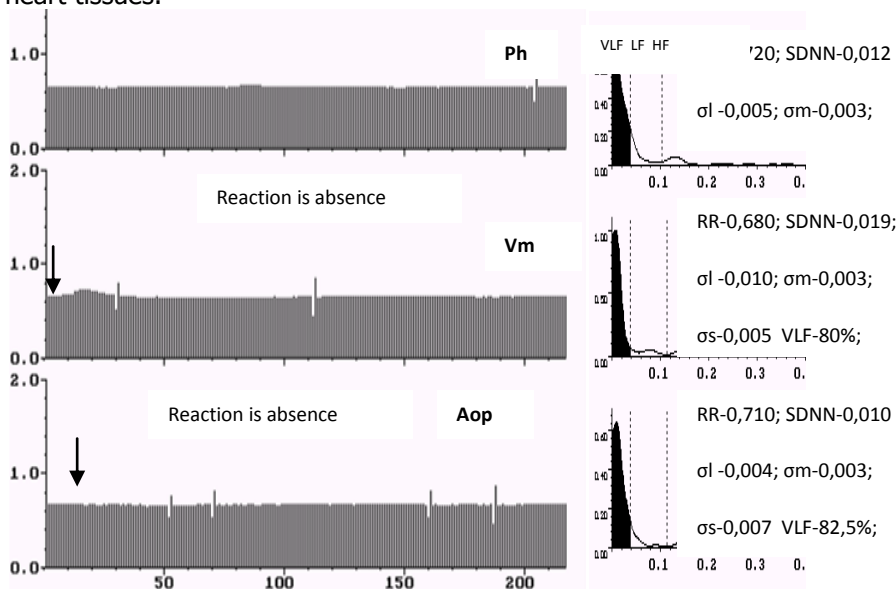
Ph

VLF LF HF

'20; SDNN-0,012

σl -0,005; σm-0,003;

Reaction is absence

Vm

RR-0,680; SDNN-0,019;

σl -0,010; σm-0,003;

σs-0,005 VLF-80%;

Reaction is absence

Aop

RR-0,710; SDNN-0,010

σl -0,004; σm-0,003;

σs-0,007 VLF-82,5%;

(Fig. 4) Rhythmocardiograms, spectrograms and HRV-indices of patient with hypertension disease of 3 st. Here are the extremely low the amplitude of all waves of the HRV. HRV is stabilized. Reactions to all stimuli are absence. These symptoms are testinony about autonomic cardioneuropathy with heavy disease and the high risk of the lethal outcome.

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P13 AUTONOMIC DEREGULATION OF SINUS HEART NODE PACEMAKER ACTIVITY AT OCCUPATIONAL DISEASES

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Abstract.
Presented here results of studying of regulation cardiological breaches in patients (pts) with occupational diseases. There were investigations of 417 pts with syndrome Reyno, 578 with pneumoconiosis and 215 patients with chronic intoxication of weld aerosol intoxication by the high-resolution method rhythmocardiography for analysis of heart rate variability (HRV). HRV data were compared with standard data of cardiological investigation. Here was exposed in all patients deregulation of pacemaker activity in sinus heart node, correlated with echocardiography data. HRV data of patients with occupational diseases connect to pathogenesis of occupational diseases.

Key words: heart rate variability, occupational diseases, cardiovascular pathology

Presented here results of studying of SN regulation at the cardiological breaches in patients (pts) with occupational diseases (OD). The autonomic nerven system breaches were researched by the heart rate variability (HRV) analysis   by help of the high-resolution hardware-software complex CAP-RC-01-"Micor" for rhythmocardiography (RCG). Actuality of these researches was expounded by the high frequency of cardiovascular diseases (CVD), priority, invalidization and lethal outcome, caused by its [1-3]. In the workers, working in conditions of the professional risk had proved the increase disposition to CVD [Mironova, 2000]. In pts with OD at the standard cardiological investigation to prove etiological junction with professional risk complicatedly because absence of the specific symptoms of this CVD complication, specially at the nosological CVD pathology, because in anamnesis OD and CVD have no certain successively. The borders between OD and CVD is absent in that part of both diseases, which associated with non occupational pathology. There was supposed, that the differential symptoms may be in the early cardiovascular deregulations at the OD.

The purpose of this studying was research of the autonomic deregulation of the sinoatrial heart node at the OD in pts with local syndrome Reyno (SR), pneumoconiosis (PC) and at the chronic intoxication by weld aerosol (FMnI) by help of heart rate variability (HRV) analysis and pacemaker activity of the sinoatrial heart node (SN). There were investigated 417 pts with SR, 378 pts with PC, 215 pts with FMnI. 47 healthy men without any PR compiled the control group (C). This research was open, randomized, controled. The diagnosis of OD was corrected and evaluated, as the beginning stage of OD. The conditions of this work were from 3.1 till 3.3 classis, and the continuation of action in these conditions was 14,43±5,12 years. All pts investigated by standard cardiological methods (ECG, HM, monitoring of the BP, EchoCG, laboratory analysis). Also in every pt was investigated HRV by high-resolution complex apparatus program CAP-RC-01-"Micor" (APC). There were evaluation average HRV indices: average RR-interval, standard deviation of all intervals, average quadratic dispersion sympathetic HRV waves-σm, parasympathetic waves – σs and humoral-metabolic HRV-waves – σl. The last is peculiarities of our analysis, because other researchers aren't count up it. The humoral metabolic obligatory influences on formation of the slow potential of pacemaker cells action in SN. It is classical physiology. For the evaluation of the degree of influence of every regulative factors there was used spectral analysis with Fast Furier Transformation and spectral windows Hamming and Parsen – humoral-metabolic factor – VLF%, sympathetic influence – LF%, parasympathetic factor- HF%, correspondingly to total spectrum in 100%.

In mathematical cultivation of HRV data was used non parametric criterion Z, analogue criterion t for large volume of data. Correlative analysis made out by method Spirmen with program SPSS 12. For registration and analysis RCG was used APC of high –resolution (discritization of electrosignal - 1000±3 Hz) in posture lie (Ph) and in 4 stimulant tests-Valsalva-Burcer (Vm), Ashner (pA), active orthostatic (Aop), test with load (PWC120). At the periods of stimulation determined maximal reaction of HRV to stimuli – ΔRR, time of this reaction- tAB, time of recovery after stimuli –tr.

At the RCG-investigation in pts OD there were registered deregulations, as predictors of the CVD complication. The wave structures of the heart rhythm had the peculiarities for every forms of the OD, connecting to pathogenesis these diseases.

