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И ЛОКАЛНЕ САМОУПРАВЕ

Počasno
pokroviteljstvo

NJ.K.V. Prestolonaslednik Aleksandar i Nj.K.V. Princeza Katarina
HRH Crown Prince Alexander and HRH Crown Princess Katherine

HISPA
HYPERTENSION, INFARCTION & STROKE PREVENTION ASSOCIATION
UDRUŽENJE CENTARA ZA HIPERTENZIJU, PREVENCIJU INFARKTA I ŠLOGA

HISPA TRILATERALA

Kardiovaskularni izazovi na raskršću balkanskih puteva

u organizaciji
Udruženja centara za hipertenziju, prevenciju infarkta i šloga (HISPA)

HISPA TRILATERAL

Cardiovascular challenges on Balkan roads crossing

Organized by
Hypertension, Infarction & Stroke Prevention Association (H.I.S.P.A)

15 – 17 September 2017.
Hotel Palisad, Serbia

ORGANIZATOR KONFERENCIJE

ARIA Conference & Events d.o.o.
Karađorđev trg 34, 11080 Zemun
Tel. +381 11 2600.978
Fax. +381 11 2604.590
E-mail: office@aria.co.rs

PROFESIONAL CONFERENCE ORGANIZER

ARIA Conference & Events d.o.o.
Karađorđev trg 34, 11080 Zemun
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ORGANIZATOR / ORGANIZER
Udruženje centara za hipertenziju, prevenciju infarkta i šloga – HISPA
Hypertension, Infarction and Stroke Prevention Association – HISPA

POKROVITELJSTVO / PATRONAGE
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Ministry of health, Republic of Serbia
Ministarstvo državne uprave i lokalne samouprave
Ministry of public administration and local self-government
NJ.K.V. Prestolonaslednik Aleksandar i Nj.K.V. Princeza Katarina
HRH Crown Prince Alexander and HRH Crown Princess Katherine

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dr Dragan Bogdanić
dr Kenan Hrapović

Poštovane kolege,

Sa željom da nastavimo sa uspešnim sprovodjenjem stručnog i edukativnog programa HISPA udruženja, koje je započeto HISPA kongresom u oktobru 2016. godine u Beogradu, odlučili smo da u 2017. godini održimo regionalni simpozijum "Kardiovaskularni izazovi na raskršću balkanskih puteva" koji će se održati na Zlatiboru u hotelu Palisad od 15-17. septembra 2017. godine.

Odabrali smo zapadnu Srbiju i Zlatibor kao mesto gde ćemo sjediniti i prezentovati naš rad i program zajedno sa HISPA centrima iz Crne Gore i Bosne i Hercegovine zbog geografskog položaja, ali i visoko postavljenih standarda u organizaciji ovakvih skupova. Prirodne lepote same planine kao i visoko pozicionirane turističke destinacije u okolini - Mokra Gora, Andrićgrad, reka Drina, Zlatar, kanjon Uvca biće još jedan razlog zbog čega želimo da Vas dočekamo u našem kraju i da Vam pružimo gostoprimstvo koje će te pamtiti.

Bogat naučni program u toku simpozijuma biće prožet mogućnostima obilaska turističkih destinacija po Vašoj želji, kao i upoznavanje sa običajima i kulturnim nasledjem našeg kraja.Takodje, brojni gosti iz susednih država i insotranstva imaće priliku da čuju i vide naša dosadašnja iskustva u radu, ali i da nam prenesu svoja znanja, a uz druženje i turistički program da se upoznaju sa lepotama naše Srbije.

Pozivamo Vas da budete naši gosti i da nakon pozitivnih iskustava koje će te poneti sa Zlatibora nastavite sradanju sa HISPA udruženjem.

Dr Zoran Čitaković
predsednik Organizacionog odbora

Dear Colleagues,

After successful HISPA meeting in October 2016. in Belgrade, we decided to continue educational HISPA activities in 2017. with organization of new regional event. This event will take place in hotel Palisad on mountain Zlatibor from 15-17.september 2017. with title "Cardiovascular challenges on Balkan road crossings".

West Serbia and Zlatibor have specific geographic position for three countries: Serbia, Bosnia and Herzegovina and Montenegro and it is unique place for presentation of HISPA achievements due to high organizational standards. Natural beauty of Zlatibor mountain and surroundings like Mokra Gora, Andricgrad, river Drina, Zlatar, canyon Uvac and our generous hospitality are additional reasons to join us in congress and out-of-congress activities.

Rich scientific program will be combined with educational activities related to customs and cultural heritage of West Serbia region. Numerous guests from all over the world will present us their knowledge and experience in joint sessions.

We cordially invite You to be our guests and with positive experience from Zlatibor continue cooperation with HISPA association.

Dr Zoran Čitaković
President of Organizational Committee

HISPA Dobrodošlica / Welcome from HISPA

Drage kolege,

Velika mi je čast i zadovoljstvo da Vam u ime Naučnog Odbora poželim dobodošlicu na predivnu planinu Zlatibor i prvi HISPA Trilaterala sastanak.

Na ovom kongresu biće predstavljen sveukupni pregled najnovijih kliničkih i naučnih istraživanja na polju preventivne, interne i kardiovaskularne medicine. Želimo da upravo na ovoj divnoj planini ("Raskršće Balkanskih puteva") lekari i medicinski tehničari iz svih krajeva sveta kroz naučni rad i druženje razmenjuju ideje i iskustva.

HISPA povezuje pacijente, lekare, medicinske tehničare i pomaže društvo u celini. HISPA sastanci su istovremeno ekspertski sastanci i divno druženje kolega i prijatelja. Upravo će na ovom sastanku HISPA zdravstveni radnici prezentovati najnovije naučne radove povezane sa implementacijom personalizovanog i multidisciplinarnog HISPA programa u HISPA centrima.

Mnogi istaknuti naučnici iz celoga sveta će uzeti aktivno učešće u radu HISPA kongresa. Biće prikazana "nauka kroz prizmu kliničkog iskustva".

Posebno zahvalnost dugujemo farmaceutskoj industriji i drugim sponzorima i prijateljima zbog velikodušne pomoći HISPA programu, članovima i kolegama.

U ime naučnog odbora pridružujem se dr Zoran Čitakoviću, i želim Vam uspešan rad i druženje na našem kongresu HISPA TRILATERALA.

Iskreno Vaš,

Prof. Dr Nebojša Tasić
Predsednik naučnog komiteta
Predsednik, HISPA

Dear Colleagues,

On behalf of the Scientific Committee, it is my great pleasure to welcome you to beautifull mountian Zlatibor and to the First Trilateral HISPA meeting.

The Congress has been designed to provide a comprehensive overview of the latest research developments in the field of preventive, internal and cardiovascular medicine. It is unique opportunity, in the settings of the beautiful mountain Zlatibor ("Balkan crossing"), for exchange of ideas, experience and science between colleagues from all parts of the world.

HISPA proved to care about patients, doctors, nurses and society. HISPA meetings provides unique opportunity for exchange of expert and scientific knowledge and for exquisite social life. In this meeeting HISPA doctors and nurses will present latest scientific papers related to personalized and multidisciplinary approach in HISPA centers.

Many distinguished scientists from around the globe have joined the faculty and will take part in this Congress. You will be presented „science translated to clinical practice".

We would like to express our thanks to the pharmaceutical and manufacturing industry for their generous support, to our dedicated staff, colleagues and friends for their help.

On behalf of the scientific committee, I join dr Zoran Čitaković, in giving a warm welcome to HISPA TRILATERALA.

Yours sincerely,

Prof. Dr Nebojša Tasić
President, Scientific committee
President, HISPA

OPŠTE INFORMACIJE

Website kongresa
https://hispa-kongres.webix.tv/
Za određene sesije biće omogućen direktan prenos na internetu na sajtu www.hispa.rs

Akreditacija
Program Kongresa je akreditovan od strane Zdravstvenog saveta Srbije sa sledećim brojem bodova:
- Predavači: 9 bodova
- Usmene prezentacije: 8 bodova
- Poster prezentacije: 6 bodova
- Pasivno učešće: 5 bodova

Bedževi
Bedževi sa imenom i prezimenom se moraju nositi na svim sesijama

Adresa održavanja HISPA TRILATERALA kongresa
Hotel Palisad
Zlatibor, Serbia
Tel: + 381 112204004, Fax: +381 112204104

Predstavljanje kompanija
Molimo Vas da odvojite vreme i posetite prezentacije naših sponzora. Više informacija ćete naći na našem website-u.

Internet
Besplatan Wi-Fi je obezbeđen u hotelu Palisad tokom trajanja kongresa.

Ručak i kafe pauze
Ručak je obezbeđen za sve učesnike u subotu 14. septembra 2017. godine. Kafe pauze su predviđene prema programu.

Mobilni telefoni/Elektronika
Molimo Vas da Vaši mobilni telefoni i drugi elektronski uređaji budu utišani/isključeni tokom naučnog programa.

Posteri
Prezentacije postera će biti tokom kafe pauza i ručka. Molimo Vas da Vaši posteri budu predstavljeni tokom celog trajanja skupa. Moraju se ukloniti do nedelje, 17. septembra do 11h.

Pitanja za predavače
Tokom diskusije molimo učesnike koji žele da postave pitanja, da dizanjem ruku pozovu tehničko osoblje i sačekaju da dobiju mikrofon pre postavljanja pitanja.

Registracija
Organizator konferencije ARIA, će biti prisutan na registracionom desku, spreman da pomogne oko svih potrebnih pitanja vezanih za HISPA TRILATERALA kongres.

Vreme rada deska za registraciju:
Petak, 15. septembar 2017. 17:00-19:00 časova.
Subota, 16. septembar 2017. 08:00-18:00 časova.
Nedelja, 17. septembar 2017. 08:00-11:00 časova.

Ceremonija otvaranja
Hotel Palisad, 15. septembar 2017. u 19:00 časova.

SOCIJALNI PROGRAM

Koktel dobrodošlice
Petak, 15. septembar, posle ceremonije otvaranje

Gala večera
Subota, 16. septembar u 20 časova

Za planirane ekskurzije molimo Vas da kontaktirate organizatora

GENERAL INFORMATION

Congress website
https://hispa-kongres.webix.tv/
For some sessions live streaming will be available on site www.hispa.rs

Accreditation
Congress is accredited by Serbian Health Council:
- Lecturers: 9 points
- Oral presentation: 8 points
- Poster presentation: 6 points
- Participation: 5 points

Badges
Name Badges must be worn all time throughout the meeting.

Conference Venue Full Address
Hotel Palisad
Zlatibor, Serbia
Tel: + 381 112204004. Fax: +381 112204104

Exhibition
Please ensure you take time to visit and support the companies exhibiting at HISPA TRILATERALA. Further information about the sponsor and exhibitors are available on the website.

Internet Access
Wi-Fi is provided free of charge for all participants.

Lunch and Refreshments
Lunch will be provided for all participants on Saturday September 16th, 2017.

Mobile/Cell Phone & Electronic
As a courtesy to speakers and other delegates, please ensure that mobile/cell phones, tablets and other electronic devices are switched to silent during sessions.

Posters

September 16th and 17th during lunch and coffee breaks. All posters should be mounted and displayed during the full meeting. Access will be available from 8:00 in the morning. All posters must be removed by 11:00 on the last day.

Questions to Speakers

During discussion periods delegates who wish to ask a question should raise their hand clearly and wait to be acknowledged by the chairperson. Please do not ask a question until you have been given a microphone.

Registration desk

The conference organizers, ARIA Conference & Events will be located at the Registration Desk and will be pleased to assist you with queries throughout the conference.

The Registration Desk will be open at the following times:
Friday, September 15th 2017. 17:00-19:00 h
Saturday, September 16th 2017. 08:00-18:00 h
Sunday, September 17th 2017. 08:00-11:00 h

Speaker Preview

All oral presenters should meet with the audio-visual technician in speaker preview room at the earliest opportunity and at the very latest two hours before the start of the session in which the presentation will take place.

Opening Ceremony

Hotel Palisad on September 15th 2017 at 7 p.m.

SOCIAL PROGRAMME

Cocktail Party
Cocktail Party will take place on Friday September 15th after opening ceremony

Gala Dinner
Gala dinner will take place in hotel Palisad on Saturday, September 16th at 20:00.

Excursions
For more information please contact Conference organizers

UDRUŽENJE CENTARA ZA HIPERTENZIJU, PREVENCIJU INFARKTA I ŠLOGA - HISPA
HYPERTENSION, INFARCTION AND STROKE PREVENTION ASSOCIATION - HISPA

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Prof. Dr Nebojša Tasić

Savet HISPA/HISPA council:
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Marija Milošević
Aleksandar Radanović
Vladan Mitić
Svetlana Krsmanović
Srđan Stefanović
Milorad Mićović

NAUČNI PROGRAM PROGRAM

SCIENTIFIC PROGRAM

PETAK, 15. SEPTEMBAR 2017 / FRIDAY, 15th SEPTEMBER, 2017

VREME/TIME	SALA / ROOM
17:30-18:00	Simpozijum INPHARM / INPHARM Symposium
18:00-18:30	Simpozijum BOERINGHER / BOERINGHER Symposium
18:30-19:00	Simpozijum AMICUS / AMICUS Symposium
19:15-20:00	Otvaranje kongresa / Opening ceremony
20:00-20:30	Svečani program / Program
20:30	Koktel / Cocktail

SUBOTA, 16. SEPTEMBAR 2017 / SATURDAY, 16th SEPTEMBER, 2017

VREME/TIME	Sala HISPA/HISPA ROOM
08:00-09:00	HISPA 1 sesija/HISPA 1 session
09:00-10:00	HISPA 2 sesija/HISPA 2 session
10:00-10:30	Kafe pauza/Coffee break
10:30-11:00	Simpozijum RICHTER GEDEON RICHTER GEDEON symposium
11:00-11:30	Simpozijum SERVIER SERVIER symposium
11:30-12:00	Simpozijum PHARMAS PHARMAS symposium
12:00-12:30	Simpozijum SWISSNATURE SWISSNATURE symposium
12:30-13:00	Simpozijum KRKA KRKA symposium
13:00-14:15	Ručak/Lunch break
14:15-15:00	Simpozijum BOERINGHER BOERINGHER symposium
15:00-15:30	Simpozijum MG MIVELA MG MIVELA symposium
15:30-16:30	Simpozijum PFIZER PFIZER symposium
16:30-17:00	Simpozijum BAIKALPHARM BAIKALPHARM symposium
17:00-17:30	Kafe pauza/Coffee break
17:30-18:30	HISPA 3 sesija/HISPA 3 session
18:30-19:30	HISPA 4 sesija/HISPA 4 session

VREME/TIME	Sala ZLATIBOR /ZLATIBOR ROOM
08:00-09:00	HISPA 5 sesija/HISPA 5 session
09:00-10:00	HISPA 6 sesija/HISPA 6 session
10:00-10:30	Kafe pauza/Coffee break
10:30-11:45	HISPA 7 sesija/HISPA 7 session
11:45-13:00	HISPA 8 sesija/HISPA 8 session
13:00-14:15	Ručak/Lunch break
14:30-15:45	HISPA 9 sesija/HISPA 9 session
15:45-17:00	HISPA 10 sesija/HISPA 10 session
17:00-17:30	Kafe pauza/Coffee break
17:15-18:45	**Skupština HISPA/HISPA assembly**

20:30 **SVEČANA VEČERA / GALA DINNER**

NEDELJA, 17. SEPTEMBAR 2017 / SUNDAY, 17th SEPTEMBER, 2017

VREME/TIME	SALA HISPA /HISPA ROOM
09:00-10:00	HISPA 11 sesija/HISPA 11 session
10:00-11:00	HISPA 12 sesija/HISPA 12 session
11:00-11:30	Kafe pauza/Coffee break
11:30-12:30	HISPA 13 sesija/HISPA 13 session
12:30	Zatvaranje kongresa/Closing ceremony

Subota, 16. septembar, 08:00-09:00 – Sala HISPA
Saturday, September 16st, 08:00-09:00 – Room HISPA

HISPA SESIJA ZAPADNA SRBIJA
HISPA SESSION WEST SERBIA

Infarkt i šlog: Gde, kada i kako prekinuti začarani kardiovaskularni kontinuum?
Infarction and stroke: Where, when and how to stop the vitious circle of cardiovascular continuum?

Predsedavajući/Chairman:
1. Zoran Čitaković, Užice
2. Aleksandar Đenić, Zlatibor

08:00-08:15	**Lečenje hipertenzije u trudnoći** Svetlana Krsmanović, Priboj
08:15-08:30	**Specifičnosti hipertenzije kod gojaznih pacijentata - Iskustva Čigota programa** Aleksandar Đenić, Zlatibor
08:30-08:45	**Primarna prevencija KVB i lečenje hipertenzije kod osoba mladjih od 40 godina** Dragana Drobnjak, Užice
08:45-09:00	**Hipertenzija kao najučestaliji faktor rizika kod bolesnika u sekundarnoj prevenciji KVB** Zoran Čitaković, Užice

Subota, 16. septembar, 09:00-10:00 – Sala HISPA
Saturday, September 16st, 09:00-10:00 – Room HISPA

ZAJEDNIČKA SESIJA UDRUŽENJA HISPA I SCREEN-FH PROJEKTA
JOINT SESSION OF HISPA ASSOCIATION AND SCREEN-FH PROJECT

Predsedavajući/Chairman:
1. Richard Češka, Prague
2. Nebojša Tasić, Belgrade

09:00-09:15	**Familial hypercholesterolemia from Czech experience to the international cooperation** Richard Češka, Prague
09:15-09:30	**Perspectives in lipoprotein(a) as a modifiable cardiovascular risk factor** Marat Ezhov, Moscow
09:30-09:45	**FH and cardiovascular risk – HISPA approach** Nebojša Tasić, Belgrade
09:45-10:00	**Familial hypercholesterolemia is not a rare disease** Ivan Pečin, Zagreb

Subota, 16. septembar, 17:30-18:30 – Sala HISPA
Saturday, September 16st, 17:30-18:30 – Room HISPA

Elektronika, mehanika , robotika i kardiovaskulane bolesti:
Da li ćemo uskoro moći da prepoznamo, dijagnostikujemo i lečimo bolest bez elektronskih uređaja?
Electronic, mechanic, robotic and Cardiovascular diseases:
Would we be able to recognize, diagnose and treat the disease without electronic devices?