Results of researches and its consideration. Except symptoms of OD in selected pts at the special criterions there were exposed the nonsyndrom breaches of the heart by Doppler echoCG. There were defined in pts with OD different types of geometric changes of the heart. In 22 pts with SR were defined the normal heart configuration and in 14 pts were some signs of concentric changes of the left ventricle form, in 12 pts was concentric hypertrophy, in 2 and 1 pts were hypertrophy of a partition between ventricles. In 27 pts with PC was the normal geometry of the heart, in 14 pts was the concentric changes of the left ventricle, in 3 pts was concentric hypertrophy. In 32 pts with FMnI was normal configuration of the heart, in 7 pts were exposed concentric, isolation hypertrophy of the left heart ventricle and of a partition between heart ventricles. These breaches were isolated and correlated with breaches of HRV in sinus node (SN) significant (r=0,515-0,574). Correspondingly to monitoring of ECG in pts with SR, PC, FMnI arrhythmias of heart were frequently in comparison to healthy control (p<0,05-0, 001). This suppose in pts with OD the cardiopathy on the background of OD.

By the RCG investigation in all pts were exposed deregulations of pacemaker activity in heart SN. In subsequent studying all pts with OD. There were selected pts without any internal diseases, because its can change HRV results. Selected pts were divided in 2 groups – with signs of changes heart configuration (1) and without these symptoms of the heart remodeling.(2). Results of the comparison between groups presented in tables 1 and 2.

Table 1. Results of comparison HRV indices in time-domain in pts with normal heart configuration (SR1, PC1, FMnI 1) and with symptoms of the heart remodeling (SR2, PC2, FMnI 2)

Compared groups in sec	**SDNN**, s –HRV-sign of middle standard deviation of all waves amplitudes	σs, s- middle quadratic dispersion of amplitude of parasympathetic HRV waves	σm,s- middle quadratic dispersion of amplitude of sympathetic HRV waves	σl s- middle quadratic dispersion of amplitude of humoral-metabolic HRV waves
Control,n-48	0.054±0.011	0.039±0.02	0.024±0.011	0.026±0.011
SR1(n-22)	0.043±0.01*	0.022±0.011**	0.017±0.010*	0.023±0.010
SR2(n-34)	0.025±0.010**	0.007±0.002**	0.011±0.009**	0.021±0.01*
PC1(n-27)	0.042±0.010*	0.028±0.011**	0.017±0.011*	0.023±0.012*
PC2 (n-25)	0.027±0.012**	0.007±0.002**	0.011±0.002**	0.018±0.011**
FMnI1 (n-32)	0.031±0.009**	0.020±0.012**	0.012±0.004**	0.020±0.009*
FMnI2 (n-26)	0.012±0.004**	0.005±0.002**	0.004±0.001**	0.012±0.004**

*p<0.05-0.01; **p<0.001*

Table 2. Results of comparison HRV spectral indices in pts with normal heart configuration (SR1, PC1, FMnI 1) and with symptoms of the heart remodeling (SR2, PC2, FMnI 2)

Compared groups	HRV sign of spectral share of humoral-metabolic influence in SN -VLF %	HRV sign of spectral share of sympathetic regulation in SN- LF %	HRV sign of spectral share of parasympathetic regulation in SN- HF %
Control, n-48	21,73±12,81	23,76±3.6	56,005±18,01
SR1(n-22)	39,12±13,20**	22,26±12,97	32,67±14,65**
SR2(n-34)	59,73±17,31**	29,104±11,94*	11,16±10,58**
PC1(n-27)	54,32±15,13**	20,43±7,35	25,25±13,25**
PC2(n-25)	66,56±10,72**	17,85±6,12*	15,59±8,71**
FMnI1 (n-32)	44,47±11,12**	18,56±9,77*	36,98±15,33**
FMnI 2 (n-26)	75,44±12,35**	11,39±4,64**	13,16±7,54**

*Примечание: * p<0.05-0.01; **p<0.001*

Table 1 and 2 data show, that SN deregulation associated with changes configuration of the heart simultaneously, not only, but in the degree of deviation correspondingly normal. It is the most significant at the significant heart remodeling. And at the absent symptoms of the heart remodeling here are authentic HRV signs of deregulation in SN correspondingly to control group, because the breaches of rhythm regulation form early than morphological pathology. Results in table1 demonstrated in a number of HRV signs breaches in regulation of the SN, and in significant changes of all HRV indices in groups 2 with symptoms of the remodeling. In the same groups 1 and 2

SR, PC, FMnI there were exposed reduction of the reactions in all tests-ΔRR, corresponding to control, independently from intensify and direction of stimulant tests in the same pts with SR, PC, FMnI. (ΔRRVm=4,3±0,843 vs 12,2±2,4%; ΔRRAop=21,1±3,3 vs 30,4±1,9 % при ПЗ и в К;ΔRRPWC=19,2±2,1vs 39,3±5,4% ПЗ и К; ΔRRpA= 4.5±1,8 vs 13,1±1,5% in pts with OD and control; p< 0,01-0,001). The time of restoration after stimuli (tr) increased- (trPWC=102,4±23,3 vs 56,8±10,7 at OD and control; p<0,01-0,001), special at the symptoms of the heart remodeling. This testimonies about the heart failure and manifested a passage of the rhythm regulation from fast and adequate sympathetic and parasympathetic autonomic level to low humoral-metabolic level. (Таблица 2). Here is spectral correlation shows the most share in very low frequency diapason (VLF%), p<0,001, connecting to the humoral metabolic influence in SN.

Spectral correlation of influences regulative factors in SN shown, that in spite of absent the morphological` remodeling in the heart there were symptoms of deregulation in SN. Main regulative factors become the humoral-metabolic medium, unadequate and non effective, at the expense of autonomic system. The pathogenesis of these breaches is different.

At the PC here are perivascular and peribronchial fibrosis in pulmonary parenchima and, as reason, decrease the blood oxygenic, pulmonary hypertension develops, and hypoxia in heart tissues.

The main pathogenesis of the heart remodeling is breaches of balance between heart contractions and metabolic processes in myocardium and epicardium connected to chronic influences of vibration in prophessional conditions. At the manganese dioxide and chronic hydrogenous phtor intoxication breach of the piridoxalphosfate and synthesis of the noradrenaline, as mediator of the sympathetic autonomic department. Sympathetic system is the main regulator of the tropic function.
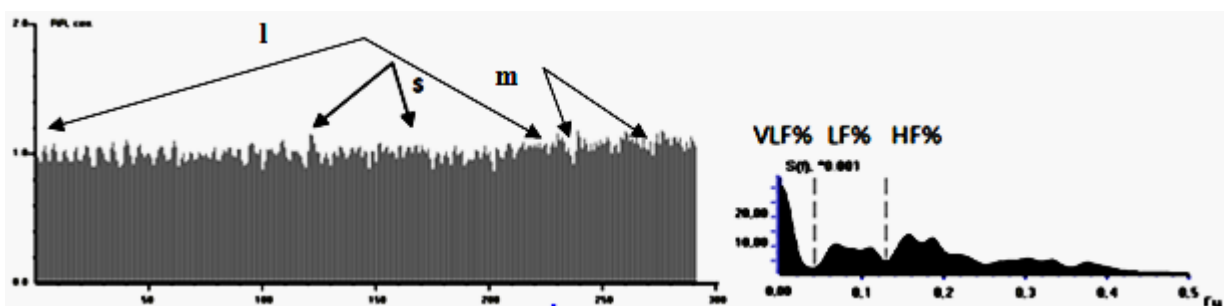
Fig.1. On the rhythmocardiogram and spectrogram of the healthy man presented three types HRV of HRV. Here are parasympathetic (s), sympathetic (m) and humoral-metabolic (l) waves of the regulation of SN. On the spectrogram the most spectral power density is the parasympathetic (HF%), and the lowest part spectrum is the humoral-metabolic (VLF%) influence..
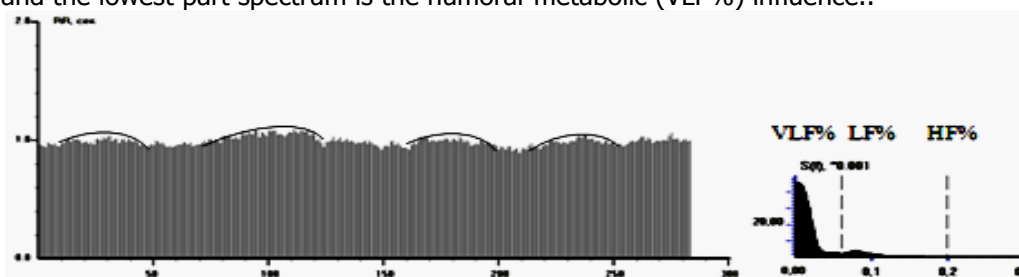
Fig. 2. Rcg and spectrogram of patient with pneumofibrosis. There were on the background of re duction HRV the very low frequency wave (marked by arcs)- l and with the most part of spectrum is VLF%, which pathogenetically connects with fibrosis in pulmonal tissues.
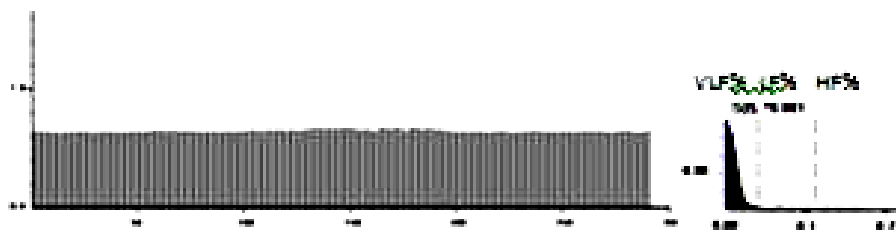
Fig.3. Rcg and spectrogram of patient with Reyno syndrome. Here is autonomic cardioneuro-pathy -HRV stabilization on the tachycardia (100 beat/ sec.). On the spectrogram here is the most part of density spectrum is in very low frequency diapason (VLF%).
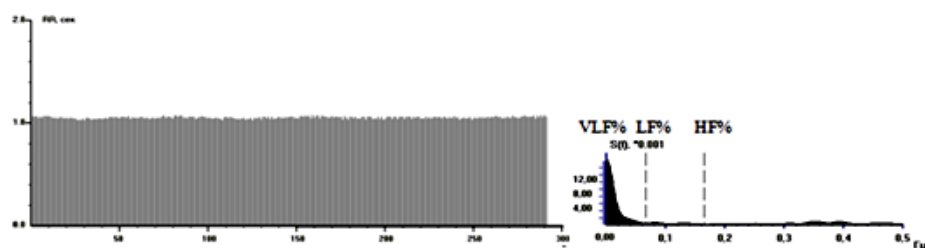
Fig. 4. Rcg and spectrogram of patient with FMn intoxication. Here is autonomic cardioneuro-
pathy - HRV stabilization but on the background of bradycardia (60 beat/ sec.). This
connects with breaches of the noradrenaline synthesis. On the spectrogram here is
the most part of density spectrum is in very low frequency diapason (VLF%).

Conclusion:

1. Rhythmocardiography is adequate and informative method of the regulative breaches diagnosis at the cardiovascular complications in patients with occupational diseases.
2. The results of high-resolution HRV analysis at time-domain and frequency-domain testimony about the peculiarities of the cardiovascular complications, connected with pathogenesis of the occupational diseases.

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P14 Circadian chronology and number of deaths from acute coronary syndrome and acute myocardial infarction (a fragment of the study "RACSMI-Uz")

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Objective: To evaluate the deaths from acute myocardial infarction (AMI) and acute coronary syndrome (ACS) depending on the daily chronology and age-gender characteristics in one of the districts of Tashkent for 2015 (a fragment of the study "RACSMI-Uz").

Material and Methods: Over 32,000 emergency medical signal sheets were examined, of which 620 patients were diagnosed with ACS / MI. Of the 620 selected, in 92 - were recorded lethal cases. Then 92 death cases were distributed in chronological order. The data were considered reliable at p <0.05.

Results: The mean age of the deceased was 57,7±8,5 (from 30 to 70) years. Amongthedeceased 63 (68.5%) weremenand 29 (31.5%) – women. The mean age of the deceased men was 57,5±8,6 (from 30 to 70) years, and women - 58,2±8,2 (from 35 to 70) years. The analysis of signal sheets of the deceased patients into daily chronological sequence installed the greatest peak of death occurred during from 8 am to noon from with they died 27 (29.4%) patients. In this case hourly component was represented by 5, 7, 9 and 6 dead, respectively. Also in the daily rhythm can be considered critical intervals from noon to 4 pm and from 8 pm until midnight,on which it was necessary on 16 died, accordingly.

When conducting a correlation-regression estimate between the age of death patients and the time of day what is the dependence was not found (p=0,856; r=0,019; t=0,181).

Conclusion: Death rate from ACS/AMI is the prerogative of men, at the same time, the age of men is younger than that of women. The most critical time is the interval from 8 am to noon, which accounts about one-third of all deaths from ACS/AMI. Nevertheless, there is no correlation between the age of the deceased and the time of day.

P15 Low systolic arterial pressure in the evaluation of the frequency of registration of heart rhythm disturbances and ST-displacement according to the data of ambulance medical care (Fragment of the study RACSMI-Uz)

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Purpose: To estimate the incidence of heart rhythm disturbances (HRD) in relation to the ST-segment displacement in patients with low blood pressure (BP) according to emergency medical care (EMC) according to the data of study "RACSMI-Uz").