Predsedavajući/Chairman:
1. Arsen Ristić, Beograd
2. Miodrag Perić, Beograd

17:30-17:45	**Pedeset godina transplantacije srca i mehaničke potpore cirkulacije** Miodrag Perić, Beograd
17:45-18:00	**Novi personalni uređaji i telemonitoring u lečenju srčane insuficijencije** Arsen Ristić, Beograd
18:00-18:15	**HISPA e-learning platforma** Slavko Radonjić, Beograd
18:15-18:30	**Philips i apnea tokom spavanja** Igor Mitrić, Beograd

Subota, 16. septembar, 18:30-19:30 – Sala HISPA
Saturday, September 16st, 18:30-19:30 – Room HISPA

HISPA SESIJA – Medicinski tehničari/sestre
HISPA SESSION – Nurses
Savremene smernice u kardiovaskularnoj medicini, IKVB Dedinje
Current guidelines in cardiovascular medicine, Cardiovascular Institute Dedinje

Predsedavajući/Chairman:
1. Goran Cucić, Beograd
2. Velisava Perović, Beograd

18:30-18:45	**Endovaskularno lečenje stenoza renalne arterije** Velisava Perović, Beograd
18:45-19:00	**Ishrana i hipertenzija** Sanja Vučinić, Beograd
19:00-19:15	**Perkutano lečenje stenoza na brahiocefaličnim arterijama** Miloš Novaković, Beograd
19:15-19:30	**Preoperativna priprema kardiohirurških bolesnika** Snežana Borić, Beograd

Subota, 16. septembar, 08:00-09:00 – Sala Zlatibor
Saturday, September 16st, 08:00-09:00 – Room Zlatibor

ZAJEDNIČKA SESIJA UDRUŽENJA HISPA/UDRUŽENJA KARDIOLOGA SRBIJE/BASICS-A
JOINT SESSION ASSOCIATION HISPA/ASSOCIATION OF CARDIOLOGY SERBIA/BASICS
Prevencija vs. intervencija: Minuti za stent vs godine za bezbednu i udobnu starost
Prevention vs. Intervention: Minutes for stent vs years for safe elderliness

Predsedavajući/Chairman:
1. Branko Beleslin, Beograd
2. Stevan Ilić, Niš

08:00-08:15	**Perkutana revaskularizacija hronično okludiranih koronarnih arterija: savremena indikacija ili OMT?** Siniša Stojković, Beograd
08:15-08:30	**Aktuelnosti novih preporuka za STEMI** Branko Beleslin, Beograd
08:30-08:45	**HISPA program – udobna i bezbedna starost** Nebojša Tasić, Beograd
08:45-09:00	**Progresija i regresija aterosklerotičnog plaka - lekcije iz IVUS-a i OCT-a** Vladan Vukčević, Beograd

Subota, 16. septembar, 09:00-10:00 – Sala Zlatibor
Saturday, September 16st, 09:00-10:00 – Room Zlatibor

HISPA CRNA GORA SESIJA
HISPA MONTENEGRO SESSION
Hipertenzija – Faktor rizika ili bolest, kontinuirana dilema
Hypertension – Risk factor or disease, ongoing dilemma

Predsedavajući/chairman:
1. Nebojša Bulatović, Podgorica
2. Mihailo Vukmirović, Podgorica

09:00-09:15	**So i hipertenzija** Nebojša Bulatović, Podgorica
09:15-09:30	**Hipertenzija kao faktor rizika za razvoj atrijalne fibrilacije** Mihailo Vukmirović, Podgorica
09:30-09:45	**Hipertenzija kao faktor rizika za nastanak akutnog koronarnog sindroma** Saša Babović, Berane
09:45-10:00	**Diskusija** Disscusion

Subota, 16. septembar, 10:30-11:45 – Sala Zlatibor
Saturday, September 16st, 10:30-11:45 – Room Zlatibor

ZAJEDNIČKA SESIJA UDRUŽENJA HISPA I MEĐUNARODNOG UDRUŽENJA ZA VASKULARNO ZDRAVLJE
JOINT SESSION OF HISPA ASSOCIATION AND INTERNATIONAL SOCIETY FOR VASCULAR HEALTH

Predsedavajući/Chairman:
1. Roland Asmar, Paris
2. Marina Deljanin ilić, Niš

10:30-10:50	**Effects of Metabolic Syndrome on arterial function in different age groups. The Advanced Approach to Arterial stiffness study (AAA Study)** Roland Asmar, Paris
10:50-11:10	**Management of Hypertension in old adults : how to choose the right treatment strategies** Athanas Benethos, Paris
11:10-11:30	**Digital health: the mobility solution in aging and elderly** Jirar Topouchian, Paris
11:30-11:45	**Diskusija** **Disscusion**

Subota, 16. septembar, 11:45-13:00 – Sala Zlatibor
Saturday, September 16st, 11:45-13:00 – Room Zlatibor

EURO –HISPA sesija
EURO-HISPA session

Predsedavajući/Chairman:
1. Yuriy Sirenko, Kiev
2. Dobrin Vassilev, Sofia

11:45-12:05	**Time to intervene** Dobrin Vassilev, Sofia
12:05-12:25	**Time to screen** Teodora Yaneva, Sofia
12:25-12:45	**Practical algorhythm in resistant hypertension** Yurij Sirenko, Kiev
12:45-13:00	**The Role of Arterial Stiffness in Assessment of Cognitive Decline** Sandra Morović, Zagreb

Subota, 16. septembar, 14:30-15:45 – Sala Zlatibor
Saturday, September 16st, 14:30-15:45 – Room Zlatibor

HISPA SESIJA
HISPA SESSION

Faktori rizika na balkanskom raskršću: Vekovna akumulacija, sadašnja eksplozija
Risk factors on Balkans crossings: Centuries of accumulation, current explosion

Predsedavajući/Chairman:
1. Marina Deljanin Ilić, Niš
2. Dragan Đurić, Beograd

14:30-14:50	**Varijabilnost krvnog pritiska - novi cilj u terapiji arterijske hipertenzije** Marina Deljanin Ilić, Niš
14:50-15:10	**Mesto fiksnih kombinacija u lečenju arterijske hipertenzije** Stevan Ilić, Niš
15:10-15:30	**Značaj osovine adiponektin-hipertenzija- gojaznost** Sanja Stojanović, Niš
15:30-15:45	**Put do željenog cilja kroz rad HISPA centra** Aleksandar Stanković, Leskovac

Subota, 16. septembar, 15:45-17:00 – Sala Zlatibor
Saturday, September 16st, 15:45-17:00 – Room Zlatibor

HISPA BH SESIJA
HISPA BH SESSION

Infarkt i šlog: Gde, kada i kako prekinuti začarani kardiovaskularni kontinuum?
Infarction and stroke: Where, when and how to stop the vitious circle of cardiovascular continuum?

Predsedavajući/Chairman:
1. Vlado Đajić, Banja Luka
2. Ranko Škrbić, Banja Luka

15:45-16:00	**Prevencija kardiovaskularnih bolesti u RS – HISPA program** Radoslav Nikolić, Doboj
16:00-16:20	**Asimptomatska karotidna bolest** Vlado Đajić, Banja Luka
16:20-16:40	**Uloga porodične medicine u prevenciji kardiovaskularnih bolesti** Maja Račić, Foča
16:40-17:00	**Interakcije lekova- implikacije na kardiovaskularni sistem** Ranko Škrbić, Banja Luka

Nedelja, 17. septembar, 09:00-10:00 – Sala HISPA
Nedelja, September 17st, 09:00-10:00 – Room HISPA

HISPA SESIJA
HISPA SESSION

Kako stići do cilja? Prevencija kardiovaskularnih bolesti u više brzina
How to reach the target? Prevention of cardiovascular diseases in several velocities

Predsedavajući/Chairman:
1. Nebojša Tasić, Beograd
2. Dara Božović Savić, Užice

09:00-09:15	**Lečenje hipertenzije kod dece – HISPA program** Dara Božović Savić, Užice
09:15-09:30	**Prevencija šloga – HISPA program kontrole atrijalne fibrilacije i sinkopa** Slađana Božović Ogarević, Beograd
09:30-09:45	**Dijagnoza i lečenje rezistentne hipertenzije – HISPA program** Danijela Tasić, Beograd
09:45-10:00	**Sleep apnea: redukcija kardiovaskularnog rizika savremenim metodama – HISPA program** Maja Filipović, Beograd

Nedelja, 17. septembar, 10:00-11:00 – Sala HISPA
Nedelja, September 17st, 10:00-11:00 – Room HISPA

ZAJEDNIČKA SESIJA UDRUŽENJA HISPA I DRUŠTVA SRBIJE ZA IZUČAVANJE ARTERIOSKLEROZE, TROMBOZE I VASKULARNE BIOLOGIJE
JOINT SESSION OF HISPA ASSOCIATION AND SERBIAN ASSOCIATION FOR ARTERIOSCLEROSIS, THROMBOSIS AND VASCULAR BIOLOGY RESEARCH

Endotelna disfunkcija: od hipoteze preko dijagnoze do savremenog lečenja
Endothelial dysfunction – From hypothesis, diagnosis to modern treatment

Predsedavajući/Chairman:
1. Dragan Đurić, Beograd
2. Vladimir Jakovljević, Kragujevac

10:00-10:15	**Endothelial dysfunction, homocysteine, paraoxonase and HDL: the missing link between lipid's and protein's theory of atherosclerosis** Dragan Đuric, Beograd
10:15-10:30	**The role of exercise in prevention and treatment of cardiovascular diseases** Vladimir Jakovljević, Kragujevac
10:30-10:45	**The role of nutrition in prevention and treatment of cardiovascular diseases – Research** Vesna Vučić, Beograd
10:45-11:00	**Endothelial dysfunction and nutritive intervention in rheumatoid arthritis** Mirjana Veselinović, Kragujevac

HISPA SESIJA – Medicinski tehničari/sestre
HISPA SESSION - Nurses

Uloga edukacije u primaroj i sekundarnoj prevenciji kardiovaskularnih oboljenja –Regionalna mreža
Role of education in primary and secondary prevention of cardiovascular disease – Regional network

Predsedavajući/Chairman:
1. Kenan Galijašević, Doboj
2. Jovana Spasojević, Užice

11:30-11:45	**Edukacija medicinskih tehničara u visokoobrazovnim institucijama – HISPA program** Kenan Galijašević, Doboj
11:45-12:00	**Edukacija i prevencija: sveobuhvatni pristup** Jelena Đurđević, Beograd
12:00-12:15	**Sveobuhvatnost djagnostičke obrade bolesnika – HISPA centar Užice** Jovana Spasojević, Užice
12:15-12:30	**Sestrinske intervencije u nefarmakološkom lečenju arterijske hipertenzije** Milena Lupšić, Beograd

INPHARM SIMPOZIJUM

PETAK, 15. SEPTEMBAR
17:30-18:00

DOBITNA KOMBINACIJA ZA HIPERHOLESTEROLEMIJU
Save Oil Plus® - činjenice, dokazi, iskustva u kliničkoj praksi
Prof. dr Nebojša Tasić, Beograd
Prim. dr Zoran Čitaković, Užice

SIMPOZIJUM BOEHRINGER

PETAK, 15. SEPTEMBAR
18:00-18:30

NOVE STRATEGIJE U LEČENJU BOLESNIKA SA DIJABETESOM TIP 2

Empagliflozin i velike promene na polju dijabetesa tip 2
Prof. dr Teodora Beljić, Beograd

Značajan korak u poboljšanju ishoda srčane insuficijencije u dijabetesu tip 2
Prof. dr Dragan Simić, Beograd

AMICUS

Modern Medicines for All

SIMPOZIJUM AMICUS

PETAK, 15. SEPTEMBAR
SALA
18:30-19:00

Trinomia - terapija, komplijansa i komfor u jednoj kapsuli
Prof. dr Nebojša Tasić, Beograd

RICHTER GEDEON

SIMPOZIJUM RICHTER GEDEON

SUBOTA, 16. SEPTEMBAR
SALA
10:30-11:00

Manje tableta, veća efikasnost - kombinovana terapija u redukciji krvnog pritiska
Prof. dr Ivan Tasić, Niš

SIMPOZIJUM SERVIER

SUBOTA, 16. SEPTEMBAR
SALA HISPA
11:00-11:30

Prexanil porodica – pronadjite dobitnu kombinaciju za vase pacijente sa hipertenzijom
Prof. dr Nebojša Tasić, Beograd

PharmaS®

SIMPOZIJUM PHARMAS

SUBOTA, 16. SEPTEMBAR
SALA HISPA
11:30-12:00

Prirodni statini, izazovi u lečenju dislipidemije
Prof. dr Dragan Simić, Beograd

Swiss Nature

SIMPOZIJUM
SWISS NATURE

SUBOTA, 16. SEPTEMBAR
SALA HISPA
12:00-12:30

Portulaka i kurkuma: moćni duet u zaštiti srca i krvnih sudova
Prof. dr Nebojša Tasić, Beograd

KRKA

SIMPOZIJUM
KRKA

SUBOTA, 16. SEPTEMBAR
SALA HISPA
12:30-13:00

Snaga Sinergije u eliminisanju hipertenzije i hiperholesterolemije
Prof. dr Dragan Simić, Beograd
Prof. dr Svetlana Apostolović, Niš
Svetlana Popović, Beograd

Boehringer Ingelheim

SIMPOZIJUM BOEHRINGER

SUBOTA, 16. SEPTEMBAR
SALA HISPA
14:15-15:00

ANTIKOAGULANTNA TERAPIJA U 2017.

Dabigatran - bezbednost, efikasnost, kontrola
Prof. dr Nebojša Tasić, Beograd

Antikoagulantna terapija - Zašto je važno imati antidot?
Prof. dr Goran Rađen, Beograd

Mg++ mivela
Mg++ mivela BLAGO GAZIRANA
Voda vašeg srca!

SIMPOZIJUM MG MIVELA

SUBOTA, 16. SEPTEMBAR
SALA HISPA
15:00-15:30

Magnezijum i voda – sigurna kardiovaskularna i cerebrovaskularna protekcija
dr Danijela Tasić, Beograd

SIMPOZIJUM PFIZER

SUBOTA, 16. SEPTEMBAR
SALA HISPA
15:30-16:30

Atrijalna fibrilacija i antikoagulancija
Slađana Božović Ogarević, Beograd

Izazovi u antikoagulantnoj terapiji kod AF pacijenata
Danijela Tasić, Beograd

Od kliničkih studija do realnog života
Dalibor Dragišić, Beograd

Eleprenon: zašto, kome i kada?
Aleksandra Milošević, Beograd

SIMPOZIJUM BAIKALPHARM

SUBOTA, 16. SEPTEMBAR
SALA HISPA
16:30-17:00

Dihidrokvercetin – kako očistiti aterosklerotski plak i zaštiti krvne sudove?
Prof. dr Nebojša Tasić, Beograd

ABSTRACT BOOK

„WHITE-COAT EFFECT“ AS A CAUSE OF „PSEUDO-RESISTANT“ HYPERTENSION

Davidovic Goran[1], Vuleta Marko[1], Petrovic Marijana[1], Dragisic Dalibor[2], Tasic Nebojsa[3], Milanov Srdjan[1]
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[3]Cardiovascular Institute „Dedinje“, Belgrade

Background: „White-coat effect“ is defined as the rise in blood pressure that occurs in the medical environment regardless of the daytime ABPM level or the use of antihypertensive drugs. In general, „white-coat effect“ is present when the office BP is higher than the awake ambulatory BP. Patients with an office BP at least 20 mmHg systolic and/or 10 mmHg diastolic higher than the awake ambulatory BP have been designated as having a „clinically important white-coat effect“. Aim was to investigate the presence of „white-coat effect“ in our patients.

Methods: Research included 200 patients observed in HISPA center Kragujevac, Serbia, during the one year period. Patients had baseline and control visits, after 3 or 6 months, with the results of all specific diagnostic methods. Data on previous hypertension and antihypertensive treatment, including the number of drugs were collected anamnestically and via previous medical reports. Office blood pressure was measured on baseline and control visit, in a supine position, after at least 5 minutes of resting. Office hypertension was defined according to the latest ESC/ESH recommendations as >140 mmHg for systolic and/or >90 mmHg for diastolic BP. All patients underwent ambulatory blood pressure monitoring between two visits. We used awake average values >135 mmHg for systolic and/or >85 mmHg for diastolic BP for confirmation and estimation of hypertension. All data were statistically analyzed in the SPSS for Windows.

Results: Study population consisted of 135 (67.5%) of male and 65 (32.5%) of female subjects. Mean age of the population was 55.19±11.24 years. Previous hypertension was present in 165 (82.5%) of patients (x^2; p=0.000), duration of hypertension was in 87 (43.3%) patients between 1 and 10 years (x^2; p=0.003), and 154 (77%) already were on antihypertensive therapy (x^2; p=0.000). Baseline average values of systolic BP were 144.19±21.62 mmHg (t-test; p=0.000), and for diastolic BP 87.38±14.93 mmHg (t-test; p=0.000). Awake systolic blood pressure was >135 mmHg in 104 (52%) patients with mean values 134.13±18.40 mmHg (t-test; p=0.504). Awake diastolic BP was >85 mmHg in 112 (56%) patients with mean values 83.20±12.13 mmHg (t-test; p=0.037). The majority of patients already had 3/more antihypertensives in therapy on baseline visit. This group has 122 (21%) patients (x^2; p=0.000).

Conclusions: „White-coat effect“ is a recognized cause of „pseudo-resistant“ hypertension and may be present in normotensives or anyone treated for hypertension, regardless of the number of drugs being taken which was confirmed in our population of patients. Treated patients with office BP at least 140/90mmHg and normal awake BP levels on ABPM could be designated as having „pseudo-resistant hypertension due to white-coat effect“, as they have apparent hypertension based upon office readings, but are actually normotensive. This effect was not clinicaly significant because the difference was not >20 mmHg for systolic or >10 mmHg for diastolic BP, but it was probably the reason for perhaps unnecessary previous administration of 3/more drugs in the treatment of these patients.

Keywords: white coat effect, pseudo-resistant hypertension, office blood pressure, ABPM

THE ASSOCIATION BETWEEN OBESITY AND VISIT-TO-VISIT VARIABILITY N SYSTOLIC BLOOD PRESSURE: A PROSPECTIVE STUDY

Marina Deljanin Ilic[1], Sanja Stojanovic[1], Stevan Ilic[1], Nebojša Tasic[2], Dalibor Dragisic[3], Bojan Ilic[1], D. Petrovic[1]
[1]Institute of Cardiology “Niska Banja”, Medical Faculty University of Nis, Serbia
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Background: With the prevalence of obesity, which should already be considered as a pandemic phenomenon (with all accompanying health risks), both prevention and health education, as well as identifying predictors for the development of obesity-related diseases are primary. The pathophysiological relationship between obesity and visit-to-visit variability in systolic blood pressure (SBPV) has not been completely resolved. The aim of the study was to investigate the association between obesity and visit-to-visit variability in systolic blood pressure in hypertensive patients.

Methods: Prospective study included 300 randomly selected hypertensive patients (147 men and 153 women, mean age 67.76±9.84 years), who were divided, according to body mass index (BMI≥30 kg/m^2), to groups of obese (n=249) and non-obese examinees (n=51). The study comprised three visits during the follow up period of 22-months. Obesity was defined as BMI, as the parameter of total obesity and it was defined as waist circumference (WC), as the parameter of central obesity. SBPV for each examinee was defined using the standard deviation (SD) from 3 values of systolic blood pressure (SBP). In order to estimate detailed evaluation of distribution SBPV quartiles of SBP-SD were formed.

Results: The values of SBP and SBP-SD were significantly higher in the group of obese hypertensive patients than in the group of non-obese patients (126.67±8.22 vs. 120.45±7.79 mmHg, 11.00±5.64 vs. 7.34±3.96; p<0.01). There was statistically stronger correlation between SBP-SD and BMI compared to large WC (ρo=0.425 vs. ρo=0.356, p<0.01). The analysis showed statistically significant average decrease of SBP-SD for 8.2 mmHg, BP for 31/8 mmHg, BMI for 3.8 kg/m^2 and WC for 10 cm. The highest SBPV was recorded in the 4th quartile in obese patients (43.13±7.50 mmHg).

Conclusion: Our findings suggest an association between parameters of obesity and increased visit-to-visit variability in systolic blood pressure in hypertensive patients. During follow-up 22-months periods, reduction of body weight was associated with reduction of blood pressure values, and lower value of blood pressure variability. Persistently decrease both body weight and visit-to-visit variability may explain lower cardiovascular risk in obese-related disease.

Keywords: Obesity, hypertension, visit-to-visit systolic blood pressure variability

THE SIGNIFICANCE OF ADIPONECTIN AS A MARKER OF PREHYPERTENSION AND HYPERTENSION IN PATIENTS WITH METABOLIC SYNDROME

Sanja Stojanovic[1], Marina Deljanin Ilic[1], Stevan Ilic[1], Nebojša Tasic[2], Dalibor Dragisic[3], Bojan Ilic[1], Dejan Petrovic[1], Dragan Marinkovic [1]
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Background: Hypertension is associated with significant differences in adipose tissue metabolism (especially decreased adiponectin concentration), with an increase in total and central obesity and the higher risk of cardiovascular events. The aim of the study was to determine adiponectin concentration in patients with metabolic syndrome (MetS) and prehypertension (Pre-HT) or hypertension (HT) and to estimate relationship between adiponectin concentration and components of MetS.

Methods: This cross-sectional study involved randomly selected 120 subjects (60 men and 60 women, mean age 54.23±15.53 years), who were divided in four groups: MetS+normotensive, n=30; MetS+Pre-HT, n=30; MetS+HT, n=30; Control group (no MetS, no Pre or HT, n=30). In all subjects serum adiponectin concentration was measured by ELISA method, and serum triglyceride concentration, fasting plasma glucose (FPG), Homeostasis Model Assessment of Insulin Resistance index (HOMA-IR), total cholesterol (TC) and high-density lipoprotein (HDL) were determined. Obesity was evaluated through body mass index (BMI), waist circumference (WC), and body fat percentage (BFP).

Results: Serum adiponectin was the lowest in group with MetS and HT (1092.06±488.91 pg/mL), significantly lower ($p<0.01$) in MetS+ Pre-HT group (1134.15±510.11 pg/mL), and it was the highest in the control group (1670.27±500.12 pg/mL). Adiponectin negatively correlated with most components of MetS ($p<0.01$); blood pressure ($r=-0.286$), systolic blood pressure ($r=-0.313$), waist circumference ($r=-0.309$), triglycerides ($r=-0.295$), FPG ($r=-0.208$), HOMA-IR ($r=-0.259$), and positively with HDL-cholesterol ($r=0.156$, $p>0.05$). In logistic regression analysis, the level of adiponectin and WC were distinguished as the strongest predictors of Pre-HT and HT. In patients with MetS value of adiponectin ≥1266.54 pg/mL was associated with a lower risk of Pre-HT, and value of ≥1159.98 pg/mL was associated with a lower risk of HT.

Conclusion: Patients with metabolic syndrome have low adiponectin levels and this hypo-adiponectinemia may indicate prehypertension or hypertension. There is a strong relationship between adiponectin level and components of MetS.

Keywords: adiponectin, prehypertension, hypertension, metabolic syndrome

A ROLE OF MATRIX METALLOPROTEINASE-9 IN PATHOGENESIS OF DISSECTING AORTIC ANEURISM

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"Dedinje" Cardiovascular Institute, Institute of Onkology and Radiology, Belgrade, Serbia

Background : The aime of this study was to determine matrix metalloproteinase-9 (MMP-9) expression in dissected aortic tissue.

Methods: Specimens of aorta from 23 patients who underwent surgery for acute dissection with the entrance tear in the ascending aorta. Aortic tissue samples were evaluated for MMP-9 expression and were compared with 10 control aortic specimens, free of any vascular diseases. Expression of MMP-9 was graded as 0 (absent), 1+ (mild), 2+ (moderate), and 3+ (intense).

Results: Mean age of patients was 54±9 years (ranging 24-72 years), with 20/23 (87%) of them being male, and 3/23 (13%) female. A total of 14/23 (61%) patients had exit rupture in the aortic wall, whereas 9/23 (39%) did not have exit tear. In group without exit tear expression of MMP-9 was absent (0) in 4 and mild (1+) in 5 patients, whereas in patients with exit tear expression of MMP-9 was intense (3+) in 10 patients, and moderate (2+) and mild (1+) in 2 each. Expression of MMP-9 in group without exit tear was lower than in patients with exit tear (0.55±0.52 vs 2.57±0.76, respectively, $p<0.001$). Expression of MMP-9 was absent in all control specimens, and was significantly lower than in both groups with aortic dissection ($p<0.001$).

Conclusion: Expression of MMP-9 in the aortic media is enriched in dissected aortic tissue. In acute aortic dissection with existence of the exit rupture in the aortic wall expression of MMP-9 higher than in group without exit tear.

Keywords: matrix metalloproteinase-9 expression, aortic tissue

AGE AND SEX-BASED DIFFERENCES IN MAJOR CORONARY HEART DISEASE RISK FACTORS

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[5]General Hospital „Uzice", Uzice, Serbia

Background: Traditionally, coronary heart disease (CHD) has been considered as a disease predominantly affecting men. Women with clinically manifest CHD are in general older than men, with a higher expression of cardiovascular risk factors. To investigate relationship of age, sex and major coronary heart disease risk factors.

Methods: This study included 4005 patients, mean age 58,9±12,6 years, 1975 or 49,3% males and 2030 or 50,7% femals. Patients were divided in four groups according to age: group I 30-39 years, II 40-59, III 60-65, IV > 65 years and also were sex-stratified. All patients were evaluated for hypertension, systolic and diastolic blood pressure, dyslipidemia, diabetis, obesity, smoking, exposure to stress and left ventricular hypertrophy (estimated by echocardiography, based on left venticular mass index-LVMI, and relative wall thickness-RWT).

Results: The results are presented in Table 1. Hypertension was more common in younger and middle aged women and RWT significantly higher especially in group of women older then 65 years, suggesting a higher percentage of left ventricular concentric hypertrophy or concentric remodeling in women. Furthermore, family history had a more negative influence on CHD in women (1718 (84,6) vs 1601 (81,1), p=0,002) compared to men in the whole group of patients. Smoking was more common and incidence of myocardial infarction significantly higher among men. BMI was significantly higher among men, and also LVMI, with lower RWT probably due to the large number of patients with eccentric left ventricular remodeling.

Conclusion: This finding indicates that the pathogenesis of CHD is very similar for men and women. Smoking has been found to have a greater impact on CHD risk in men compared to women, while family history has a more negative influence on CHD in women than in men. The majority of cardiovascular risk factors show no important differences between the genders.

Keywords: coronary heart disease, risk factors, age differences, sex differences

BLOOD PRESSURE LOAD AND BLOOD PRESSURE VARIABILITY AS MARKERS OF POOR CONTROL OF HYPERTENSION

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[1]HISPA center Kragujevac, Clinic of Cardiology, Clinical center Kragujevac, , Kragujevac, Serbia
[2]University Hospital Center "Dr Dragisa Misovic-Dedinje", Belgrade, Serbia
[3]Cardiovascular Institute „Dedinje", Belgrade, Serbia

Background: Blood pressure load is defined as the percentage of readings in a given period, usually 24-h, which exceed a predefined threshold value, typically set at the proposed normality level for average BP values of that period. Studies have shown that normal values are <15% for systolic and <9% for diastolic blood pressure load. Clinical evidence shows that both short- and long-term blood pressure variations occurring during a 24-h period increase progressively as subjects advance from normotensive to hypertensive. Unstable BP may also be an indication that antihypertensive treatment is being ineffective and ABPM will demonstrate both the efficacy of treatment and the smoothness of BP reduction. Aim was to investigate the level of BP load and variability as markers of poor control of hypertension.

Methods: Research included 200 patients observed in HISPA center Kragujevac, Serbia, during the one year period. Patients had baseline and control visits, after 3 or 6 months, with the results of all specific diagnostic methods. All patients underwent ABPM and the parameters were estimated according to the latest ESC/ESH recommendations. We calculated 24-h, daytime and nighttime BP loads separately for systolic and diastolic BP. We used 20% as threshold for higher BP load. For 24h blood pressure variability we used a threshold for standard deviation of 15% for systolic and 9% for diastolic to define the groups with normal and higher variability. All data were statistically analyzed in the SPSS for Windows.

Results: Study population consisted of 135 (67.5%) of male and 65 (32.5%) of female subjects. Mean age of the population was 55.19±11.24 years. Previous hypertension was present in 165 (82.5%) of patients (x^2; p=0.000), duration of hypertension was in 87 (43.3%) patients between 1 and 10 years (x^2; p=0.003), and 154 (77%) already were on antihypertensive therapy (x^2; p=0.000). Mean values of BP load were in mmHg: dSBP-38.18±28.24; nSBP-54.04±35.73; 24h-SBP-43.38±28.70; dDBP-31.64±25.42; nDBP-31.07±27.02; 24h-DBP-30.99±23.95. All blood pressure load parameters in patients on antihypertensive therapy were significantly elevated, higher than 20%, except for 24h-DBP load. Blood pressure variability, defined through standard deviation of 24h values was >15% for systolic BP in 144 (72%) patients (x^2; p=0.000), with an average of 19.04±7.16 mmHg (t-test; p=0.000), and >9% for diatolic BP in 168 (84%) patients (x^2; p=0.000), with an average of 16.06±6.76 mmHg (t-test; p=0.000). Average 24h BP values were normal in the significant majority of patients.

Conclusion: 24h blood pressure values can entice us to think that hypertension is controlled, but we should look beyond this values for furhter estimation. High blood pressure load and blood pressure variability levels in study group showed us that although it seems that hypertension is controlled according to average BP values, it was significantly uncotrolled according to these parameters. Possible reasons for poor control could be bad adherence, subdosing of antihypertesives or inadequate daily dosing. BP load and BP variability should therefore be parameters we include when we make the individual therapeutic approach.

Keywords: blood pressure load, blood pressure variability, uncontrolled hypertension

CAROTID INTIMA MEDIA THICKNESS –GENDER AND AGE DISTRIBUTION AT OBESE ADOLESCENTS

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Background: Carotid intima media thickness c IMT, ultrasound (US) measurement from the common carotid artery in children, is useful tool for screening risk factors for CVD. Increased prevalence of high risk children for subclinical atherosclerosis in obesity, dyslipidemia and diabetes, with growth trend CVD risk factors, indicate using reliable and reproducible method for determining c IMT. Detection in early stage of atherosclerotic process by US as a useful tool is possible through use of trained person and quality equipment. Data analysis using noninvasive assessment is a great help to medical providers in prevention vascular complications. Evaluate relation c IMT and BMI according the gender and age in obese children, patients from endocrinology and cardiology ambulance, with BMI higher that P 97.

Methods: US was performed with Vivid US system, with linear sound by one educated person for US diagnostic. Included criteria was, children from 10 to 18 age, group I with BMI up P 90 to P 97, and group II, obese BMI over P 97, with evaluated lipid status (HOL ,HDL. LDL, TG), dyslipidemia, and positive atherogenic index HOL/HDL, LDL/HDL.

Results: Data collected from 72 pediatric patients (8-18 years old), find 35 adolescents (13-18 years old) 21girls and 14 boys with higher cIMT, (from 0,6 to 1,1 mm, med 0,7). High BMI, 45% according age, and 68% according gender, by med for age, more form 12 to 15 age. Positive correlation cIMT with BMI at girls more in older. At boys, higher cIMT no correlation with BMI and age. In group I, no gender difference, but higher changes cIMT at girls in group II.

Conclusion: EASO guide propose evaluation comorbidity before obese diagnosis. Explore cIMT at obese adolescents shows positive risk for CVD. Detection elevated cIMT is important tool for planning needs for obese therapy instruments.

Key words: children obesity, IMT a.c. children, correlation BMI and IMT according gender, EASO guide

COMPARATIVE CLINICAL AND ANGIOGRAPHIC CHARACTERISTICS OF PATIENTS WITH ARTERIAL HYPERTENSION, DIABETES AND MYOCARDIAL INFARCTION

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Background: Arterial hypertension is one of the most significant risk factors for the development of blood vessels atherosclerosis, coronary artery disease and myocardial infarction. Diabetes mellitus is an independent risk factor for coronary disease associated with the rapid progression of obstructive atherosclerotic lesions of the coronary arteries and myocardial infarction. The aim of this study was to examine the influence of hypertension and diabetes on the clinical and angiographic characteristics of patients with myocardial infarction.

Methods: The study included 125 patients with infarction, 67 with hypertension, non-diabetic patients (57.2 ± 8.3), 52 (77.9%) men and 15 (22.4%) women and 58 with hypertension, diabetics (58.6 ± 8.9), 42 (724%) men and 16 (27.6%) women. There was no statistically significant difference in age (p> 0.05) and poles (p> 0.05) between groups. Clinical, laboratory, ECG and echocardiographic examinations and selective coronarography were applied.

Results: Patients with hypertension, non-diabetic patients, compared to diabetics, have a frontal infarction of 50.7% vs 48.3% (p> 0.05), anterior-lower in 13.4% vs 10.4% (p> o, O5) and lower in 35.8% versus 41.4% (p> 0.05). Myocardial reinfarction had 19.4% non-diabetics and 27.6% diabetics (p> 0.05). The average ejection fraction of left ventricle, non-diabetic patients, is 50.7% ± 10.2%, and diabetics 47.2 ± 10.3% (p> 0.05). Rhythm and conduction disorders were found in 11.9% of non-diabetic patients and 32.7% of diabetics (p <0.01). In non-diabetics there was hyperlipidemia in 77.5% and the incidence of smoking in 65.6%, and in diabetics, hyperlipidemia in 91.4% and smoking in 43.1%. Significantly greater incidence of hyperlipidemia in diabetic patients compared to non-diabetic patients (p <0.05), and the incidence of smoking is significantly higher in non-diabetic patients (p <0.01). Three-vessels coronary disease was found in 40.3% of non-diabetic patients and 87.9% of diabetics (p <0.01), and multi-vessels disease, in 59.7% of non-diabetics and 91.4% of diabetics (p <0.01). Single-vessels disease had 37.3% non-diabetics and 5.2% diabetics (p <0.01). Without stenosis there were 3.0% non-diabetics and 3.4% diabetics (p> 0.05). Of individual coronary arteries, most commonly there was LAD stenosis, in 76.1% of non-diabetic patients and 93.1% of diabetic patients (p <0.01). The main tree disease was 8.9% non-diabetic and 10.3% diabetic (p> 0.05).

Conclusion: Patients with hypertension and diabetes have significantly more frequent hyperlipidemia, rhythm and conduction disturbances, a three-vessels and multi-vessels coronary disease and LAD disease, more left main coronary artery disease and a lower ejection fraction of the left ventricle compared to patients with hypertension, non-diabetics, which means that diabetes melitus is a remarkable risk factor for the formation of more complex lesions of the coronary arteries and poorer parameters of the cardiac function.

Keywords: boldarterial hypertension, diabetes, myocardial infarction

CORRELATION BETWEEN OBESITY AND HIGH BLOOD PRESSURE OF PATIENTS IN HISPA CENTER IN PIROT: A PROSPECTIVE STUDY

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Background: HISPA center in Pirot was established on 24.09.2015. For 2 years, in our center have been registered 145 patients. With the prevalence of obesity, which should already be considered as a pandemic phenomenon (with all accompanying health risks) both, prevention and health education, as well as identifying predictors for the development of obesity-related diseases are primary. The aim of the study was to investigate the correlation between obesity and high blood pressure values of patients which are registered and treated in HISPA center in Pirot.

Methods: Prospective study included 145 randomly selected hypertensive patients (92 men and 53 women, age 66.30±18.70 years), who were divided, according to body mass index (BMI≥30 kg/m^2), to groups of obese (n=41) and non-obese examinees (n=104). The study includes values which are measured on reception of the patient after first visit, before adding antihypertensive therapy to their daily routine, and consulting about non-medical measures and life style changes of losing weight and lowering blood pressure. Obesity was defined as BMI, as the parameter of total obesity. Values of systolic blood pressure (SYS) and diastolic blood pressure (DIA) were measured in sitting position on left upper arm and recorded after one measure.

Results: The values of SYS and DIA were significantly higher in the group of obese hypertensive patients than in the group of non-obese patients. The average value of SYS in group of obese patients was 143.54mmHg, the highest recorded value was 180mmHg, the lowest was 110mmHg, and 73.17% of patients in obese group had value of SYS above 140mmHg. The average value of SYS in group of non-obese patients was 134mmHg, the highest recorded value was also 180mmHg, the lowest was 90mmHg, but 44.23% of patients in this group had value of SYS above 140mmHg. The average value of DIA in group of obese patients was 87.73mmHg, the highest recorded value was 110mmHg, the lowest was 60mmHg, and 58.54% of patients in obese group had value of DIA above 90mmHg. The average value of DIA in group of non-obese patients was 83.34mmHg, the highest recorded value was also 110mmHg, the lowest was 60mmHg, but 28.85% of patients in this group had value of DIA above 90mmHg.

Conclusion: Our findings suggest an association between parameters of obesity and increased values of systolic and diastolic blood pressure. In the coming period of time, after scheduled control inspections, we are going to keep track of how patients' parameters changing after taking antihypertensive therapy and following non-medical measures and life style changes and see how reduction of body weight was associated with reduction of blood pressure values, which may explain lower cardiovascular risk in obese-related disease.

Keywords: obesity, hypertension, cardiovascular risk

DOES THE AGE AND USE OF ORAL ANTICOAGULANTS CORRELATE WITH INCIDENCE OF STROKE IN PATIENTS WITH NON VALVULAR ATRIAL FIBRILLATION? INSTITUTIONAL EXPERIENCE

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Background: Atrial fibrillation (AF) is strong independent risk factor which increases the incidence of stroke. It is proven that oral anticoagulants (OAC) and novel oral anticoagulants (NOAC) significantly reduces the risk of stroke for more than 70%. Our goal is to confirm the effect of age and OAC/NOAC on outcome in patients with stroke and non valvular AF.

Methods: We identified 292 patients with acute brain infarction, mean age 81 years (193 female and 99 male) with previous history of hypertension and non valvular AF. In all patients were performed blood analysis, ECG, cranial MSCT, color Doppler ultrasonography of the main neck arterial vessels (CDS MAV), and all patients were examined by a specialist of internal medicine and neurologist.

Results: Among of all patients due to the results of cranial MSCT we detected in 135 pts (46.2%) a severe cerebral infarction, in 147 (50.4%) lacunar and smaller stroke, and in 10 pts. (3.4%) intracranial hemorrhage. CDS MAV showed severe atherosclerotic changes in only 46 pts. (15.8%). Prior to the stroke, 101pts (34.6%) was taking OAC, and 191 pts (65.4%) was without OAC or NOAC. In the group of pts. taking OAC, 20 pts. died (19. 8%), and in the group of pts who did not receive OAC died 139 patients (72.8%).

Conclusion: The results of this study shows the decreased death rate among the patients older than 75 years with the acute stroke and AF who received OAC, compared with the group of patients with AF and acute stroke who did not received OAC.

Keywords: stroke, atrial fibrillation, oral anticoagulants OAC/NOAC

EARLY DETECTION OF ASYMPTOMATIC LEFT VENTRICULAR DYSFUNCTION IN HYPERTENSIVE PATIENTS

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Background: Hypertension is potent risk factor for congestive heart failure (CHF). Development of overt CHF may be preceded by a phase of asymptomatic left ventricular systolic dysfunction. The aim of this study was early detection of alteration in left ventricular systolic function.