Material and methods: Over 32,000 signal sheets were surveyed in 2015, of which 620 cases were suspected for acute coronary syndrome (ACS) ormyocardial infarction (AMI). Of the 620 selected cases, systolic blood pressure (SBP) <100 mm Hg was recorded in 55 (8.9%) (mean SBP = 85.64 ± 17.29 mmHg).

Results: It was found that out of 55 respondents, in 14 (25.5%) cases ST-segment displacement was recorded (7 - with ST-elevation and 7 - with ST-depression); In 24 (43.6%) cases, various HRDs were recorded on the ECG (3 with paroxysmal atrial fibrillation, 2 with paroxysms of ventricular tachycardia and 19 with paroxysms of supraventricular tachycardia).

The average SBP in individuals with HRDs was 88.75 ± 10.35 mm Hg and the mean heart rate = 147.10 ± 32.51beats/min, while for respondents without HRDs, similar indicators were 83.23 ± 21.04 mm Hg. and 78.22 ± 11.94 beats/min (p <0.001).

Analysis of ST- displacement showed that in most patients with HRDs (5 out of 7 cases) was recorded ST-depression and ST-elevation was recorded only in 1 case, while in patients without HRDs more often ST-elevation took place, rather than a decrease of the ST segment (6 vs 2 cases, respectively).

Conclusion: in patients with suspicion of ACS / AMI, a low systolic blood pressure is observed in 8.9% of cases. A decrease in systolic blood pressure in 25.5% of cases is accompanied by a displacement of the ST segment and in 43.6% by various heart rhythm disturbances. The combination of low blood pressure and cardiac arrhythmias in most cases is accompanied by ST-depression.

P16 Arterial hypertension and its effects in estimation of clinical-laboratory data in acute coronary syndrome and acute myocardial infarction (according to register "RACSMI-Uz")

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Purpose: To conduct a comparative analysis of clinical and laboratory indicators in patients with acute coronary syndrome (ACS) or myocardial infarction (AMI), depending on the presence or absence of arterial hypertension (AH) (the data of study "RACSMI-Uz").

Material and methods: The material of the study was the database of hospitalized patients (according to emergency medical care or family polyclinics) or who died of this pathology (according to the forensic medical examination)during 1 (2015) year. For the evaluation of clinical parameters, two groups were identified: 1 group - 47 without AH (control group) and 2 patients - 385 people with AH of varying severity.

Results: Analysis of bad habits did not reveal significant differences between groups (all p> 0.05). Reliable, but somewhat paradoxical, differences were found in the assessment of blood lipid spectrum. Namely, the number of people with hypercholesterolemia was 1.5 times higher among patients 1gr. (without AH), which was confirmed by digital indicators in blood tests. Nevertheless, the mean level of triglycerides in patients without AH was 1.5 times lower than in the comparison group.

Analysis of the main ECG changes in ACS / AMI in the groups of patients revealed that for patients with AH the most typical are depression of the ST segment (35.6% in 2 gr.vs 25.5% in 1 gr., p = 0.228, $\chi 2$ = 1.455) and inversion of T-wave without ST-displacements (16.3% in 2gr, vs 8.5% in 1gr, p = 0.234, x2 = 1.418), while ST-elevation was lesser than in 15% of cases.

Conclusions: The lipid spectrum of patients with ACS / AMI comorbid with arterial hypertension was characterized by hypertriglyceridemia and relatively safe values of total cholesterol of the blood, while the ECG was more often recorded phenomena of depression of the ST segment and T-wave inversion, than ST-elevation.

P17 Ventricular extrasystole in the evaluation of chronotropic and angiographic indices in coronary heart disease

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Purpose: To make a comparative analysis of clinical angiographic (CAG) data in coronary heart disease (CHD) depending on the presence or absence of ventricular extrasystole (VE).

Material and methods: 75 patients with CHD were examined, mean age = 55.26 ± 10.16 years. All were conducted general clinical studies, CAG with stenting. The presence of VE was determined by daily monitoring of ECG (DM-ECG) with analysis of chronotropic indicators and calculation of circadian index (CI). Depending on the presence or absence of VE, 2 groups were randomized: 1gr. - 41 patients with VE and 2g. - 34 patients without VE.

Results: The groups were comparable in age, but in terms of gender in 1yr, women were 8.3% more. Chronotropic indicators of DM-ECG did not differ significantly. Nevertheless, in 1gr. the maximum HR was lower (by 6.5 beats / min), and the average nightly rate was higher (by 1.1 beats / min) than in 2g. In addition, in patients 1gr. was observed a relatively high QTc% (by 9.11%), which was probably due to the presence of VE in this group of patients. Analysis of CAG also did not reveal significant differences between groupshowever the length of atherosclerotic lesion in patients 1gr. was on 0.6mm lesser than in 2gr. (all p> 0.05)

Conclusion: The presence of VE in CHD is more often associated with female sex; on DM-ECG is characterized by a relatively high chronotropic activity at night and an extension of QTc%; on CAG - a relatively larger length of lesion of the coronary vessels; but all the revealed differences did not reach the level of authenticity.

P18 ECG-determined left ventricular hypertrophy and blood pressure: a closer look at possible significance

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Objectives: Over the past decade, appropriate investments in judicious evidence have been interchangeably rendered for every ECG-LVH definition; an abrupt twist of appearing achievement, researchers rest assured that predictive role of ECG-LVH for further cardiovascular complications grasping angina pectoris, myocardial infarction, stroke, congestive heart failure, sudden cardiac death is proved within much-vaunted clause, as it's a principle.

Methods: We executed EPOGH (n=300), used ECG-LVH criteria, adjusted Cornell voltage (Norman-Levy), clock-time-dependent method narrow-approach for ambulatory BP.

Results: That's why it's an elusive thing, but it's temporarily; conceptual reasoning should be applied to ECG-LVH designations comparison. The amendments embody the ripped tidings. Below we have adduced five notable challenges, highlighting the enriched outlets expressing facts from essential trials. This was one of the key issues, Cornell voltage bypassed Sokolow-Lyon voltage in LVH performance in both Korean men and women. What's more, NHANES III findings plunged into a deep well; though LVH is risk factor for cardiovascular disease independent of BP, we defined correlation of adjusted Cornell voltage with clinic SBP, DBP (r=0.374, r=0.410), home SBP, DBP (r=0.378, r=0.326), 24-hour SBP, DBP (r=0.470, r=0.373), day SBP, DBP (r=0.459, r=0.349), night SBP, DBP (r=0.430, r=0.351), p<0.001, 24-hour Hr (r=-0.157, p=0.007), day Hr (r=-0.167, p=0.004), night Hr (r=-0.121, p=0.038). Crucially, advent of decisive discretion concerning acquisition of ECG-LVH, echo-LVH great assets to stroke risk was hailed in CHS identity. The wisdom is tough, because it entails reasons; next queries received endorsements alleging that ECG-LVH, echo-LVH acclaimed divergent risks in patients with sudden cardiac arrest, mirroring two prominent warnings in turn conceding electrical vs. anatomic remodeling, underlining possibility of ECG-LVH detection with higher arrhythmogenic risk without anatomic echo-LVH.