Methods: 120 hypertensive patients, with preserved ejection fraction (EF), were divided in three groups according LV diastolic function: normal (n=40), abnormal relaxation (Grade I, n=37) and pseudo normal (Grade II, n=43). Left atrial diameter (LA), left atrial volume index (LAVI), left ventricular mass index (LVMI), left ventricular dimensions and volume indexes (EDVI and ESVI) and EF were estimated by echocardiography. We measured corresponding velocities from tissue Doppler at the level of the septal mitral annulus (Em; Am; Sm), including E/Em. The same measurements were repeated after three years.

Results: Close correlations were found between Sm and EF (r=0.349;p=0.0009), LVMI (r=-0.222; p=0.015), EDVI (r=-0.394; p=0.0004) and ESVI (r=-0,394; p=0.0009), LA (r=-0,290; p=0.001) and LAVI (r=-0.419; p=0,0002). Levels of LA (3,56 vs. 3,83 vs. 4,39; p=0.0001), LAVI, (32.0vs35.5vs44.5; p=0.0001), LVMI (104.3vs112.5vs123.0; p=0.0004) and ESVI (32,6vs41.9vs44.9; p=0.0004), progressively increased from the normal group through LVDD Grade I and II groups. Significantly different values of EF (63vs61vs59; p=0.003) and Sm (0.074vs0.067vs0.059; p=0.003) were obtained between groups too, but with progressively decrease from the normal group through LVDD Grade I and II groups. General linear model for repeated measures showed increase of EDVI (F=50.009; p<0.01), ESVI (F=42.744; p<0.01), LVMI (F=27.648; p<0.01) and LAVI (F=17.083; p<0.01) during three years, with significant time difference, but without significant difference between groups, these parameters enlarged in all groups almost at the same manner. Sm also significantly changed during three years with significant time difference (F=128.24;p<0.01) and with significant difference between groups (F=4.597;p< 0,05), Sm decrease in all groups, but most expressed in LVDD Grade II

Conclusion: Left ventricle EF was not sensitive indicator for detection of subclinical systolic dysfunction, but decrease of Sm appeared as the first sign of systolic abnormalities following established diastolic dysfunction and was the clear reflection of LV remodeling process. This suggests that Sm may aid in the identification of patients at high risk for development of CHF who need preventive treatment.

Keywords (boldirano): left ventricular dysfunction, hypertension

ENDOTHELIAL DYSFUNCTION, HOMOCYSTEINE, PARAOXONASE AND HDL: THE MISSING LINK BETWEEN LIPID'S AND PROTEIN'S THEORY OF ATHEROSCLEROSIS

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Homocysteine (Hcy) is an independent risk factor (or risk marker) for heart attack, stroke, birth defects, Alzheimer's disease, neurodegenerative diseases, renal failure, osteoporosis and cancer. It is believed that hyperhomocysteinemia leads to oxidative stress, endothelial cell damage, reduction in the distensibility of vessels, and alters the process of haemostasis. Furthermore, hyperhomocysteinemia may lead to an enhancement of the adverse effects of risk factors like hypertension, smoking, increased lipids as well as promotion of the development of inflammation and oxidative stress. The thioester homocysteine thiolactone (Hcy-thiolactone), product of an error editing process during protein synthesis to remove the non-protein amino acid homocysteine (forms when Hcy is mistakenly selected by methionyl-tRNA synthetase), is extremely prooxidant/toxic metabolite (including LDL cholesterol), and also risk factor for many diseases. The accumulation of Hcy-thiolactone and N-Hcy-protein greatly increases in genetic or nutritional hyperhomocysteinemia. Mammalian organisms, including human, have evolved the ability to eliminate Hcy-thiolactone with enzyme paraoxonase 1 (subtype PON1), which has the ability to hydrolyze Hcy-thiolactone, thus decreasing Hcy-thiolactone and N-Hcy-protein accumulation. The paraoxonase family comprises three enzymes (PON1, PON2 and PON3) with structural homology and common antioxidant properties. The enzymatic activities of PONs include paraoxonase, arylesterase and lactonase, which catalyse the hydrolysis of organophosphates, aromatic esters and lactones, respectively. Serum paraoxonase 1 is synthesized in the liver and attached to high-density lipoproteins (HDL) in the blood, but recent studies demonstrate that PON1 is also present in the brain. PON1 protects against high-fat diet-induced atherosclerosis in mice and humans, and could protect against cardiovascular risk by hydrolyzing Hcy-thiolactone, thereby minimizing protein damage. A finding that the natural Hcy-thiolactonase activity of PON1 is a predictor of coronary heart disease is consistent with such function. However, PON1 exhibits a wide range of physiologically important activities, including Hcy-thiolactone detoxification, drug metabolism, and detoxification of nerve agents. PON1 hydrolyzes the toxic oxon metabolites of organophosphorous insecticides, including parathion, diazinon, and chlorpyrifos, nerve agents, such as sarin and soman, aromatic esters, a variety of aromatic and aliphatic lactones as well as Hcy-thiolactone. In addition, drugs used for the prevention or treatment of cardiovascular disease may modulate plasma homocysteine levels (especially lipid-lowering drugs and anti-hypertensive drugs) and influence complex Hcy metabolism. Thus, a drug induced homocysteine increase may counteract the desired cardioprotective effect. This work has been supported by the Ministry of Education, Science and Technological Development of Republic of Serbia, grant number 175043, COST Action BM1005 "Gasotransmitters: from basic science to therapeutic applications (ENOG: European Network on Gasotransmitters, 2011-2015)", and COST Action CA16225 "Realising the therapeutic potential of novel cardioprotective therapies (EU Cardioprotection, 2017-2021)".

Keywords: endothelial dysfunction, homocysteine, paraoxonase, HDL

EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN NEWLY DIAGNOSED OSA PATIENTS WITH ESH GRADE I HYPERTENSION AND PRESERVED EJECTION FUNCTION

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Background: Obstructive sleep apnea is a serious and very common sleep disorder which is associated with many cardiovascular comorbidities. The aim of this study is to evaluate effect of OSA on diastolic left ventricular function in newly diagnosed patents with ESH grade I hypertension.

Methods: Thirty-one patents with newly diagnosed obstructive sleep apnea and ESH grade I hypertension with preserved ejection fraction and twenty-seven patents without obstructive sleep apnea but with ESH grade I hypertension and preserved ejection fraction are enrolled in this study. All patients underwent polysomnography, 24h ambulatory blood pressure measurement and echocardiographic examination which included standard transthoracic echocardiographic measurements and derived tissue Doppler measurements. Both groups were age and sex matched, without any known comorbidity except ESH grade I hypertension.

Results: Study showed that there were significant difference in E/A ratio which was abnormal in 21 patients (67.7%) with newly diagnosed OSA group compared with 11 patients (40.7%) in control group ($p<0.005$), mean value of mitral inflow E wave was 0.68±0.13 in newly diagnosed OSA group compared to 0.89±0.15 in control group ($p<0.005$), isovolumetric relaxation time in newly diagnosed OSA group were prolonged, OSA group 94.4±12.1 ms compared to 84.3±8 ms in control group ($p<0.005$).Tissue doppler E` wave velocity in newly diagnosed OSA group was 6.9±2.4 m/s compared to control group 8.1±1.4 m/s ($p<0.005$).

Conclusion: Obstructive sleep apnea independently contributes to impaired diastolic function in patents with ESH grade I hypertension and preserved ejection function.

Keywords: OSA, echocardiography, hypertension, diastolic function

FIRST HUNDRED PATIENTS – RETROSPECTIVE EPIDEMIOLOGICAL STUDY – HISPA CENTER VRANJE

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Background: HISPA Center "Vranje" was founded on 7th of May 2015. It works within the specialist clinics of the Department of Internal Medicine General Hospital Vranje. It actively started to work 1st of March 2016, due to technical, organizational and other problems. It has a team of doctors from the Department of Internal Medicine headed by Dr. Vladan Mitic – internist. The Center is open in order to identify, diagnose and treat patients with high cardiovascular risk, namely patients who have a high probability for the occurrence of heart attack and stroke. We use the space, infrastructure and diagnostic equipment of the Department of Internal Medicine. Work at the Center is based on the personal commitment and enthusiasm of employees, with one aim: lead to a higher level the health status of our population.

Results: Patients who have appeared in our HISPA Center "Vranje" and live in our environment are evenly distributed by gender (♂ 51% , ♀ 49%), obese (body mass index aver. 28,8, waist volume aver. 97cm), heterogeneous age (from 21 to 76 years). The largest number of patients (89% ♂ , and 86% ♀) was in the age group of 40 to 70 years. Patients in our Center occurred due to a variety of ailments but they usually were: fatigue, shortness of breath and palpitations. The most important risk factors for cardiovascular disease were: hypertension, dyslipidemia, stress and family burden. The values of ambulatory measured blood pressure were in the zone of optimal values: 136,9 mmHg systolic, diastolic 87,4 mmHg. 29,5% of our patients had a systolic blood pressure higher than 140 mmHg and 28,4% of them had a diastolic blood pressure higher than 9 0mmHg. More than 85% of patients were in the zone of low to moderately high cardiovascular risk. The most common diagnoses sets in our Center were: hypertension, dyslipidemia, obesity and diabetes.

Conclusions: We have to to treat better comorbid conditions and disease with consultative examinations of other specialists. Pharmacological therapy: equal representation of all antihypertensive drugs, we should be given more AT II receptor blockers, fixed drug combinations, earlier introduce of supplements. Non-pharmacological therapy: more advise a healthy diet, the emphasis placed on enhancing physical activity and more frequently advise a reduction in body weight.

Keywords: risk factors, hypertension, blood pressure, dyslipidemia

FIXED COMBINATIONS IN THE TREATMENT OF ARTERIAL HYPERTENSION

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Background: The approach in the treatment of hypertension (HTN) can be accomplished through single or combined drugs. However, achievement of targeted blood pressure with a single antihypertensive agent is difficult. In fact, studies have shown that only a small number of patients with high blood pressure undergo monotherapeutic treatment. In addition, in certain groups of patients, especially those with significantly increased blood pressure and at high risk of unwanted cardiovascular events, it is recommended to start therapy with a combination of two drugs. The aim of our study is to determine the incidence of various therapeutic modalities (i.e. monotherapy, free individual combinations, single-pill combinations as well as their common application) and examine the relationship between patients characteristics (i.e. age and duration of HTN) in relation to their antihypertensive treatment in the Center for HTN of the Institute for Cardiovascular Diseases Dedinje (ICVDD).

Methods: We collected and analyzed data (i.e. blood pressure, demographic data, medical history, duration of HTN, current therapy and family history) of 300 outpatients with primary HTN grade 1 and 2 who were treated from January to December 2014 at the Center for HTN of ICVDD.

Results: More than three quarters of the patients were receiving a combined therapy (two or more drugs), while the rest were under monotherapeutic treatment. In relation to the method of administration of drugs, from 76.7% of the patients who received polytherapy, 27.7% received free individual combination, 16.3% single-pill combination and 32.7% received both free individual and single-pill combination. Oder patients as well as those who have hypertension for a long time have received more substances in therapy. The percentage of patients achieving target blood pressure of ≤140 / 90mmHg was 45.7%, with a greater percentage of women among them. The majority of patients had hypertension for one to five years.

Conclusion: HTN treatment is done mainly by combination therapy at the Center for HTN of ICVDD. The number of drugs the patients received correlates directly with their age and duration of high blood pressure. Blood pressure control is at the same level as well as in developed countries.

Keywords: hypertension, monotherapy, combination therapy

FREQUENCY OF DYSLIPIDEMIA, LIPID LEVEL AND ATHEROGENIC INDEX VALUES IN INDIVIDUALS WITH DIFFERENT CATEGORIES OF OBESITY

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Background: Abnormalities in lipid metabolism are very common in obese people. About 60-70% obese people with dyslipidemia and 50-60% with increased body weight. Aim. The aim of the paper was to determine the frequency of dyslipidemia, lipid levels and atherogenic index values in persons with different categories of obesity.

Methods: The study is covered 184 persons (68.3 ± 22.8), 105 women (69.0 ± 12.0) and 79 men (68.3 ± 11.8) (p> 0.05), 42 normal (BMI <25.0 kg / m^2) and 142 overweight (BMI≥25.0 kg / m^2). Based on BMI, respondents were classified into different categories of nutrition: normal (18.5-24.9) 42 (70.3 ± 11.8), increased body weight (25.0-29.9) 60 (71.7 ± 11,1), obesity I (30,0 - 34,9) 43 (66,2 ± 11,8), II (35,0 - 39,9) 31 (63,7 ± 11,2) , III degree (> 40.0) 8 (67.3 ± 8.7), total obese 82 (65.3 ± 11.4).

Results: The incidence of dyslipidemia in obesity I is 34.9%, II 41.9%, III degree 62.5%, total obese 40.2%, increased body weight 21.7%, normally fed 19.0%. Obese have a significantly higher incidence of dyslipidemia than normally fed (p <0.01) and with increased body weight (p <0.05). Normally nourished have lower levels of cholesterol, LDL-C and HDL-C compared to total obese, but this is statistically not significant (p> 0.05). Obese have a significantly higher triglycerides (TG) level (p <0.01) and significantly higher incidence of elevated triglycerides (p <0.01) than normal naturally fed. Normally nourished have a lower incidence of elevated cholesterol (p> 0.05) and significantly lower incidence of elevated LDL-C versus obesity (p <0.01). Obese have an insignificantly lower incidence of diminished HDL-C levels compared to normally fed (p> 0.05). Cholesterol / HDL-C ratio is normally fed 4.04 ± 1.13, total obese 4.08 ± 1.11, obesity I 4.01 ± 1.30, II 4.06 ± 1.19, III degree 4 , 05 ± 1.49. There is no significant difference in the value of risk factors between naturally fed and total obese (p>0.05). The index of atherosclerosis of LDL-C / HDL-C is normally fed to 2.18 ± 0.78, total obese 2.35 ± 0.92, obesity I 2.37 ± 1.01, II 2.36 ± 0.87, III degree 2. 24 ± 0.59 (p>0.05). The average value of TG / HDL-C ratio is normally fed to 0.93 ± 0.36, total obese 1.37 ± 0.70, obesity I 1.22 ± 0.66, II 1.47 ± 0.69, III degree 1.76 ± 0.46. There is a significantly higher value of TG / HDL-C ratio obesity (p <0.05) obesity II (p <0.01), III degree (p <0.01) than normal naturally fed.

Conclusion: With BMI growth, frequency increases dyslipidemia, cholesterol level and levels of LDL-C, HDL-C, TG. Obese have significantly higher levels of TG, values of TG/HDL-C ratio, higher incidence of elevated TG, LDL-C. There were no significant differences in levels of total cholesterol, HDL-C and LDL-C, values of cholesterol/HDL-C and LDL-C/HDL-C ratio between obese and normally fed.

Keywords: obesity, lipids, dyslipidemia, aterogenic index

HOMA-INDEX IN THE EVALUATION OF THE MAJOR ADVERSE CARDIAC EVENTS IN HYPERTENSIVE PATIENTS - SIX MONTHS AFTER REVASCULARIZATION

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Background: HOMA-index (homeostatic model assessments insulin-resistance) is parameter of a direct evaluation of insulin sensitivity. The ability to predict major adverse cardiac events (MACE) by the parameters of insulin sensitivity is still controversial. High blood pressure (HBP) is the most common single risk factor for CAD. Evaluation of the HOMA-IR index in the patients after complete revascularization, which have or not have HBP, in assessing the existence of coronary artery disease (CAD), its extensiveness and frequency of MACE occurrences one and six months after revascularization.

Methodology: HOMA-index is mathematical formulation defined as a ratio of serum glucose level and fasting insulin. HBP was defined by values of systolic and diastolic pressure. Hypertensive patients were graded in relation to the recommended values (have/have no HBP). After invasive cardiology diagnostics, patients were divided into group with or without CAD and CAD is graded in relation to the number of severely narrowed vessels, the one-, two-, three-, four-and-more-vessel disease.

Results: The study included 188 patients (60±8.7years), 75.5% were male, who underwent clinical and labaratory assessment. HBP have 88,9% pts. (SBP 129.9±22mmHg; DBP 75.4±11mmHg). There was no differences in SBP in relation to gender, but DBP was significantly highter in male pts. (p=0.625; p=0.04). HOMA index was significantly higher in male group (9.7 vs 7, p=0.05). We found negative correlation between value of HOMA-index in HBP pts who have or not have CAD. HOMA index was higher in pts. without of HBP and CAD in contrary of group with HBP and CAD (11.4±9 vs. 9.53±9, p=0.05). There is pozitive correlation in HOMA index among pts. with CAD and with and without of HBP (9.5±9 vs 6.3±2, p=0.05). HOMA-index was significantly higher in HBP patients with more extensivity of CAD (p=0.0001). We found negative correlation between value of HOMA-index and presence of MACE after one month among pts with or without HBP (7.3 vs, 10, p=0.03) and pozitive correlation according to not have MACE after one month in HBP pts. (8.7 vs, 7.1, p=0.843). Hypertensive pts with elevated value of HOMA-index have significantly more MACE after 6 months (5.2 vs, 10.6, p=0.003)

Conclusion: HOMA-index is an excellent predictor MACE in hypertensive patients in med-term follow-up.

Keywords: HOMA index, hypertension, revascularization

INCIDENCE AND RISK FACTORS OF ISCHEMIC STROKE IN HYPERTENSIVE PATIENTS

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Background: Of the risk factors for stroke, hypertension appears to be the most important. The aim of this study was to describe the epidemiology of ischemic stroke in hypertensive patients.

Methods: The study included 3112 hypertensive patients (1468 or 47,2% males and 1644 or 52,8% femals, mean age 60±14,0 years), divided into two groups according of ischemic stroke: group of 2994 hypertensive patients without of ischemic stroke history and group of 118 patients with previous ischemic stroke (IS). All involved patients underwent clinical examination, with anthropometric measurements (body mass index (BMI) and waist size), ECG analysis and echocardiography. Left atrial diameter, end-diastolic and endsystolic left ventricular diameters, left ventricular ejection fraction, relative wall thickness and left ventricular mass index were measured by echocardiography. All patients were evaluated for traditional risk faktors hypertension, dyslipidemia, diabetis, smoking and exposure to stress.

Results: Hypertensive patients with IS were significantly older (65,7 ± 10,0 vs 59,9 ± 14,1, p<0,001), with significantly higher systolic blood pressure (147,4 ± 24,2 vs 139,8 ± 23,0, 0,006) and greater duration of hypertension (11,8 ± 8,6 vs 8,7 ± 8,0, p=0,001) compared with hypertensive patients without IS. Furthermore, diabetes was more common in patients with IS (34 (28,8%) vs 528 (17,6%), p=0,002), and with a large number of smokers (52 (44,1%) vs 1239 (41,4%), p=0,001) compared to group without IS. There were no diffeneces in gander, BMI, waist size, dyslipidemia, exposure to stress, eletrocardiography criteria for left ventricular hypertrophy and echocardiography parameters between two groups.

Conclusions: In hypertensive patients ischemic stroke was associated with age, systolic blood pressure level and duration of hypertension. Higher incidence of ischemic stroke is also connected with the association of hypertension with diabetes and smoking habits.

Keywords: ischemic stroke, hypertension

INFLAMMATION AS A PREDICTOR FOR CAROTID RESTENOSIS AFTER EVERSION ENDARTERECTOMY

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Background: The aim of this paper is to evaluate predictive value of inflammatory markers (high-sensitivity (hs)-CRP, fibrinogen, C3 complement) in carotid restenosis development after eversion endarterectomy.

Methods: From March 1st till August 1st 2010, a total of 300 patients underwent eversion carotid endarterectomy (CEA). HsCRP, C3 complement and fibrinogen were analysed on the day of the surgery (06h), 48h after the surgery and after 1 month, 6 months, 1 year and 2 years thereafter. During the follow up, all patients underwent colour duplex scan evaluation and computed tomography (CT) angiography if indicated. We have also created 'Inflammation score' consisted of values of inflammatory factors (hsCRP, C3 complement and fibrinogen) taken just before and just after the surgery (6 parameters altogether).

Results: Patients with increased hs-CRP just before the surgery (06h) had increased risk of carotid restenosis after one year follow up as well as patients with increased fibrinogen 48h after the surgery. Patients who were not taking aspirin after the surgery had increased risk of carotid restenosis as well. Gender showed to be independent predictor of restenosis with females having higher risk during the follow up, (odds ratio = 0.351; p=0.030). Males taking aspirin with inflammation score >2 had increased risk of restenosis when compared to males with inflammation score <2. We have created 3R formula (Restenosis Risk Rate) using the data referring to aspirin use (taking/not taking) and fibrinogen values 48h after the surgery (normal/elevated) to identify patients with high risk of early restenosis. An algorithm of therapeutic options has been also created to decrease restenosis rate in such patients. Patients with hypothyreosis had increased risk of restenosis as well.

Conclusion: Inflammation plays a significant role in carotid restenosis development after eversion endarterectomy. Identification of high-risk patients for restenosis by 3R formula we could influence more aggressive statin and antiplatelet therapy following endarterectomy that might result in decreased overall restenosis rate.

Keywords: carotid restenosis, hsCRP, fibrinogen, inflammation.

METABOLIC SYNDROME AS A RISK FACTOR FOR IN PATIENTS WITH PREVIOUS CARDIAC EVENTS - MYOCARDIAL INFARCTION, PERCUTANEOUS OR SURGICAL REVASCULARIZATION

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Background: According to the latest World Health Organization data, 17.5 million people die each year from cardio vascular disease (CAD), an estimated as 31% of all deaths worldwide.

Objective: We would like to evaluate the incidence of metabolic syndrome (MetS) in patients with previous myocardial infarction (MI), or previous revascularization and to determine the impact of MetS, in the progression of atherosclerosis.

Methods: MetS is defined by International Diabetes Foundation criteria. We evaluated previous MI, percutaneous coronary intervention (PCI) and aorto-coronary bay-pass (ACB). Coronary artery disease (CAD) is graded in relation to the number of vessels which were severely stenostic (normal findings, one-, two-, three-, four-and multi-vessel CAD disease).

Results: The study included 837 consecutive patients. 75.6% met the criteria for MetS. Incidence for CAD in those who have or not MetS, was not significantly different (p=0.088). MI had 436pts (52%) MI more often had men (p<0.01), mostly younger than 50 years (61.6%)(p=0.095). MetS was not significantly presented among those who had or not MI (75.9% vs.75.3%) (p=0.882). Previous PCI had 96pts (11.5%), ACB 88pts (10.5%). No differences between gender in the PCI group (p=0.770), ACB is slightly more common in male pts. (p=0.051). In the oldest group, PCI was less frequent (p=0.083). ACB significantly more frequent in the oldest group (p<0.05). Pts. who had previous MI and have MetS, have frequently higher degree of CAD (p=0.022), compared with those who do not have MetS. In patients who had previous PCI procedure, MetS were more frequent in two and three vessel disease, while those who do not have MetS were almost equally represented in all groups irrespective of the severity of CAD (p=0.05). Patients who had previous ACB, had a significantly higher percentage of pts with MetS in all CAD groups compared to those who did not have MetS (p=0.023).

Conclusion: Relative presentation of MetS in patients with previous MI, PCI or AOC is significantly high, and have positive relation to severity of CAD.

Keywords: metabolic syndrome, myocardial infarction

METHIONINE VERSUS HOMOCYSTEINE: FUTURE DIRECTIONS IN CARDIOVASCULAR RESEARCH

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L-methionine, the principal sulfur-containing amino acid in proteins, has important roles in cell physiology as an antioxidant, and in the breakdown of fats and heavy metals. Methionine is the precursor of homocysteine, and participates in the methylation and transsulfuration pathways. Elevated total plasma homocysteine (hyperhomocysteinemia) is associated with atherosclerosis, thromboembolic disease and cancer. Whether homocysteine *per se* or a coincident metabolic abnormality (homocysteine-related compounds, thiolactone metabolites) causes vascular disease is still an open question. Animals with genetic hyperhomocysteinemia have so far not displayed atheromatous lesions. However, when methionine-rich diets are used to induce hyperhomocysteinemia, vascular pathology is often observed. Such studies have not distinguished the effects of excess dietary methionine from those of hyperhomocysteinemia. It is known that high methionine diet, not only red meat for example lamb, beef, pork but also chicken meat can induce cardiovascular dysfunction but the mechanisms are unclear. It has been hypothesized that a diet rich in methionine can malfunction the cardiovascular system in three ways: (1) by augmenting oxidative stress, (2) by inflammatory manifestations, and (3) by matrix/vascular remodeling. However, some evidence indicates that an excess of methionine can be harmful for other systems, and can increase the risk of developing type-2 diabetes, certain types of cancer, brain alterations such as schizophrenia, and memory impairment. However this is still controversial because previous studies suggesting the use of L-methionine as a treatment for depression and other diseases indicate that it might also improve memory (role in brain function). Thus, the direction of our research is to further elucidate mechanisms of cardiovascular and neural effects of homocysteine vs. methionine overload.

Keywords: L-methionine, homocysteine

MYOCARDIAL INFARCTION IN THE ELDERY: INCIDENCE AND RISK FACTORS

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Background: Cardiovascular heart disease represents the leading cause of death in both men and women older than 65. Hypertension, dyslipidemia, impaired glucose tolerance, and obesity remain the major modifiable risk factors for most of the coronary disease afflicting the elderly. To determine the incidence of acute myocardial infarction (AMI) in patients over 65 years and its relation to common risk factors.

Methods: We retrospectively studied 1316 patients older than 65 years (mean age 73±13,5), 758 male (57,6%) and 558 female (42,4%), with high percentage of obese and overweight patients (BMI 28,4±4,3). Patients were evaluated for age, sex, dyslipidemia, diabetes, hypertension, smoking and left ventricular hypertrophy.

Results: History of AMI had 128 patients (9,7%), type 2 Diabetes mellitus 303 (23%), arterial hypertension 1106 (84%), dyslipidemia 756 (57,4%) and 345 (26,2%) history of smoking. There was a statistically significant correlation between AMI and smoking duration (p=0,061, p=0,029) and number of cigarets per day (p=0,062, p=0,027).

The relative risk was significantly increased in male over female patinets (RR=0,683, p<0,001); in diabetic patients (RR=0,651, p=0,003); hypertensive patients (RR=0,085, p=0,002), patients with dyslipidemia (RR=0,778, =0,001) and in smokers (RR=0,492, p<0,001).

Conclusions: Patients older then 65 have an increased risk for the development of AIM with male sex and with traditional risk factors such as diabetes, hypertension, dyslipidemia and smoking. Unfortunately hsCRP, homocysteine or novel cardiovascular risk factors (activation of the cytokine cascade, increased oxidative stress, and the presence of modified lipoproteins (Lpa)) were not evaluated. Further research is needed for the study of the importance of novel risk factors for the increased risk of coronary heart disease in older patients.

Keywords: myocardial infarction, risk factors

NEUROGENIC HYPERTENSION – ENTITY WE FORGOT. ARE WE TREATING IT CORRECTLY?

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Background: Essential hypertension is considered as „neurogenic" when sympathetic overactivity has the min role in its development and maintenance. It was estimated that the prevalence of neurogenic hypertension is about 50% of all cases of essential hypertension. Despite years of investigation, the origin of the sympathetic activation characterizing the essential hypertensive state still remains largely unknown, but it is known that it has its role in both, short and long-term effects on blood pressure levels. Efficacy of RAAS inhibiors made sympathetic overactivity and central antihypertensives very neglected. Aim was to investigate the prevalence of neurogenic hypertension as special entity and level of sympathetic activity.

Methods: Research included 200 patients observed in HISPA center Kragujevac, Serbia, during the one year period. Patients had baseline and control visits, after 3 or 6 months with the results of specific diagnostic methods. Level of stress was estimated using Mayo Clinic test for stress assesment with 6 questions regarding behaviour in common stressfull situations. Heart rate variability obtained by ECG Holter monitoring was used to estimate the level of sympathetic activity. LF/HF ratio > 2.0 was used as a marker of sympathetic overactivity. We used both time and frequency domain analysis of HRV as confirmation. Data on previous hypertension and 24h average blood pressure levels were used for estimation of the sympathetic control of hypertension.

Results: Study population consisted of 135 (67.5%) of male and 65 (32.5%) of female subjects. Mean age of the population was 55.19±11.24 years. Previous hypertension was present in 165 (82.5%) of patients (x2; p=0.000) and 154 (77%) already were on antihypertensive therapy (x2; p=0.000). ACE inhibitors were administrated in 141 (70.5%) patients (x2; p=0.000), beta-blocker in 120 (60%) patients (x2; p=0.005); central antihypertensives in 40 (20%) patients. Moderate and intensive stress, as assessed per Mayo Clinic criteria was present in 149 (74.5%) patients (x2; p=0.000). LF/HF ratio was >2.0 in 70% of patients confirming that autonomic balance is shifted towards sympathetic activity (t-test; p=0.000). Average values of LF/HF were 4.13±3.06, showing significant sympathetic overdrive (t-test; p=0.000). Moreover, the average values of LFnu confirmed the presence of sympathetc overload (LFnu: 172.15±728.99; t-test; p=0.023). Values of 24h BP assessed by ABPM were higher than 130 mmHg for systolic in 108 (54%) with an average of 130.67±18.23 mmHg and higher than 80 mmHg for diastolic in 104 (52%), with average of 79.69±11.27 mmHg.

Conclusions: Neurogenic hypertension was confirmed in the majority of patients according to level of stress and the proof of sympathetic overload. Level of sympathetic activity was high regardless the use of beta blockers in the majority of patients. Possible explanations are subdosing of beta blocker and lower usage of central antihypertensives. Average blood pressure levels were mostly normal which can be the influence of other antihypertensives, especially ACE inhibitors. Remnant of sympathetic overdrive could influence the transit from controlled to uncontrolled hypertension due to its long-term effects.

Keywords: neurogenic hypertension, sympathetic overactivity, heart rate variability, beta-blockers, central antihypertensives

POLYPHARMACY AND HYPERTENSION

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Background: Hypertension represents one of the most common diseases in family medicine. In the treatment there are several types of drugs. To be selected medication depends on the condition of the patient and the additional diseases (diabetes, cardiac or renal failure, etc.) what could results in such patients taking other medication which leads to polypharmacy. The term polypharmacy is considered to be taking three or more drugs.

The objective of this study was to examine the type and percentage of the most frequently used drugs (ACE-blockers and calcium antagonists) in the treatment of hypertension, the percentage of patients who are on combination therapy and patients who have hypertension and in addition other diseases and the number of patients receiving three or more drugs.

Methods: The study used electronic patient records. The study covers the period of one year and patients were selected randomly. The study included 100 patients.

Results: 80% of patients treated with ACE inhibitors; 44% is receiving beta-blockers and 30% Ca antagonists in therapy. Of these, 37% of patients on combination therapy and 70% of patients have other diseases (heart or renal failure, diabetes, etc.).

Conclusion: They are often experienced by doctors in a dilemma which drug given priority. It is known that the best compliance obtained by use of one drug, once daily. Research shows strong preferences of ACE inhibitors and to the significant number of patients are on combination therapy. Because other diseases, patients have three or more medications, which is why a long-term view can expect side effects becouse of interactions between of drugs.

The most common used drugs are ACE inhibitors, after them beta blockers and Ca antagonists. Patients because of longtime disease and taken a lot of drugs have a side effects because of polypharmacy.

Keywords: hypertension, drugs, ACE inhibitors, beta blockers, Ca antagonists

PREVALENCE OF HYPERTENSIVE END ORGAN DAMAGE IN PATIENTS IN HISPA CENTER KRAGUJEVAC, SERBIA

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Background: The classic manifetations of hypertensive end organ damage are left ventricle hypertrophy, coronary artery disease and systemic atherosclerosis, rethinopathy, vascular and hemorrhagic stroke, proteinuria and renal failure. The early detection of hypertensive end organ damage can slow or prevent damage, or allow disease regresion with adequate therapy. Aim was to investigate the prevalence of end organ damage in our patients.

Methods: Research included 200 patients observed in HISPA center Kragujevac, Serbia, during the one year period. Patients had baseline and control visits, after 3 or 6 months, and out of 500 patients observed during this period, only 200 with complete assessment of hypertension were included into analysis. Diagnosis of early end organ damage was obtained according to the latest ESC/ESH recommendations. Left ventricular hypertrophy was estimated by echocardiographic criteria – relative wall thicknes (concentric hypertrophy) and left ventricle mass; carotid intima-media thickness >0.9mm or carotid atherosclerotic plaque and renal resistive index >0.7 were used as markers of systemic atherosclerosis. Rethinopathy was assessed by fundoscopy. Serum kreatinin >133mmol/L in men and >124mmol/L in women and glomerular filtration rate (eGFR) <90 ml/min/1.73m2 were used for diagnosis of hypertensive nephropathy. All data were statistically analyzed in the SPSS for Windows.

Results: Study population consisted of 135 (67.5%) of male and 65 (32.5%) of female subjects. Mean age of the population was 55.19±11.24 years. Previous hypertension was present in 165 (82.5%) of patients (x^2; p=0.000), duration of hypertension was in 87 (43.3%) patients between 1 and 10 years (x2; p=0.003), and 154 (77%) already were on antihypertensive therapy (x^2; p=0.000). Left ventricular hypertrophy defined as concentric hypertrophy was present in 112 (56%), x2; p=0.090. IMT > 0.9mm was measured in 116 (58%) which was significant (x^2; p=0.024); renal RI was >0.7 in 102 (51%) – x^2; p=0.770. Serum creatinin was normal in the majority of patients, 178 (89%), x^2; p=0.000 and eGFR showed that 109 (54.5%) had chronic renal failure grade I (x^2; p=0.000). Fundoscopy revealed that rethinopathy, at least grade I, was present in 111 (55.5%), x^2; p=0.120.

Conclusions: Our research showed that initial carotid atherosclerotic changes and I grade of chronic renal failure were the most significant end organ changes in the study population. Lasting of hypertension and previous antihypertensive therapy probably influenced on the lower prevalence of concentric hypertrophy and prevention of further development of serious systemic atherosclerosis and renal damage.

Keywords: end organ damage, concentric hypertrophy, renal damage, atherosclerosis

PREVALENCE OF METABOLIC SYNDROME AND ITS COMPONENTS IN PATIENTS OBSERVED IN HISPA CENTER KRAGUJEVAC, SERBIA

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Background: Metabolic syndrome, sometimes known by other names, is a clustering of several medical conditions: central obesity, hypertension, atherogenic dyslipidaemia and elevated fasting glucose/diabetes mellitus. Hypertension is one of the central components of metabolic syndrome with the estimated prevalence of about 85% in patients with metabolic syndrome. Every component by itself represents significant risc factor for cardiovascular morbidity and mortality, and rates of serious events increase with the number of components of metabolic syndrome. Aim was to investigate the prevalence of metabolic syndrome in patients examined in HISPA center Kragujevac, as well as the number of present components.

Methods: Research included 200 patients observed in HISPA center Kragujevac, Serbia, during the one year period. Patients had baseline and control visits, after 3 or 6 months, and out of 500 patients observed during this period, only 200 with complete assessment of hypertension were included into analysis. Definition of metabolic syndrome was made by using IDF criteria for diagnosis: central obesity (waist circumference >94cm in man and >88cm in woman) plus at least 2 of the following criteria: elevated serum triglycerides (>1.7 mmol/L); lower serum HDL (<1.03 mmol/L for man and <1.29 mmol/L for woman); high blood pressure (>130 mmHg systolic or >80 mmHg diastolic) or data on previous hypertension treatment; high fasting glucose (>5.6 mmol/L) or previously diagnosed diabetes mellitus type 2.

Results: Study population consisted of 135 (67.5%) of male and 65 (32.5%) of female subjects. Mean age of the population was 55.19±11.24 years. Central obesity was highly prevalent in the study population. BMI was >25 kg/m^2 in 170 (85%), showing that majority of subjects were overweight/obese (x^2; p=0.000), average BMI was 31.6±6.38 kg/m2. Waist circumference was in 150 (75%) patients >94/88cm (x^2; p=0.000), average values were 109.54±13.7 cm. Triglycerides were normal in 116 (58%) patients and elevated in only 26 (13%). HDL was significantly lower (x^2; p=0.000), with 102 (51%) of patients having values <1.03/1.29 mmol/L. Fasting glucose was >5.6 mmol/L in 90 (45%), with an average value of 5.80±1.08 mmol/L (t-test; p=0.000), and diabetes was already diagnosed in only 40 (20%). Hypertension was present in 165 (82.5%) of patients (x^2; p=0.000) with 154 (77%) already were on antihypertensive therapy (x^2; p=0.000). Metabolic syndrome was diagnosed in 136 (68%) patients (x^2; p=0.000). Prevalence of patients with three, four or five components was: 62 (31%), 48 (24%) and 26 (13%) patients (x^2; p=0.000).

Conclusions: Prevalence of metabolic syndrome is very high so we can conclude that are patients have a higher cardiovascular risk. Central obesity, hypertension and low HDL were the most often components of metabolic syndrome. The most prevalent were patients with three components.

Keywords: metabolic syndrome, central obesity, hypertension, high triglycerides, low HDL, high fasting glucose

PREVALENCE OF NOCTURNAL HYPERTENSION AND NON-DIPPING PATTERN OF BLOOD PRESSURE IN PATIENTS EXAMINED IN HISPA CENTER KRAGUJEVAC, SERBIA

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Background: Nocturnal hypertension and non-dipping of blood pressure during sleep are distinct entities that often occur together and are regarded as important signs of poor cardiovascular prognosis. Nocturnal sympathetic overactivity has been suggested as mediating nocturnal hypertension and non-dipping BP pattern. It is estimated that approximately 22% of patients with essential hypertension have a non-dipping pattern, and isolated nocturnal hypertension, which may be present in 7% of hypertensive patients, can only be diagnosed with ABPM. Aim was to investigate the prevalence of nocturnal hypertension and non-dipping pattern in patients examined in HISPA center Kragujevac.

Methods: Research included 200 patients observed in HISPA center Kragujevac, Serbia, during the one year period. Patients had baseline and control visits, after 3 or 6 months, and out of 500 patients observed during this period, only 200 with complete assessment of hypertension were included into analysis. ABPM parameters were estimated according to the latest ESC/ESH recommendations. Nocturnal hypertension was defined as nocturnal systolic blood pressure >120 mmHg or nocturnal diastolic blood pressure >70 mmHg. Threshold for dipping was -10% of blood pressure values between day and night period. According to the dipping status patients were diveded into two groups – dippers, which included normal and extreme dipping; and non-dippers, which included non-dippers and risers. All data were statistically analyzed in the SPSS for Windows.