Conclusions: It was serious to carry out accusatory discretion; we attempted to implement preliminary vetting of several assumptions, which yield insights into cardiovascular disease consequences, requiring assiduous research.

P19 FEATURES OF ELECTROPHYSIOLOGICAL REMODELING OF THE HEART IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDILITIS

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Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are often accompanied by heart damage.

Objective: to identify the comparative features of electrophysiological remodeling of myocardium in patients with RA and AS.

Materials and methods: the study included 149 patients: 1st group – 71 patients with RA, 2ndgroup – 78 patients with AS. All patients was conducted by vectorcardiographywith the definition the square loop P, QRS, T, as well as the maximum vector (MV), MV-azimuth and MV-ascent. To compare two independent groups on quantitative grounds used nonparametric methods and Mann-Whitney test. Data are shown as mean, minimum and maximum values.

Results: in the 1st group the mean value of the square loop P was 11.7 [3.92; 36.39] mV, square loop QRS – 901.5 [258.55; 2235] mV, square loop T – 51.7 [16.5; 149.88] mV, MV – 1589.26 [711; 3229] μv, MV-azimuth – 69.8 [20; 86]°, MV-ascent – 65.18 [34; 90]°. In the 2nd group the mean value of the square loop Pwas 34.6 [4.7; 91.6] mV, square loop QRS – 1418.05 [118.7; 4989.6] mV, square loop T – 70.66 [18.7; 149.88] mV, MV – 2290.6 [1152; 3833] μv, MV-azimuth – 53 [13; 94]°, MV-ascent– 51.3 [12; 92]°. When comparing both groups revealed that in the group of patients with ASsignificantly higher value of the squareloops P, QRS, T and the maximum of the vector (p<0.05) than in the group of patients withRA. It suggests that in patients with ankylosing spondylitis, in which echocardiography revealed no pathology, the electrophysiological remodeling of both atria and ventricles is more likely than in patients with rheumatoid arthritis.

Conclusion: the electrophysiological remodeling allows predicting the development of structural-geometric remodeling at the stage of the absence of significant changes in the myocardium. Early diagnosis allows for timely start prevention of remodeling in patients with rheumatologic diseases.

P20 Diagnosis and treatment of cardiac papillary fibroelastoma

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Introduction: Papillary fibroelastomas constitute 0.7-10% of all primary heart tumors which until recently were considered just as a pathoanatomical finding during intracavitary operations on the heart.

Aim: To show the possibilities of echocardiographic diagnosis and treatment of cardiac papillary fibroelastoma.

Material and methods: For this study, 14 patients (6 females, 8 males) aged 40-69 years (mean age 52.6 ± 2.6 years) with papillary fibroelastomas were considered. Echocardiography was helpful in detecting neoplasms of valvular structures and heart chambers in 12 (85.7%) and 2 (14.3%) patients respectively. In 10 (71.4%) patients, neoplasmspresented as solitary tumors. In 3 (21.4%) patients were observed a multifocal growth pattern of neoplasms. The tumor sizes ranged from 1.2x0.3 to 1.5x2.0 cm, in one observation the size of neoplasm attained 3.0x3.5 cm. During histological studies, it was noted that the cardiac papillary fibroelastomas originated from the epicardium, their roots continued into the avascular region. Tumor invasions into endocardial linings were not detected.

Results and discussion: An asymptomatic course of the disease or a combination of various nonspecific symptoms (arrhythmias, syncope, heartburn and embolic syndromes) were noted. A short history of the disease (average 12.9 ± 4.4 months) from initial visit to the doctor was common.

Electrocardiographic changes were absent in 2 (14.3%) patients. The remaining 12 patients showed various electrocardiographic changes: arrhythmias and conduction disorders. Intraoperative transesophageal echocardiography(TEE) was performed on 10 patients, the diagnosis was confirmed in 8 patients. The operations were performed by longitudinal median sternotomy. The volume of surgical intervention was based on the echocardiogram and TEE findings; however, it was finally determined during the course of the surgery. In most cases (83.3%), valve-preserving operations were performed. There was no hospital lethality.

Conclusion: Echocardiography are non-invasive method that help in identifying cardiac neoplasms. Minimal volume of surgical intervention like isolated removal of papillary fibroelastomas is recommended.

P21 ALGORITAM OF ATRIAL FIBRILLATION IN PATIENTS WITH STROKE

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Abstract

Detection of paroxysmal atrial fibrillation is important for optimal prevention of secondary stroke. In diagnosis of AF, it should be kept in mind that standard ECG is not a method of choice. An insertable cardiac monitor (ICM) automatically provides non-stop long-term ECG recording with very high sensitivity and specificity for PAF detection. A retrospective study was conducted at the Neurological Clinic of the University Clinical Center of the Republic of Srpska in Banja Luka. Of the 200 patients with recent brain infarction, newly detected AF was present in 12 patients. In the population of the patient we investigated, there was insufficient attention toward atrial fibrillation. Atrial fibrillation is often diagnosed for the first time only after brain infarction. Atrial fibrillation in this study was not adequately treated in primary prevention of the stroke.

Key words: Fibrillatio atriorum, infarction of cerebri, ECG, ICM, antiplatelet therapy, anticoagulants.

INTRODUCTION

Detection of paroxysmal atrial fibrillation (pAF) is important for optimal secondary stroke prevention. [1]. Many studies have shown increased rates of mortality in ischemic stroke in patients with AF. The prevalence of AF increases with age.

Although older age could explain the increased mortality rate in patients with AF, but the effects of larger lesions, more severe stroke or especially AF on the improvement process should be discussed. The effect of AF on neurological and functional results and the length of hospitalisation is not defined obviously [2].

Strokes due to atrial fibrillation are common and frequently devastating (70 to 80% of patients die or become disabled), yet they are largely preventable with anticoagulant therapy (64% reduction in the risk of stroke and 25% reduction in mortality). However, because atrial fibrillation is often intermittent and asymptomatic, it can be a silent risk factor that easily evades detection.

Since patients with stroke or transient ischemic attack (TIA) due to atrial fibrillation are facing a high annual risk of repeated stroke, strategies to improve the detection and treatment of atrial fibrillation promise to reduce the severity of recurrent strokes. In the absence of atrial fibrillation, the standard treatment of secondary stroke prevention is antiagregation therapy. However, when atrial fibrillation is present, antiaggregation therapy is only partially effective (22% reduction in risk, compared to placebo), and anticoagulation therapy is recommended as a substitute (39% to 63% reduction in risk of stroke compared to antiagregation therapy) .