Results: Study population consisted of 135 (67.5%) of male and 65 (32.5%) of female subjects. Mean age of the population was 55.19±11.24 years. Out of total number 154 (77%) already were on antihypertensive therapy (x2; p=0.000). Nocturnal systolic BP was >120 mmHg in 120 (60%) patients (x2; p=0.000), with the average of 125.67±20.38 mmHg (t-test; p=0.000); nocturnal diastolic BP was >70 mmHg in 116 (58%) patients, with the average values of 74.31±11.91 mmHg (t-test; p=0.000). Overall, nocturnal hypertension, systolic, diastolic or both, was present in 141 (70.5%) patients (x2; p=0.000). Non-dipping pattern of systolic BP was present in 139 (69.5%) patients (x2; p=0.000), average values were -5.74±9.75 mmHg (t-test; p=0.000); and for diastolic BP in 108 (54%) patients (x2; p=0.258), with an average value of -9.62±13.18 mmHg (t-test; p=0.680). There was no significant correlation between the use of different groups of antihypertensives and the presence of nocturnal hypertension or non-dipping status. LF/HF ratio was >2.0 in 70% of patients confirming that autonomic balance is shifted towards sympathetic activity (t-test; p=0.000).

Conclusions: Nocturnal hypertension was highly prevalent, even several times higher than previously reported. Although the non-dipping status was also highly prevalent we should emphasize that this group included „riser" pattern as well. Among treated hypertensive patients, nocturnal hypertension and non-dipping may be partly related to the absence of uniform 24-hour therapeutic antihypertensive coverage, perhaps especially in those treated with single morning doses and/or short-acting antihypertensive medications. Other explanation for this high prevalence is the maintainance of sympathetic overactivity during the nighttime.

Keywords: nocturnal hypertension, non-dipping, ABPM, sympathetic overactivity

PULMONARY EMBOLISM – AN ETERNAL RIDDLE (CASE REPORT)

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Background: Pulmonary embolism (PE) is a major contributor to global disease burden, including a high short-term mortality risk. The epidemiology of PE is difficult to determine because it may remain asymptomatic or its diagnosis may be an incidental finding; in some cases the first presentation of PE may be sudden death. In the absence of hemodynamic instability at presentation, the diagnostic work-up of a patient with suspected acute PE begins with the assessment of the clinical or pre-test probability of PE. Clinical prediction rules (Wells or revised Geneva) should be used to assess the pretest probability of a PE diagnosis before laboratory or imaging procedures. Whereas patients with high clinical probability for PE (PE-likely) should directly undergo an imaging test, D-dimer testing is recommended as the next diagnostic step in patients with low or intermediate pre-test probability (PE-unlikely). According to the recommendations of the European Society of Cardiologists from 2014., a strategy for the treatment of PE is based on risk assessment from dying after which the patients are divided into three groups. Patients with PE who are at high risk are hypotensive (indicating the limit of systolic arterial blood pressure of 90 mmHg), patients with intermediate risk are with dysfunction of the right ventricle and without hypotension and low the risk is patients who have no right ventricular dysfunction and they are not hypotensive. The basic treatment strategy for PE is reperfusion therapy for high risk patients, anticoagulant therapy and monitoring for patients with intermediate risk and anticoagulant therapy and quick release from the hospital or complete outpatient treatment for patients with low risk. Anticoagulation treatment for acute PE should cover at least 3 months. Direct oral anticoagulants are effective and safe alternatives to standard anticoagulation regimens. In this case-report we presented a patient with a intermediate risk to PE as well as a diagnostic procedure that we performed during his treatment in our department. A 44 years old male was recivied with problems in the form of dyspnoea, smallnes, weakness, accelerated heartbeat, sweating. The risk factors that our patient has are: hypertension, diabetes mellitus, dyslipidemia, obesity. The blood pressure was 80/60mmHg, pulse frequency 182/min, the saturation with oxygen was 85%. By the doctor on reception, it was percieved as a paroxysmal supravenricular tachycardia and was treated in that direction. After stabilization of the patient's overall condition and urgently performed analyses, the patient was diagnosed with standard diagnostic procedures and adequate therapy was included which resulted in a favorable outcome. 6th day of hospitalization were released in stable condition with oral anticoagulants included.

Keywords: embolism, risk factors, D-dimer, anticoagulant,

RADIOFREQUENT CATHETER ABLATION LEFT ACCESSORY PATHWAY

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Background: The safety and efficacy of radiofrequent (RF) catheter ablation of an accesory AV pathway have made ablation the tretment of choice in patients who have VR tachycardia, and or atrial fibrillation (AF) associated with a rapid ventricular response over the AP. To compare results of the left-sided AP RFA in first 58 cosecutive patients with manifested preexcitation, traeted at Dedinje Cardiovascular Institute in Belgrade.

Results: Total procedure time was significantly different (p<0,05) between the localization of AP on the MA (60,0±26,0 for anterior; 45,2±28,4 for anterolateral; 73,9±27,9 for lateral; 59,1±25,5 for posterolateral and 83,1±29,6 for posterior). Also significant difference was noted in the number of applied RF pulses (9,0±4,5 for anterior; 4,3±4,7 for anterolateral; 8,1±5,8 for lateral; 4,0±2,9 for posterolateral and 8,1±4,2 for posterior; p< 0,05). The fluoroscopy time did not differ significantly (p=0,078). Atrial fibrillation was present in 25,5 % patients before the procedure. Transaortic approach is more offten used (74,1%) for ablation left-sided pathways, than tras-septal approach. There were no significant differencse between groups in primary success rates (100% for anterior and anterolateral, 82,1% for lateral, 100% for posterolateral and 88,9% for posterior, p=0,672), reccurence rates (10,7% lateral and 5,5% for posterior; p=0,023) and final success rates (100% for anterior, anterolateral and posterolateral, 94,8% for lateral and 89,3% for posterior; p=0,421).

Conclusion: Although total procedure time and the number of applied RF pulses were highest for lateral and posterior pathways, succes rate was similar for RF ablation of all AP along the MA localisations.

Keywords: radiofrequent catheter ablation, atrial fibrillation, tachycardia

RECOVERY OF ISCHEMIC MYOCARDIUM AFTER CORONARY ARTERY BYPASS SURGERY : THE ROLE OF HIBERNATION

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Background: The aim of this study was to investigate the morphologic characteristics of the hibernating human myocardium and ,thrue the correlation its with dobutamine stress echocardiography (DSE), to study the potential for myocardial recovery in coronary artery disease.

Methods: We evaluated 15 patients with coronary disease (58+/-12 years old, ejection fraction 38 +-/14%) with a corresponding wall motion abnormality on DSE (up to 10 micrograms kg (-1) min(-1) before coronary bypass surgery. During surgery, transmural myocardial biopsies from hypokinetic or akinetic area were perfomed (n=37). The samples of myocardium were analyzed by histopathology and immunohistochemestry to investigate the extent of interstitial fibrosis, intracellular and interstitial proteins.

Results: Among the 15 patients included in the study, 7 recovered function as assessed with an echocardiography, one month after bypass surgery, 8 with DSE viability showed less fibrosis and less vimentin expression,more glycogen, a higher ration of alpha-smooth muscle actin, actin and desmin then those without recovery. The degree of severity of the morphological changes (three stages) correlated well with the demonstration of inotropic reserve during DSE and with the extent of postoperative functional recovery (wall-motion score index, NYHA).

Conclusion: Myocardial hibernation as the adaptation to a reduced oxygen supply in coronary artery disease, have an important role in potential recovery of ischemic myocardium after coronary artery bypass surgery, as shown by more favourable histopathologic features.

Keywords: ischemic myocardium, bypass surgery, hibernation

RELATION OF BODY MASS INDEX AND HEIGHT OF ARTERIAL BLOOD PRESSURE IN PERSONS WITH NORMAL AND EXCESSIVE NUTRITION

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Background: Excessive weight, especially when combined with increased visceral obesity, is the major cause of arterial hypertension. The aim of this study was to examine the relationship and correlation between the body mass index and the height of arterial blood pressure in people with normal and excessive nutrition.

Methods: The study included 184 persons (68.3 ± 22.8), 105 women (69.0 ± 12.0) and 79 men (68.3 ± 11.8) (p> 0.05), 42 normally nourished (BMI <25.0 kg / m^2) and 142 overweight (BMI≥25.0 kg / m^2). The body mass index (BMI) was calculated.

Based on BMI, respondents were classified into different categories of nutrition: normal (18.5-24.9) 42, increased body weight (25.0-29.9) 60, obesity I (30.0 - 34.9) 43, obesity II (35.0 - 39.9) 31, obesity III degree (> 40.0) 8.

Results: The average value of blood pressure normally fed is 134.0 ± 16.3 / 83.0 ± 8.1, increased body weight 142.5 ± 19.9 / 86.0 ± 6.2, I degree 151.3 ± 18.5 / 88.9 ± 6.3, II degree 161.1 ± 23.6 / 92.5 ± 7.6, III degree 154.5 ± 21.8 / 93.7 ± 7.4, total obesity 155.2 ± 20.5 / 90.7 ± 7.2, overweight 149.8 ± 21.3 / 88.7 ± 7, 4. Total obese persons have significantly higher systolic (p <0.01) and diastolic pressure (p <0.01) than normal persons. Overweight have significantly higher systolic (p <0.01) and diastolic pressure (p <0.01) than normal persons. In patients with I and II degree of obesity, there is a positive correlation between BMI and systolic pressure (r = 0.239 p> 0.05; r = 0.649 p <0.01) with equations of the regression direction y = 2.769x + 61.938 and y = 10.881x - 242.912. In people with I and II degree of obesity, there is a positive correlation between BMI and diastolic pressure (r = 0.336 p> 0.05; r = 0.267 p> 0.05) with equations of regression direction y = 1.327x + 46.171, y = 5.938x - 127.978 . In total obesity, a positive, significant correlation of BMI and systolic (r = 0.383; p <0.01) and BMI and diastolic pressure (r = 0.305; p <0.01) were found with BMI and systolic y = 1.940x + 86.87 and BMI and diastolic pressure y = 0.542x + 71.64 In overweight, there is a positive, significant correlation between BMI and systolic (r = 0.417 p <0.01) and BMI and diastolic pressure (r = 0.417 p <0.01) with equations of direction of regression for BMI and systolic y = 1.77x + 93.27 and BMI and diastolic pressure y = 0.794x + 63.36.

Conclusion: The direction of linear regression, the positive and significant correlation of body mass index (BMI) and blood pressure, and the finding of statistically significantly higher systolic and diastolic pressure in obese individuals compared to normally nourished, suggests that obesity is a significant risk factor in the onset of arterial hypertension.

Keywords: obesity, body mass index, arterial hypertension

SEX-BASED ASSOCIATION OF SERUM URIC ACID AND LEFT VENTRICULAR REMODELING IN HYPERTENSIVE PATIENTS

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Background: Serum uric acid is a risk factor for cardiovascular disease. Increased uric acid serum levels are a common finding in patients with high blood pressure. Left ventricular (LV) hypertrophy, which is likely to be involved in cardiovascular disease, is the most common cardiac complication caused by hypertension. Several studies have shown that serum uric acid (UA) is associated with left ventricular (LV) hypertrophy. The aim of the study was to determine sex-based association of serum uric acid and left ventricular hypertrophy in hypertensive patients.

Methods: The study included 130 hypertensive patients (70 or 53,8% males and 60 or 46,2% femals, mean age 61±11,4 years). All patients underwent clinical examination, with anthropometric measurements (body mass index (BMI) and waist size), ECG analysis and echocardiography. Left atrial diameter (LA), enddiastolic and endsystolic left ventricular diameters (LV EDD, LV ESD), left ventricular ejectin fraction, relative wall thickness (RWT) and left ventricular mass index (LVMI) were measured by echocardiography. To determine the factors influencing the LVMI, multiple regression analysis was carried out.

Results: Patients in studi compared based on gander were without differences by age, BMI, hypertension duration, systolic and dyastolic blood presure values. Men more common were smokers (35 (50%) vs 16 (26,7%), p=0,01) and alcohol users (15 (21,4) vs 1 (1,67), p=0,001) compared to women. Serum uric acid was significantly higher in men (0,373±110,9 vs 308,5±11,8, p<0,001) and further analysis was calculated according to sex. There were significant correlations between serum uric acid and BMI (r=0,378, p=0,011), LV EDD (r=0,576, p=0,016), LV ESD (r=0,619, p=0,008) and LVMI (r=0,518, p=0,033) but only in women. Regression analysis also revealed that the LVMI was independently associated with serum uric acid concentration in women (B=0,986, p=0,045), but not in men (B=0,996, p=0,409).

Conclusion: In hypertensive patients link between serum uric acid and left ventricular geometry is much stronger in females than in males. It remains unclear whether uric acid is only a marker or also a causal factor of left ventricular remodeling.

Keywords: serum uric acid, left ventricular remodeling, hypertension

SIMILARITIES AND DIFFERENCES IN EPIDEMIOLOGY AND RISK FACTORS OF CEREBRAL AND MYOCARDIAL ISCHEMIC DISEASE

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Background: Ischemic heart disease and cerebral ischemia represent the leading causes of mortality worldwide. Both entities share risk factors, pathophisiology and etiologic aspects by means of a main common mechanism, atherosclerosis.

The autors aimed to considering the differences and similarities in epidemiology and risk factors that could be found in between both entities.

Methods: In a retrospective sudy 403 patients were included and divaded into two groups: group of 289 patients with history of myocardial infarction (AMI), and group of 114 patients with hisory of ischemic stroke (IS). All patients were evaluated for nonmodifiable risk faktors, which included age and sex, and modifiable, suck as hypertension, dyslipidemia, diabetis, obesity, physical activity and smoking. Differences in some epidemiological aspects were also considered: profession, marital status, alcohol consumption, exposure to stress

Results: Patients with history of IS were significantly older then AMI patientes (68,6 ± 30,7 vs 64,3 ± 10,0, p=0,036), with higher diastolic blood pressure (87,1 ± 10,2 vs 83,6 ± 10,4, p=0,003) and also with higher Sokolow-Lyon index in ECG, as a index of left ventricular hypertrophy (19,2 ± 9,1 vs 14,7 ± 6,5). There were no significant differences between groups in the estimated body mass index and waist size. Also differences between groups in stress exposure, profession, alcohol consumption or physical activity were no significant. Patients in AMI group were more frequently male (199 (69%) vs 59 (52%), p=0,001), married (252 (87%) vs 88 (77%), p=0,037), smokers (162 (56%) vs 50 (44%), p=0,027) and with higher incidence od dyslipidemia (217 (75%) vs 73 (64%), p=0,026) compared with SI group. Incidence of arterial hypertension and diabetes was similar in both groups.

Conclusion: Both entities share similar pathophysiological mechanisms and, consequently, main traditional risk factors. However, incidense of myocardial infarction increases with male sex, dyslipidemia, smoking and marital status, while incidense of ischemic stroke increases with age, higher diastolic blood pressure and also with higher Sokolow-Lyon index in ECG.

Keywords: cerebral disease, myocardial ischemic disease, risk factors

SUCCESS OF RADIOFREQUENCY ABLATION IN TREATMENT OF PATIENTS WITH CARDIAC ARRHYTHMIAS

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Background: Numerous trials have shown high success of radiofrequency ablation (RFA) in treatment of patients with cardiac arrhythmias.

We aimed to examine RFA initial success in treatment of different cardiac arrhythmias and success after 6 months of follow-up.

Methods: The present study included 320 patients in which RFA was performed in the Cardiovascular Institute "Dedinje" during 2012 year. We evaluated RFA immediate success and success after 6 months of follow-up. For statistical analysis we used T-test, chi-square test and linear regression analysis (P<0.05).

Results: RFA initial success is for RFA of AV node and atrioventricular nodal reentrant tachycardia (AVNRT) 100%, RFA of pulmonary veins 99%, RFA of ventricular tachycardia 94%, RFA of atrial flutter 92%, RFA of premature ventricular complexes (PVC) and Wolf-Parkinson-White (WPW) syndrome 87% and RFA of atrial tachycardia 78%. Success of RFA after 6 months of follow-up is for RFA of AV node 100%, RFA of AVNRT 94%, RFA of atrial flutter 90%, RFA of WPW syndrome 86%, RFA of ventricular tachycardia 85%, RFA of pulmonary veins 79% (paroxysmal atrial fibrillation 88% and persistent form 63% with significant difference P<0.05), RFA of PVC 78% and RFA of atrial tachycardia 67%. Significant negative correlation was found between number of PVC and left ventricular ejection fraction (P<0.05) before RFA of PVC.

Conclusion: This study proved very high RFA initial success in treatment of cardiac arrhythmias and satisfactory RFA success after 6 months of follow-up.

Keywords: radiofrequency ablation, premature ventricular complex, ejection fraction

SUCCESS, FOCUS LOKALIZATION PREMATURE VENTRICULAR COMPLEXES END COMPLICATION IN TREATMENT PATIENTS OF RADIOFREQUENCY ABLATION

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Background: The aim of this study was to examine the effectiveness of radiofrequency ablation (RFA) in the treatment of patients with ventricular premature complex (VPC), focus localization and complications during the RFA.

Methods: The present study included 302 patients in which RFA was performed in the Institute for Cardiovascular Diseases “Dedinje” during period 2010.-2013. year. We evaluated RFA immediate success and success after 6 months of follow-up, localization PVC end complications RFA.

Results: Acute success RFA of PVC: 87% successful, 13% unsuccessful. Success of RFA after 6 months of follow-up is for RFA of PVC 78%, 22% unsuccessful. Focus localization PVCs: ~ 90% of all IPVCs are outflow PVCs. RVOT 66% (RVOT septal 48.3 %, RVOT free wall 14.3%, PA 2.0%, para Hiss 1.4%). LVOT 33.9% (LCC 18.4%, RCC 6.1%, GCV+AIV 2.0%, AMC 2,0%, MA 5.4%).Complication RFA: 1.vascular access – 19 patients (dissection a. femoralis 2, hematoma 16, pseudoaneurism 1) 2. tamponada 1 patient.

Conclusion: This study proved very high RFA initial success in treatment of PVC and satisfactory RFA success after 6 months of follow-up.PVC from outflow tract (RVOT,LVOT) are the most frequent idiopathic clinic arrhythmia ~90%. Catheter ablation allows permanent elimination of focuses of VES / VT and actual healing process. Intervention approach in resolving off focuses VES/VT is the first option of treatments for patients with: 1. arrhythmia induced by Cardiomyopathy, 2. frequent episodes of monomorphic VES / VT and severe symptoms, 3. when a patient does not want to take antiarrhythmic drugs.

Keywords: radiofrequency ablation, premature ventricular complex, focus PVC

SYSTEMIC HEMODYNAMIC ATHEROTHROMBOTIC SYNDROME (SHATS) – ENTITY THAT WE SHOLUD INCLUDE IN DAILY CLINICAL PRACTICE

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Background: Systemic hemodynamic atherotrombotic syndrome (SHATS) is defined by both vascular (one or more clinical/subclinical vascular diseases) and blood pressure components (one or more phenotypes of BP variability), although the precise definition and criteria of SHATS are not clearly established yet. SHATS is clinically important for predicting future sustained hypertension in younger subjects. Early detection of SHATS may raise the alert for prevention of organ damage in this early stage. Aim was to investigate the possible presence of SHATS in our patients combining marker of atherosclerosis and values of BP variablity.