Undiagnosed atrial fibrillation is often suspected as the cause of many cryptogenic strokes, but anticoagulation is not recommended unless atrial fibrillation has been documented. [3]. About 10% of patients with acute IM have first time detected AF.

Additionally, in 11% of patients,an AF is determined with continuous monitoring of heart rhythm in the period of one month after discharge from the hospital. Longer heart rate monitoring (up to 6 months) did not further increase the number of newly diagnosed patients.

In AF diagnosis, it should be kept in mind that routine ECG is not a method of choice. It is necessary to apply ECG holter and keep in mind that the longer the monitoring is, the greater the percentage of diagnosed AF diagnosis would be.

It is recommended that the patient should be wearing an holter ECG for more than 24 hours. It is preferred that the patient wears the holter ECG from 48 to 72 hours.

According to some authors, if ECG is monitored shorter, it will be 7.7% of AF patients, and if monitoring is longer, up to 23.7% of AF patients will be reached. It is particularly important that patients who have experienced IM or TIA have a well-conducted diagnosis in order to determine the existence of AF. Longer monitoring of the above is achieved with the use of a loop recorder that is implanted subcutaneously and records the ECG for several months.

An insertable cardiac monitor (ICM) automatically provides non-stop long-term ECG recording with very high sensitivity and specificity for PAF detection. Studies using ICM have suggested a detection rate of approximately 25 % [4].

THE OBJECTIVE OF RESEARCH
Affirmation of the treatment of atrial fibrillation in patients with a recent brain infarction.

MATERIAL AND METHODS
In the period from 01.06.2015 to 01.09.2016, we analyzed 200 patients with stroke. All patients were treated at the Neurological Clinic of the University Clinical Center of the Republic of Srpska in Banja Luka. Patients were selected by random selection.

RESULTS
We had 154 patients with brain infarction and 46 patients with various types of intracranial hemorrhage (intracerbial hematomas, subarachnoidal haemorrhages, subdural hematomas).
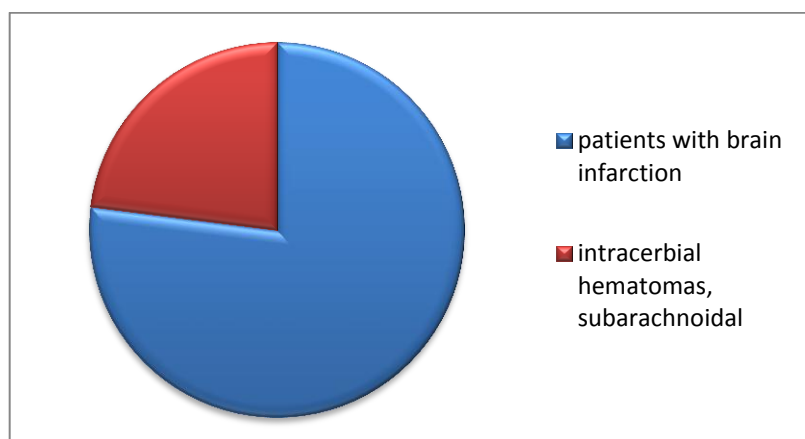
Graph. 1

Of the 154 patients, 35 of them had atrial fibrillation. Of the 35 patients with atrial fibrillation, 24 did not receive anticoagulant therapy before stroke, while 11 patients had atrial fibrillation and received anticoagulant therapy before the onset of brain infarction. In 26 patients AF was diagnosed with routine ECG, and with holter ECG in 9 patients. Of the 200 patients with recent brain infarction, newly detected AF was present in 12 patients, like we see in Graph.2.
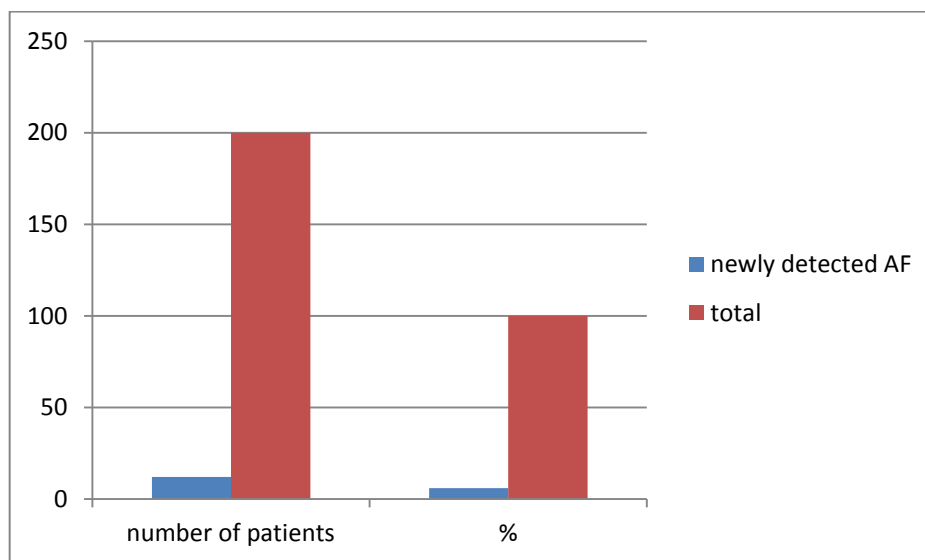
Graph.2.

In 24 patients, AF was noticed before the onset of stroke but did not undergo anticoagulant therapy because:
• 8 patients refused to take medication,
• In 11 patients there wasn't diagnosis of AF or the patient did not receive an anticoagulant therapy from the specialist

• 3 patients received anticoagulant therapy, which was soon self-indulgently stopped
• 2 patients had unstable values of INR or complications of anticoagulant therapy that led to end of taking the drug.
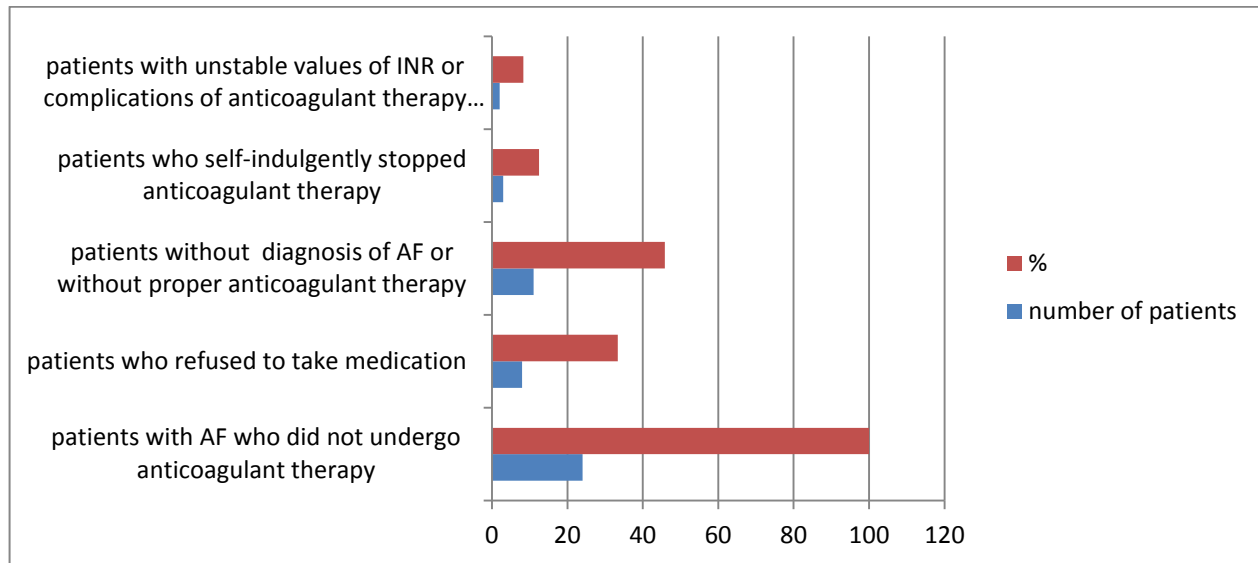
Graph.3.