Methods: Research included 200 patients observed in HISPA center Kragujevac, Serbia, during the one year period. Patients had baseline and control visits, after 3 or 6 months, and out of 500 patients observed during this period, only 200 with complete assessment of hypertension were included into analysis. All blood pressure parameters were estimated according to the latest ESC/ESH recommendations. For 24h blood pressure variability we used a threshold for standard deviation of 15% for systolic and 9% for diastolic to define the groups with normal and higher variability. Carotid intima-media thickness >0.9 mm or carotid atherosclerotic plaque, renal resistive index > 0.7 and pulse pressure > 40 mmHg were used as markers of clinical/subclinical vascular disease. For pulse pressure we used 24h average values from ABPM. Limitation of the study was lack of pulse wave velocity estimation.

Results: Study population consisted of 135 (67.5%) of male and 65 (32.5%) of female subjects. Mean age of the population was 55.19±11.24 years. IMT > 0.9mm was measured in 116 (58%) which was significant (x2; p=0.024); renal RI was >0.7 in 102 (51%) – x2; p=0.770. Pulse pressure was > 40 mmHg in 160 (80%) which was a significant majority of patients (x2; p=0.000). Average values of pulse pressure were 51.20±12.8 mmHg (t-tes; p=0.000). Blood pressure variability, defined through standard deviation of 24h values was >15% for systolic BP in 144 (72%) patients (x2; p=0.000), with an average of 19.04±7.16 mmHg (t-test; p=0.000), and >9% for diatolic BP in 168 (84%) patients (x2; p=0.000), with an average of 16.06±6.76 mmHg (t-test; p=0.000). Statins were administrated in only 99 (49.5%) patients on baseline (x2; p=0.888)

Conclusions: High markers of clinical/subclinical vascular disease, carotid IMT and pulse pressure showed that the atherosclerosis was significantly present in a study group. Blood pressure variability was significantlly pronounced. Combined with markers of vascular disease, it shows us that we should consider the presence of SHATS in daily clinical practice for prompt end organ damage evaluation, especially in younger subjects. Considering that patients were mostly middle-aged further reserch should include pulse wave velocity estimation as more reliable marker than pulse pressure in this age group. Use of statins in a prevention of future atherosclerotic changes should be higher.

Keywords: systemic hemodynamic atherothrombotic syndrome, blood pressure variability, IMT, pulse pressure

THE ASSOCIATION BETWEEN OBESITY AND VISIT-TO-VISIT VARIABILITY IN SYSTOLIC BLOOD PRESSURE- A PROSPECTIVE STUDY

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Background: With the prevalence of obesity, which should already be considered as a pandemic phenomenon (with all accompanying health risks), both prevention and health education, as well as identifying predictors for the development of obesity-related diseases are primary. The pathophysiological relationship between obesity and visit-to-visit variability in systolic blood pressure (SBPV) has not been completely resolved. The aim of the study was to investigate the association between obesity and visit-to-visit variability in systolic blood pressure in hypertensive patients.

Methods: Prospective study included 300 randomly selected hypertensive patients (147 men and 153 women, mean age 67.76±9.84 years), who were divided, according to body mass index (BMI≥30 kg/m^2), to groups of obese (n=249) and non-obese examinees (n=51). The study comprised three visits during the follow up period of 22-months. Obesity was defined as BMI, as the parameter of total obesity and it was defined as waist circumference (WC), as the parameter of central obesity. SBPV for each examinees was defined using the standard deviation (SD) from 3 values of systolic blood pressure (SBP). In order to estimate detailed evaluation of distribution SBPV quartiles of SBP-SD were formed.

Results: The values of SBP and SBP-SD were significantly higher in the group of obese hypertensive patients than in the group of non-obese patients (126.67±8.22 vs 120.45±7.79 mmHg, 11.00±5.64 vs 7.34±3.96; p<0.01). There was statistically stronger correlation between SBP-SD and BMI compared to large WC (ρo=0.425 vs ρo=0.356, p<0.01). The analysis showed statistically significant average decrease of SBP-SD for 8.2 mmHg, BP for 31/8 mmHg, BMI for 3.8 kg/m^2 and WC for 10 cm. TT The highest SBPV was recorded in the 4th quartile in obese patients (43.13±7.50 mmHg).

Conclusion: Our findings suggest an association between parameters of obesity and increased visit-to-visit variability in systolic blood pressure in hypertensive patients. During follow-up 22-months periods, reduction of body weight was associated with reduction of blood pressure values, and lower value of blood pressure variability. Persistently decrease both body weight and visit-to-visit variability may explain lower cardiovascular risk in obese-related disease.

Key words: Obesity, hypertension, visit-to-visit sistolic blood pressure variability.

THE SIGNIFICANCE OF ADIPONECTIN AS A MARKER OF PREHYPERTENSION AND HYPERTENSION IN PATIENTS WITH METABOLIC SYNDROME

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Background: Hypertension is associated with significant differences in adipose tissue metabolism (especially decreased adiponectin concentration), with an increase in total and central obesity and the higher risk of cardiovascular events. The aim of the study was to determine adiponectin concentration in patients with metabolic syndrome (MetS) and prehypertension (Pre-HT) or hypertension (HT) and to estimate relationship between adiponectin concentration and components of MetS.

Methods: This cross-sectional study involved randomly selected 120 subjects (60 men and 60 women, mean age 54.23±15.53 years), who were divided in four groups: MetS+normotensive, n=30; MetS+Pre-HT, n=30; MetS+HT, n=30; Control group (no MetS, no Pre or HT, n=30). In all subjects serum adiponectin concentration was measured by ELISA method, and serum triglyceride concentration, fasting plasma glucose (FPG), Homeostasis Model Assessment of Insulin Resistance index (HOMA-IR), total cholesterol (TC) and high-density lipoprotein (HDL) were determined. Obesity was evaluated through body mass index (BMI), waist circumference (WC), and body fat percentage (BFP).

Results: Serum adiponectin was the lowest in group with MetS and HT (1092.06±488.91 pg/mL), significantly lower (p<0.01) in MetS+ Pre-HT group (1134.15±510.11 pg/mL), and it was the highest in the control group (1670.27±500.12 pg/mL). Adiponectin negatively correlated with most components of MetS (p<0.01); blood pressure (r=-0.286), systolic blood pressure (r=-0.313), waist circumference (r=-0.309), triglycerides (r=-0.295), FPG (r=-0.208), HOMA-IR (r=-0.259), and positively with HDL-cholesterol (r=0.156, p>0.05). In logistic regression analysis, the level of adiponectin and WC were distinguished as the strongest predictors of Pre-HT and HT. In patients with MetS value of adiponectin ≥1266.54 pg/mL was associated with a lower risk of Pre-HT, and value of ≥1159.98 pg/mL was associated with a lower risk of HT.

Conclusion: Patients with metabolic syndrome have low adiponectin levels and this hypo-adiponectinemia may indicate prehypertension or hypertension. There is a strong relationship between adiponectin level and components of MetS.

Keywords: adiponectin, prehypertension, hypertension, metabolic syndrome

THE IgM ISOTYPE OF ANTI-B2GPI ANTIBODIES: SIGNIFICANT DIFFERENCE IN HYPERTENSIVE AND NORMOTENSIVE PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) is an autoimmune disease that is characterized by the recurrent thrombosis and/or pregnancy losses and by the presence of antiphospholipid antibodies (anticardiolipin (aCL), anti-b2gpI (aB2gpI), lupus anticoagulants (LA)). In the absence of any additional diseases APS is designated as primary (PAPS). It was reported that arterial hypertension might be an independent factor for thrombosis recurrence in APS. Therefore, we analyzed the prevalence of hypertension in a group of PAPS patients and potential differences in regard to the presence of aPL Abs in subgroups of PAPS patients with and without hypertension.

Methods: This study included 33 (23 female and 8 male) patients with primary APS (mean age: 40.64 ± 13.51 years). Antiphospholipid and Abs against oxidized LDL (anti-oxLDL Abs) were determined by ELISA.

Results: Hypertension was present in 12/33 (36.36%) of PAPS patients. Patients older than 40 years of age more frequently had hypertension ($\chi 2 = 5.308$, $P = 0.021$) In addition, hypertension was present in: 8/24 patients with positive LA, in 3/18 patients with positive IgM isotype of aCL, in 7/18 patients positive for the IgG aCL, in 5/15 patients positive for the IgG isotype of ab2gpI Abs. Mann-Whitney test revealed that the IgM aB2gpI Abs levels were significantly different between hyper- and normotensive PAPS patients. In 8/21 patients with positive finding of anti-oxLDL Abs hypertension was observed. In addition, hypertension was observed in 6/8 PAPS patients with myocardial infarctions ($\chi 2 = 6.812$, $P = 0.009$).

Conclusion: Strict control of blood pressure in PAPS patients might be inexpensive and efficient way to prevent recurrence of thrombotic episodes in these patients that frequently suffer from recurrent thrombotic episodes despite life-long anticoagulation therapy.

Keywords: antiphospholipid syndrome, IgG and IgM isotypes of antiphospholipid antibodies, hypertension

THE IMPACT OF OBESITY ON THE SHORT-TERM AND LONG-TERM OUTCOMES AFTER PERCUTANEOUS CORONARY INTERVENTION

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Background: Impact of obesity on prognosis among those with established coronary disease is less clear. The aim of this study was to determine the significance of the obesity on outcome in patients after elective percutaneous coronary intervention (PCI).

Method: We examine 200 patients (mean age 58±8.7, 83.5% men) who had successful elective PCI between Jun 1-November 30, 2009. Obesity was defined according to body mass index (BMI): overweight –25–30 kg/m^2; obese class I – 30-34.9 kg/m^2; obese class II >35 kg/m^2, waist circumference (WC) men/woman was > 94/80 cm and waist hip ratio (WHR) >0.90/0.84. MACE included myocardial infarction (IM), stroke and cardiac hospitalization. We compare 30 days, 12 months and 36 months outcome.

Results: Obese (BMI, WHR, WC) had higher value of diastolic and systolic pressure and lower HDL value. There was no statistically significant difference in MACE among obese and non obese patient (BMI, WC, WHR) after 12 and 36 months. In contrast, incidence of 12 months MI was significantly lower in obese (WC) (4.8% vs 14.3 %; p= 0.04), and incidence of 12 months target vessel revascularization was lower in obese (WHR) (12.3%, vs 27.3% p=0.015) compared with normal weight.

Conclusion: Obese (WC and WHR) had lower rates of 12 months IM and TRL, which may be explained by better use of guideline-recommended medical and lower smoking rate.

Keywords: obesity, percutaneous coronary intervention

THE PREVALENCE OF ARTERIAL HYPERTENSION IN PATIENTS WITH ATRIAL FIBRILLATION

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Background: With a prevalence of 3% in population, atrial fibrillation (AF) is the most common arrhythmia on discharge from the hospital. AF is more common in older people and patients who suffer from high blood pressure (hypertension), ischemic heart disease, heart failure, diabetes and renal failure. The arrhythmia itself carries fivefold increased risk for stroke. On the other hand hypertension is the most important and the most common risk factor for stroke. To determine the prevalence of hypertension in patients suffering from atrial fibrillation.

Methods: The present study included 167 patients with AF, of which 115 men (68.86%) and 52 women (31.14%). Data on AF and comorbidities were noted in a special form and a database taken from medical history and medical examination.

Results: Of 167 patients with AF them 128 (76.65%) suffered from hypertension, of whom 106 (82.81%) had regulated and 18 (14.06%), unregulated blood pressure while 4 patients (3.12%) had no comment on the matter. The highest prevalence of HTA is noted in permanent and the lowest in paroxysmal AF. The most commonly used drugs in patients with AF were beta blockers 151p (80.42%), followed by ACEI 128p (75.65%) and diuretic 91p (54.49%), and the rarest AT1 blockers 9p (5.39%).

Conclusion: Our study showed high prevalence of hypertension in patients with atrial fibrillation, especially in the group of patients with permanent atrial fibrillation.

Keywords: arterial hypertension, atrial fibrillation

THROMBECTOMY IN THE TREATMENT OF THE STROKE – CASE REPORT

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Background: Each year, around 300/100.000 people in Serbia experiences stroke. Significant number of patients has permanent consequences-disability, in case when the treatment has not been applied within first 3 hours of the symptoms onset. Mechanical thrombectomy is one of the newer of treatment options in patients with thromb in cerebral circulation who have difficult symptomatology and poor prognosis due to the presence of various risk factors. Presentation of patient with stoke treated with thrombectomy.

Method: Data for this article have been obtained from the medical records of patients (i.e. discharge list, e-chart, medical reports).

Presentation of case: 60-year old male patient with history of hypertension, dilated cardiomyopathy with EF of 20%, permanent arrhythmia absoluta and pacemaker inserted in 2012. On 11-Jul-2017 at 10.30, while in the waiting room of local ambulance (village), patient experienced symptoms of acute stroke including left-sided hemiplegia, dysarthria, left central facial palsy. He was immediately transferred to Special Hospital for CVA "Sveti Sava" with the thrombolysis initiated at 13.00. CT of endocranium on admission showed an ischemic lesion in development in right insuloopercular and frontal right corticosubcortically region, with an thrombosis in right ACM in the M1 segment. Following CT, selective angiography of the right ACI was performed where the thrombosis of the upper branch of the ACM was observed. Subsequently, mechanical extraction of thrombus with stent with aspiration was performed and complete TICI3 lumen reconstruction was achieved. Control CT of endocranium on 12-Jul-2017 revealed clear demarcation of the small acute ischemic lesion in the insular right area, with a very small (4mm) ICH in the right corona radiata. CT of endocranium on 24-Jul-2017 showed no blood densities, but the loss of the corticosubcortical border was maintained insuloopecularly to the right. On 27-Jul-2017, the patient was considered stabile and was transferred to SBIB Mladenovac for further treatment and evaluation on the cardiology department. Upon admission, neurology examination revealed left central facial paslsy and left-sided hemiplegia. He was hospitalized until 04-Aug-2017 and discharged with significant improvement. The patient is currently undergoing rehabilitation at RHC "Selters" and is able to walk with the support of other person or kin. There is no evidence of left central facial palsy, but the dysarthria is still present.

Conclusion: Prevention of cerebrovascular accidents through identification and control of risk factors is crucial. It is highly recommended that the health system is better organized with the well-trained staff and improvement of technical equipment in several healthcare institutions on the territory of the Republic of Serbia, so that patients who have experienced stroke can be transferred as soon as possible to an institution where adequate care can be applied. Delay in treatment decreases chances for recovery, especially when it comes to high-risk patients as mechanical thrombectomy is one of the most important procedures in treating the stroke.

Keywords: stroke, mechanical thrombectomy, time

WHAT IS HAPPENING IN EVERY DAY PRACTICE IN ERA OF NEW ANICOAGULATS? PERSISTENCE OF VITAMIN K ANTAGONISTS IN PATIENTS WITH NONVALVULAR AF AND STROKE

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Background: The clinical practice guidelines recommend Vitamin K antagonists and NOACS in all patients with non valvular atrial fibrillation for their efficacy in preventing stroke. The aim of this study was to assess the adherence to stroke prevention guidelines in patients with cardioembolic stroke due to nonvalvular AF and provide an overall picture on the extent to which prior and current recommendations correspond to actually, every day practice population.

Methods: We enrolled patients admitted to the hospital for cerebrovascular disease "Sveti Sava" in first nine months with cardioembolic stroke due to the nonvalvular AF. All patients were taken medical history of nonvalvular AF and prior medical therapy, performed ECG, cranial MSCT, and color Doppler ultrasonography of the main neck arterial vessels.

Results: In 93 patients referred due to ischemic stroke, 61 was female (mean age 75,6 years), 32 male (mean age 75,8 years). All of them had previous history of nonvalvular AF and hypertension. Only 17 pts (18%) received VKA on the day of the admission, and their INR ratio was within therapeutic ranges. Mostly VKA was not recommended by family doctor or specialist, and they had no contraindications or comorbidities for prescribing VKA.

Conclusions: In every day practice VKA prescription for non valvular AF is extremely low and can not be scientifically explained in light of well-known guidelines. Is it, than, real to expect the adherence to stroke prevention in these pts with the novel anticoagulants?

Keywords: non valvular AF, stroke, OAC, NOAC

ROLE OF NUTRITION IN PREVENTION AND TREATMENT OF CARDIOVASCULAR DISEASE

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Nutrition plays a pivotal role in the development and prevention of *cardiovascular disease* (*CVD*). Numerous studies have found association between an excessive intake of fats (especially trans and saturated fats), refined carbohydrates, salt and alcohol, and inadequate intake of complex carbohydrates, dietary fibres, antioxidants and unsaturated fatty acids. In order to prevent development of CVD, World Health Organization (WHO) and European Heart Network (EHN) recommend diets rich in vegetables, fruits, wholegrain cereals, nuts and seafood, with limited intake of sugars, processed meat and refined grains. Intake of trans fats should be as low as possible (up to 1% of energy). Intake of unsaturated fats, in particular oleic acid and omega-3 fatty acids, should be increased since they exert protective effects against CVD. Among vitamins, vitamin D is of special importance in both prevention and treatment of CVD. However, supplementation is not as effective as dietary intake of vitamin D, or endogenous synthesis. According to WHO and EHN, the recommended daily intake of dietary fibre is more than 20g of non-starch polysaccharide. Nevertheless, dietary fibre intake in Europe is below these recommendations. A number of observational and clinical studies have shown that Mediterranean diet has anti-atherogenic effect and is considered as the healthiest dietary pattern for the prevention of CVD.

Keywords: Cardiovascular disease, nutrition

ENDOTHELIAL DYSFUNCTION AND NUTRITIVE INTERVENTION IN RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA), higher mortality is mainly due to cardiovascular disease, as a consequence of accelerated atherosclerosis found in these diseases. Endothelial dysfunction and the early stages of cardiovascular (CV) disease may occur in the absence of any clinical symptoms. Hence, finding methods for assessing vascular dysfunction during the early stages of the disease is important, particularly in patient groups at high CV risk. Multiple studies have shown that consumption of n-3 polyunsaturated fatty acids has a special role in reducing chronic inflammation. Evidence shows the impact that control of chronic inflammation has on the reduction of the risk of cardiovascular disease.

The first aim of the study was to investigate whether early signs of atherosclerosis and endothelial dysfunction, as measured by IMT and brachial artery flow-mediated (FMD) vasodilatation, were present in patients with RA compared with controls. The second aim of this study was to assess the oxidative stress status in patients with rheumatoid arthritis who used concentrated fish oil only or concentrated fish oil in combination with evening primrose oil in period of 3 months, by measuring markers of free radical production and levels of antioxidant.

Methods: Sixty patients with RA and 30 matched healthy controls without clinically evident CV disease were studied. Brachial and carotid ultrasonography was performed to determine FMD and IMT, respectively. Patients with RA completed a 12-week, prospective, randomized study of supplementation with fish oil (I group) and fish oil with primrose evening oil (II group) and control group was without supplementation. We also assayed immunological, inflammatory and metabolic laboratory markers.

Results: IMT was significantly higher in RA patients (1.00 ± 0.16 mm) patients than in controls (0.89 ± 0.13 mm) (P = 0.001). FMD% was significantly lower in RA (9.16 ± 7.03) as compared to controls (12.60 ± 5.49) (p = 0.005). It showed statistically higher values of vWF in the RA patients compared to the control group (p=0.01). Plasma levels of TBARS and NO2-, were statistically significant increased, also there was statistically significant increased GSH levels in erythrocytes and statistically significant decreased plasma levels of H2O2 in RA patients who completed a 12-week study with marine n-3 fatty acids and ɤ-linolenic acid (GLA).