Of the 11 patients who took oral anticoagulants, 10 of them had vitamin K antagonists and only one patient was taking rivaroxaban.

DISCUSSION

A lot more attention should be committed to patient with atrial fibrillation in the population we have examined.
A large number of patients did not receive anticoagulant therapy in primary prevention of brain infarction. CHAD2VAS2C and HAS BLED score are not applied sufficiently.

The overall percentage of patients with stroke, known to have atrial fibrillation, seems to be higher than previously estimated. Accordingly, more patients can be treated with oral anticoagulants and prevent repeated strokes [10].
The threshold for anticoagulation is generally lower when it is intended for secondary prevention than for primary, and the low threshold seems reasonable for patients who have had a high probability of atrial fibrillation, excess atrial ectopia at basic holter monitoring and increased risk of stroke [13,14, 15].

With the availability of new anticoagulants, empirical anticoagulation for susceptible but untested atrial fibrillation is tempting, but controversial and has the potential for overuse if no ECG screening is performed [17].
Absence of atrial fibrillation at prolonged monitoring can help to justify antiplatelet therapy and reduce unnecessary long-term anticoagulation in presumed low-risk patients with cryptogenic stroke.

However, when atrial fibrillation is detected, anticoagulation is strongly recommended, whether atrial fibrillation is paroxysmal or constant, because the risks of stroke are similar, and patients with any type of atrial fibrillation benefit from anticoagulation. Finding even short atrial fibrillations in this population is considered important, according to increasing evidence that short subclinical atrial fibrillation predicts subsequent episodes of atrial fibrillation and represents an independent risk factor for repeated stroke [12].Prolonged monitoring almost doubles the percentage of patients who should then receive anticoagulant therapy for secondary stroke prevention - this finding is interpreted as a clinically significant change in treatment that has the potential to prevent recurrent stroke [3].

These findings are implying to clinical practice and wide applicability for secondary prevention of stroke in regions where cardiac monitoring is available.

Prolonged ECG monitoring provides greater opportunities for detecting and treating one of the most common and important risk factors that can cause repeated stroke. In some regions there is no proper monitoring. We can use the loop recorder but for now it available to small number of patients. There are concerns about the administration of anticoagulant therapy with vitamin K antagonists, because additional problems are that the rural population is not able to control INR regularly, and new oral anticoagulants are still expensive and a small number of patients can afford them [5].

Only recently, new oral anticoagulants appear on the fund lists and patients in the Republic of Srpska can

receive them at an additional cost (the so-called B list). Improving the detection of atrial fibrillation as well as proper therapy, will be more important for aging the population. Future studies in this region are needed to determine the extent of the risk reduction associated with extended monitoring and its cost-effectiveness.

CONCLUSIONS

1. Atrial fibrillation is a significant risk factor for the development of brain infarction
2. Atrial fibrillation is often diagnosed for the first time only after brain infarction
3. Atrial fibrillation in this study was not adequately treated in the primary prevention of brain infarction

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P22 Data driven learning predictorsfor Syncope recognition and characterization

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Introduction

Artificial neural networks (ANN) are data driven learning structures based on the principles of morphological and functional organization of biological neurons. Basic quality of trained neural structures, generalization, association and self-organization, enable them reliable nonlinear multi-variate regression, classification and clustering. The models trained on the representative sample generalized knowledge on the unknown test sample with high reliability even at low level of representativeness of the training set.

Research goal

Use plasticity of ANN structure for modeling complex causal relationship between the selected predictive variables obtained on the basis of standard cardiologic examination and diagnosis of syncope.

Data and methodology

Total number of predictive variables is 53, from the categories of ECG time domain Spectral domain variables and parameters (Task Force parameters).The state of a sample of 496 adult patients was characterized by predefined set of 53 variables, diagnosed in accordance with the following distribution: control (negative) group comprising 131 individuals while positive group includes 365 patients who experienced syncope. The available set of patients was divided into two groups: Traininggroup of 284 patients, of which 50 in the control group, and Test group of 262 patients, of which 131represent complete control group. Feedforward ANN, performing supervised learning technique (backpropagation) was created to provide mapping of set of input vectors into a corresponding output binary signal, 0 for the control group and 1 for patients with syncope. The knowledge gained on the training set ANN generalized during the exploitation phase with the unknown sample. The aim is to form a simple model with good performance. The output signal in response to the input feature vector x of length 53, represents the examined patients diagnosis. When the value of the output signal Oequal to0 ($O = 0$) the patient belongs to a healthy group. When the value output equal to1 ($O = 1$), means that the patient or belongs to a category that has experienced syncope. All patients who cross the zone outputs $O> 0.5$ should be treated as a risk group. Such trained models weused to test the relevance of the partial impact of individual input variables of the model in the formation of the output signal, so as to enable the kind of visualization or internal insight into the process, through a graphical presentation of the output as a function of individual input variables. The dependence of the output of individual predictive variables is obtained, using the trained model to which we bring the transformed original input data. These datawe obtained from the original so that all predictive variables, except one, are represented by its fixed mean value, and only variable analyzed is presented by their original values sorted in ascending order.

Results

Classification on the test sample was very accurate (small FP and FN values). A small number of examples (near boundary decision) showed a slight deviation from the discrete value of 0 and 1. The model indicates that there is a coincidence of parameters that are strongly correlated with the occurrence of syncope and thus they enable a reliable discrimination of healthy and diseased patients. It is possible to find the smallest group of variables of maximal relevancy. The following results refer to the Numeric Sensitivity Analysis (NSA) of the impact of certain variables on the output signal of the model.

It should be noted that the graphical results coincide well with the current knowledge about the dependence of these displayed parameters and myocardial pathology, but this presentation has advantages because it gives an insight into the internal nature of this variation depending on the value of variable from minimum to maximum. It should be noted that these models, although formed in a relatively large sample, however, represent a model of that sample, and to increase the training data sample led to increasing the level of generality and applicability of such a models. But in terms of classification of patients this model gives unexpectedly good results, so its future practical application is quite certain.

Conclusion

ANN models can be used in modeling different types of pathology and diagnostics. In this particular case the ANN structure enabled us a highly reliable discrimination of patients with syncope and patients without risk, based on standard cardiologic examination procedure.

P23 New score table for calculation of risk from myocardial infarction occurance

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Cardiovascular risk is the risk of occurrence of fatal cardiovascular event during a ten-year period and it is most frequently evaluated with SCORE (Systematic Coronary Risk Evaluation) table for the population 40-60 years old. Up to date, the risk factors taken into account were: age, sex, the length of smoking habit, systole pressure and the level of total serum cholesterol whereas the psychosocial stress which acts via the autonomic nervous system, was not taken into account.There are two SCORE tables:1. for calculating cardiovascular risk in persons who did not have a cardiovascular incident such as myocardium infarct and who do not have diabetes.2. in persons who already suffered from myocardium infarct or diabetes, with more strict criteria, which is methodologically incorrect. This was first observed by ZlatkoŠabotić, so we made the SCORE table 3, where the psychosocial stress was included. We calculated the index of psychosocial stress by applying "A II S II" Personality types, by authors SmajoŠabotić and SavkaŠabotić. Just like Roseman (1950) and Friedman (1957) who, using the Borthner questionnaire, identified psychosocial types: "A" that was associated with coronary disease and Type "B" that was not associated, Smajo and SavkaŠabotić (1998 and 2005), based on RGM questionnaire ,identified Type "A II S 2", which highly correlates with coronary disease and myocardium infarct, six times more than classical risk factors, and Type "BII S2" that is not associated with coronary disease and myocardium infarct. The SCORE table value is obtained when the value of table 1 is divided by the number of risk factors minus 2 (sex and age) and then multiplied by 6. We used clinical-epidemiological methodology of research – in 100 patients with myocardium infarct. The males suffer from the disease 1.7 times more often (63:37). Up till the age of 59, most frequently males suffer from the disease and over the age of 60 it is the females. All of the examinees had positive Type "AII S2".According to the SCORE table 1, 75% of patients have moderate SCORE risk, 13% high and only 12% very high.According to the SCORE table 2, 40% has moderate, 30% high and 30% very high. According to the SCORE table 3, 14% of patients have high and 86% very high cardiovascular risk. This new and original Zlatkoˈs formula proved to be 2.87 times more precise than the present ones (86%:30%).

P24 Characteristic of blood pressure profile as a predictor of sleep apnea after acute ischemic stroke

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BACKGROUND AND PURPOSE: Prevalence of sleep-disordered breathing is higher in patients with acute ischemic stroke irrespective of type or timing after stroke (50–70%) than in the general population. Sleep apnea (SA)has been acknowledged as a cause of systemic arterial hypertension from 35% to 80%, and appears to be influenced by SA severity. A persistently high nighttime BP is associated with increased cardiovascular morbidity. The objective of the present study was to assess the association between SA and reverse dipper pattern as a proposalto test for SA in acute stroke patients.

METHODS: The study sample comprised33 patients, median age 68 years (19 [58%] women), admitted within 24 hours after ischemic stroke onset. We selected patients at risk for central and obstructive sleep apnea according to clinical evaluation (Epworth sleepiness score) to the first group (n=23) and patients with abnormal circadian reverse dipping pattern BP to the second group (n=10). Breathing during sleep was monitored with an ambulatory device (SOMNOcheck micro,Weinmann), which monitorsnasal airflow and pulse oximetry.Mild-to-moderate SA (MMSA) was defined by an apnea-hypopnea-index (AHI) > or =5/hour, and severe SA (SSA) was defined by an AHI >30/hour. The percentage of the oxygen desaturation-index (ODI) with the magnitude≥3% were calculated. Twenty-four-hour BP monitoring was performed by ABP device (BR-102plus, Schiller)during the first 48 hours after admission. Night time-daytime (night-day) BP ratio was calculated both for systolic and diastolic BPs.

RESULTS: Patients with abnormal circadian rhythm of BP were older age group (77 years versus 58 years, p=0.005). SA was foundin 18 (78.3%) patients of the first group and in 8 (80%) of the second group. There were no statistically significant differencesin the presenceor severity of SAbetween the two groups (p>0.1).The proportion of reverse dipper pattern in systolic and diastolic blood pressure was obviously greater in patients admitted toSSA group (90%versus 10.5% in systolic BP,p=0.000; 66.7%versus 0% in diastolic BP, p=0.001).

CONCLUSIONS: This finding suggests that a reverse dipper pattern could be aspossible predictors of SA in patients with stroke.

P25 Addison disease and ileostomy, therapy challenges- Case report

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Background: Addison's disease is defined as inability of adrenal cortex to produce adequateamounts of glucocorticoid and mineralocorticoid hormones. Incidence varies from 0,8 to 60 cases per 100000 people. Most common cause is autoimmune adrenalitis, followed by secondary tuberculosis. Gold standard for diagnosis is Synacthen test. Guidelines recommend Hydrocortisone 15-25 mg/day or cortisone acetate 20-35 mg/day as primary substitution therapy.

Case description: A 68 years old woman was admitted to Endocrinology department with symptoms that included extreme fatigue, hypotension, swatting, and loss of appetite and body weight. In total body examination, she exhibited a large number of spots and larger hyperpigmentation on skin and she had a gingival margin. Synacthen test was performed that confirmed the diagnosis of primary adrenal insufficiency and she received supplementation therapy with excellent response on follow-ups. Three months later, she was admitted to General surgery department due to obstructive ileus.Extensive right hemicolectomy was performed with the creation of terminal ileostomy due to differentiated intestinal adenocarcinoma. After the surgery and receiving first chemotherapy cycle the patient was again hospitalized to the Department of Endocrinology due to the diarrheal syndrome that resulted with immenseelectrolyte imbalance. In patients that have ileostomy, drug absorption can be altered, and they are prone to dehidratation. In our patient, the response to the same doses of hydrocortisone was different before the terminal ileostomy was performed and after. After ileostomy, she needed higher doses,therefore she was discharged with greater doses of hydrocortisone than traditional, after which stable replacementtherapy was achieved during follow up.

Conclusion: This case report points to the importance of individualizing therapy and adequate drug titration in patients with Addison disease that have ileostomy or bowel absorption problems.

Key words: Addison's disease, ileostomy, hydrocortisone

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