Conclusions: The RA patients displayed accelerated development of atherosclerosis,as indicated by the increased IMT of carotid artery and impaired FMD. Our findings indicate that intakes of fish oil and evening primrose oil may be important to decrease inflammation, disease activity and oxidative stress biomarkers, through increased activities of antioxidant enzymes.

Keywords: rheumatoid arthritis, endothel, n-3 PUFA

CORONARY ARTERY ANOMALIES IN ADULT POPULATION: AN ENTITY IN SEARCH OF IDENTITY

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Background: Coronary artery anomalies are infrequent but anticipated findings during percutaneous interventions. Their prevalence ranges from 0.5% to 1.3%. Compared to consistent reporting in angiographic series, they seem to be underreported in interventional studies. During the last year primary PCI program, we encountered two patients with the solitary ostium for all three coronary arteries in the right aortic sinus of Valsalva and successfully managed both cases with implantation of drug eluting stents. In general, both patients belonged to the class of the Anomalous Origination of the Left Coronary Artery from the Opposite Sinus of Valsalva (left ACAOS).

Up to the present, several classifications of coronary artery anomalies have been used, some of them been fragmental. The latest classification came from Angelini's group in 2007. Coronary artery abnormalities are classified into 4 categories: A. anomalies of origination and course; B. anomalies of intrinsic coronary arterial anatomy; C. anomalies of coronary termination; and D. anomalous anastomotic vessels. Ectopic left coronary artery (or LAD) arising from right coronary sinus has 4 possible paths: 1. between aorta and pulmonary artery (interarterial), 2. intraseptal (or sub-pulmonary), 3. anterior to pulmonary outflow, 4. posterior. Ectopic circumflex arising from right aortic sinus may have following courses: 1. posterior atrioventricular groove, or 2. retroaortic.

Misdiagnosis of unsuspected aberrant origin of coronary arteries is a potential problem for busy operator leading to erroneous conclusion that the artery is occluded. Also, it is particularly important to have this entity in mind when dealing with acute coronary syndromes since the culprit lesion may be missed if the aberrant coronary anatomy is not identified. Selective coronary arteriography remains the gold standard for diagnosis of coronary artery anomalies, but occasionally it may fail to identify the proximal course of coronary arteries, where multi-slice CT gives more detailed information on the proximal tract of coronary arteries and on their relationship with the surrounding structures. For diagnostic purposes we summarize useful hints for successful angiographic recognition of dominant variants of anomalous origin and course of left coronary artery from the right sinus of Valsalva from the single RAO projection based on evocative "dot and eye" described by Serota in 1990.

Also, we debate on the functional significance of coronary anatomy anomalies emphasizing the novel findings that ischemic risk and risk of sudden death exist not only in the traditionally described inter-arterial course of left main originating from the right coronary sinus, applying particularly for the population of young competitive athletes. In certain cases, for further risk stratification supplementary studies, such as exercise stress testing, pharmacological stress echocardiography and ECG Holter monitoring should be required.

Finally, when facing with coronary artery anomalies, particularly with anomalous origin, either on diagnostic coronary angiography or during percutaneous procedures, operators should not limit themselves just to reporting them, but they should try to define their precise anatomy and to establish exact trajectory of the course of main coronary arteries. For that reason, we call for the inclusion of specific training in coronary artery anomalies into the interventional cardiology fellowship curriculum.

Keywords: coronary artery anomalies, ACAOS, percutaneous coronary intervention, sudden death

THE ROLE OF EXERCISE IN PREVENTION AND TREATMENT OF CARDIOVASCULAR DISEASE

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Results from substantial number of surveys have shown beneficial effects of physical activity and exercise training on cardiovascular system, both in prevention and treatment of cardiovascular disease. Recent investigations have focused on assessing the effects of different modalities of exercise training and which of them has the most favorable effect. Two modalities of physical activity are most often compared, high-intensity interval versus moderate-intensity continuous training. Bearing in mind the large number of variables that can affect results, such as age, type of cardiovascular disease and consequently the limitations in exercise training, smoking, habits, diet, motivation, results are controversial and considerably vary. In recent investigation from our laboratory, which was performed on rats, it has been shown that high-intensity interval training exerts more favorable effects on heart function. We also in our previous research showed beneficial effects of regular moderate exercise on heart. One of the key determinants that affects the exercise outcomes is redox balance, that is the ratio between the speed of production and elimination of free radicals. Over all data indicate that routine prescription of exercise training have has strong scientific support in healthy population and in patients with cardiovascular diseases, but modality of exercise as well as quantity of physical activity should be adapted to each patient individually.

Keywords: exercise, cardiovascular disease, redox balance

CORONARY ARTERY ANOMALIES IN ADULT POPULATION: AN ENTITY IN SEARCH OF IDENTITY

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Coronary artery anomalies are infrequent but anticipated findings during percutaneous interventions. Their prevalence ranges from 0.5% to 1.3%. Compared to consistent reporting in angiographic series, they seem to be underreported in interventional studies. During the last year primary PCI program, we encountered two patients with the solitary ostium for all three coronary arteries in the right aortic sinus of Valsalva and successfully managed both cases with implantation of drug eluting stents. In general, both patients belonged to the class of the Anomalous Origination of the Left Coronary Artery from the Opposite Sinus of Valsalva (left ACAOS). Up to the present, several classifications of coronary artery anomalies have been used, some of them been fragmental. The latest classification came from Angelini's group in 2007. Coronary artery abnormalities are classified into 4 categories: A. anomalies of origination and course; B. anomalies of intrinsic coronary arterial anatomy; C. anomalies of coronary termination; and D. anomalous anastomotic vessels. Ectopic left coronary artery (or LAD) arising from right coronary sinus has 4 possible paths: 1. between aorta and pulmonary artery (interarterial), 2. intraseptal (or sub-pulmonary), 3. anterior to pulmonary outflow, 4. posterior. Ectopic circumflex arising from right aortic sinus may have following courses: 1. posterior atrioventricular groove, or 2. retroaortic. Misdiagnosis of unsuspected aberrant origin of coronary arteries is a potential problem for busy operator leading to erroneous conclusion that the artery is occluded. Also, it is particularly important to have this entity in mind when dealing with acute coronary syndromes since the culprit lesion may be missed if the aberrant coronary anatomy is not identified. Selective coronary arteriography remains the gold standard for diagnosis of coronary artery anomalies, but occasionally it may fail to identify the proximal course of coronary arteries, where multi-slice CT gives more detailed information on the proximal tract of coronary arteries and on their relationship with the surrounding structures. For diagnostic purposes we summarize useful hints for successful angiographic recognition of dominant variants of anomalous origin and course of left coronary artery from the right sinus of Valsalva from the single RAO projection based on evocative "dot and eye" described by Serota in 1990. Also, we debate on the functional significance of coronary anatomy anomalies emphasizing the novel findings that ischemic risk and risk of sudden death exist not only in the traditionally described inter-arterial course of left main originating from the right coronary sinus, applying particularly for the population of young competitive athletes. In certain cases, for further risk stratification supplementary studies, such as exercise stress testing, pharmacological stress echocardiography and ECG Holter monitoring should be required. Finally, when facing with coronary artery anomalies, particularly with anomalous origin, either on diagnostic coronary angiography or during percutaneous procedures, operators should not limit themselves just to reporting them, but they should try to define their precise anatomy and to establish exact trajectory of the course of main coronary arteries. For that reason, we call for the inclusion of specific training in coronary artery anomalies into the interventional cardiology fellowship curriculum.

Keywords: coronary artery anomalies, ACAOS, percutaneous coronary intervention, sudden death

ORIGINALNI NAUCNI RADOVI

ORIGINAL SCIENTIFIC PAPERS

CORRELATION OF SALT SENSITIVITY, PLASMA RENIN ACTIVITY AND ALDOSTERONE IN HYPERTENSIVE PATIENTS

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POVEZANOST SO SENZITIVNOSTI, PLAZMA RENINSKE AKTIVNOSTI I NIVOA ALDOSTERONA KOD PACIJENATA SA HIPERTENZIJOM

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ABSTRACT

Plasma-renin values vary in normotensive and hypertensive populations. Some studies consider renin to be a key factor in the aetiology of hypertension, but other studies note that renin is an important factor in cardiovascular homeostasis and functions more as a growth factor than as a pressor hormone. The aim of this study was to assess the PRA and aldosterone values under different salt intake regimes in patients with essential hypertension. The study group consisted of 50 untreated patients (27 women and 23 men; average age 42±9,2 yrs.; average BMI 27,91±4,6 kg/m^2) with essential hypertension. All patients were put on a high-sodium diet (200 mmol NaCl per day) for one week after a week on a low-sodium diet (20 mmol NaCl per day). Sodium sensitivity (SS) was defined as a 10-mmHg increase in the mean blood pressure at the end of the high- vs. the low-sodium diet. The SS group consisted of 26 patients, and the sodium-insensitive group consisted of 24 patients. The PRA and aldosterone levels were determined in 12 patients. PRA values in the SS group during rest were significantly lower compared with the salt-resistant group during all regimes of salt intake (F=10,56, p=0,0012). Salt loading in SS patients causes a significant decrease in PRA (in rest and effort) values in comparison to values during a low salt intake regime (rest: t=4,49, p<0,001; effort: t=3,45, p<0,01). The PRA values in the salt-resistant group did not vary significantly under the different salt intake regimes. The aldosterone values followed the pattern of the PRA values. It is necessary to distinguish investigations on salt intake effects based on incidence and value of blood pressure and investigations on salt restriction's effects on of blood pressure levels (i.e., non-pharmacological hypertension therapy).

Keywords: Hypertension, plasma renin activity, aldosterone, salt sensitivity

SAŽETAK

Vrednosti renina u plazmi variraju u normotenzivnoj i hipertenzivnoj populaciji. Neka istraživanja ukazuju da renin ima značajnu ulogu u etiologiji hipertenzije dok druge studije ističu njegovu ulogu u kardiovaskularnoj homeostazi kao faktora rasta. Cilj studije je ispitivanje vrednosti plazma reninske aktivnosti (PRA) i aldosterone tokom različitih režima unosa soli kod bolesnika sa esencijalnom hipertenzijom. U studiju je uključeno 50 nelečenih bolesnika. (27 žena i 23 muškaraca; prosečne starosti 42±9,2 godina.; prosečnog indeksa telesne težine 27,91±4,6 kg/m^2) sa esencijalnom hipertenzijom. Svi pacijenti su bili na dijeti bogatoj soli sedam dana (200 mmol NaCl dnevno) posle nedelju dana na dijeti sa niskim sadržajem soli (20 mmol NaCl dnevno). So-senzitivnost je definisana kao porast srednjeg krvnog pritiska za 10 mmHg na kraju povećanog unosa soli u odnosu na period sa niskim unosom soli So-senzitivnih bolesnika je bilo 26 dok je so-rezistentih bilo 24. PRA i aldosteron su određeni kod 12 bolesnika. Pokazano je da su vrednosti PRA u so-senzitivnoj grupi bolesnika bili statistički niže u mirovanje u poređenju sa so-rezistentnim bolesnicim tokom svih režima unosa soli. (F=10,56, p=0,0012). Takođe je pokazano da je opterećenje soli dovelo do značajnog sniženja PRA kod so-senzitivnih bolesnika (u miru i naporu) u poređenju sa PRA vrednostima tokom dijete sa niskim unosom soli (mirovanje: t=4,49, p<0,001; naport: t=3,45, p<0,01). PRA vrednosti u so-rezistentnoj grupi nisu značajno varirale tokom različitih režima unosa soli. Vrednosti aldosterone su pratili obrazac PRA vrednosti. Neophodno je preciznije istražiti sve obrasce so-senzitivnosti radi bolje determinacije ne-farmakološke terapije hipertenzije kod ovih bolesnika.

Ključne reči: hipertenzija, plazma reninska aktivnost, aldosteron, so senzitivnost

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INTRODUCTION

With a decrease in extracellular volume, the binding of ATII to its receptors on vascular smooth muscle cells decreases due to previous ATII bindings to the same receptors, which leads to lower blood pressure levels. At the same time, the number of ATII receptors is increased on suprarenal glands, which causes increased aldosterone production. The overall result is sodium retention without a significant increase in blood pressure. It has been reported that the modulation of the adrenal and vascular responses to ATII is non-adequate in 30-50% of hypertensive patients, who are then considered "non-modulators"[1].

Most patients with essential hypertension are not characterized as expected (i.e., higher perfusion pressure in juxta-glomerular cells and higher blood volume), with low, inhibited plasma-renin activity (PRA) but are instead characterized rather withby normal or even high PRA values. According to Sealey and co., this discrepancy is caused by nephron heterogeneity, with a special subgroup of ischaemic nephrons that contribute to high PRA values[2].

The third model of "non-modulation" was proposed by Williams and Holenberg[3]. Healthy individuals modulate the response of target tissues to ATII according to their sodium intake. Decreased sodium intake is followed by an increase in aldosterone production and a decrease in vascular response. During sodium loading, the suprarenal response is decreased, and the vascular response is increased, especially in the kidney circulation, which stimulates sodium excretion from the kidney. Williams and Holenberg reported that 50% of patients with essential hypertension with normal and/or high PRA values are characterized with disorders of ATII modulation on target tissues according to sodium intake and are considered "non-modulators". Regulatory disorders characterized by fixed ATII concentrations in target tissues lead to increased aldosterone production during sodium restriction and increased blood flow in the kidney circulation during sodium loading. The confirmation of this hypothesis was achieved by the correction of abnormalities with ACE inhibitor administration.

Numerous mechanisms of pathogenesis in hypertensive patients with low PRA values have been described[4]. In the majority of patients, low PRA values are followed by normal (not low, as expected) aldosterone values, which are explained by increased sensitivity of the suprarenal glands to ATII. Several studies have shown low rates of cardiovascular complications in patients with essential hypertension and low PRA values[5,6]. Other studies have revealed that diuretic therapy is more efficient in hypertensive patients with low PRA values than in hypertensive patients with high PRA values. In the former group, diuretic therapy leads to smaller increases in PRA values, with smaller vascular responses and aldosterone production, which cause decreases in plasma volume and blood pressure[7].

In "bipolar vasoconstriction-volume analysis", the vasoconstriction of the kidney's arterioles is caused by ATII actions, which are responsible for hypertension in patients with high PRA values, and increased plasma volume, which is responsible for hypertension in patients with low PRA values[8,9]. It should be emphasized that most clinicians and research workers rely on PRA blood values, but the tissue concentrations might be different, and the pathogenesis of the disorder might be even more complicated.

AIM OF THE STUDY

The aim of this study was to assess PRA and aldosterone values during different regimes of salt intake in patients with essential hypertension.

PATIENTS AND METHODS

The study group consisted of 50 untreated patients (27 women and 23 men; average age 42±9,2 yrs.; average BMI 27,91±4,6 kg/m^2) with essential hypertension. The causes of secondary hypertension were excluded with standardized endocrinological investigation, and antihypertensive therapy was stopped two weeks before the study. A finding of fixed elevated blood pressure ^{3}160/95 mmHg without therapy over at least four days was considered as stable hypertension. Borderline hypertension was defined as a temporary increase in diastolic pressure ^{3}90 mmHg during three different measurements. Hypertension was classified according to the Seventh Joint Committee for the detection, evaluation and treatment of hypertension. The study was conducted in hospital. All patients were put on a high-sodium diet (200 mmol NaCl per day) for one week after a week on a low-sodium diet (20 mmol NaCl per day). Sodium sensitivity was defined as a 10-mmHg increase in mean blood pressure at the end of the high- vs. the low-sodium diet. The sodium-sensitive group consisted of 26 patients, and the sodium-insensitive group consisted of 24 patients. The electrolytes in serum and urine and blood pressure were measured on the last day of normal salt intake and on 1st, 3rd and 5th days of the low- and high-sodium diets. All patients had normal sodium and potassium serum concentrations. Sodium intake was controlled by 24-hour urine sampling, and sodium excretion between 100 and 150 mmol/d was considered satisfactory. Calcium intake was standardized and was approximately 817 mg per day. During the 7-day low-sodium diet, sodium intake was balanced to achieve a sodium excretion of 40 mmol per day. During the high-sodium intake, 10 mg of salt (NaCl) was added to each participant's normal food intake. Sodium excretion more than 200 mmol/day was considered satisfactory during the high-sodium diet. Blood samples for aldosterone and PRA determinations were prepared according to standardized procedures. Aldosterone was measured using a Maia-Biodata radioimmunoassay with a normal range of 0.03324-0.4155 nmol/l in the lying position, with an interassay CV=8.8% and an intraassay CV=7.6%. PRA was measured using a Sorin Biomedica radioimmuno-

Table 1. Average PRA and aldosteron values (rest and effort) during different regimes of salt intake

Regime	Normal salt intake		Low salt intake		High salt intake	
	rest	effort	rest	effort	Rest	effort
PRA						
Salt-sensitive	0,16±0,03	0,22±0,08	0,20±0,04	0,26±0,05	0,12±0,01	0,16±0,06
Salt-resistent	0,27±0,06	0,44±0,21	0,21±0,07	0,41±0,18	0,25±0,09	0,45±0,02
Aldosteron						
Salt-sensitive	0,3±0,14	0,46±0,14	0,36±0,14	0,58±0,29	0,13±0,04	0,21±0,1
Salt-resistent	0,33±0,1	0,53±0,3	0,31±0,08	0,74±0,52	0,44±0,19	0,53±0,21

assay, with a normal range of 0.1542-2.159 nmol/l/h in the lying position and a normal range of 1.1565-4.3947 nmol/l/h in the supine position, with an interassay CV=11.5% and an intraassay CV=9.9%. Blood pressure was measured daily at 8 AM (before breakfast) and at 6 PM with the same sphygmomanometer. Blood pressure value was considered the average value of two measurements on the non-dominant arm after 5 minutes of rest. The criteria for hypertension were diastolic pressure ³ 90 mmHg, (Korotkoff phase V) and/or systolic pressure ³ 140 mmHg without therapy. Patients were divided to a salt-sensitive and a salt-resistant group according to the change in mean arterial pressure during the low- and high-salt diets (20 vs. 200 mmol/day). Average values of mean arterial pressure were used for the determinations of salt sensitivity. Increases of more than 10 mmHg in the mean arterial pressure of were considered salt sensitivity. The RMANOVA test, correlation analysis methods, and the unpaired and paired t-tests were used for statistical analyses.

RESULTS

PRA and aldosterone levels were determined in 12 patients. Two blood samples were obtained in morning hours (in rest and effort) on normal salt intake and on the 5th days of the low- and high-salt diets. After analysing the data, we divided patients into a salt-sensitive group (with low basal PRA values) and a salt-resistant group (with high basal PRA values).

Statistical analysis revealed that PRA values in the salt-sensitive group during rest were significantly lower compared with the salt-resistant group during all regimes of salt intake (F=10,56, p=0,0012).

It was also shown that salt loading in salt-sensitive patients caused significant decreases in PRA values (in rest and effort) in comparison with values during the low-salt intake regime. (rest: t=4,49, p<0,001; effort: t=3,45, p<0,01). PRA values in the salt-resistant group did not vary significantly during the different regimes of salt intake (Table 1).

Aldosterone values followed the pattern of PRA values and were significantly different in the salt-sensitive group (in rest and effort) between the high- and low-salt intake regimes (rest: 3,53, p<0,01; effort: t=2,37, p<0,05).

Correlation analysis of PRA and aldosterone values with calcium parameters revealed positive correlations between PRA, aldosterone and ionized calcium (PRA: r=0,62, r^2=0,38, p=0,034, aldosterone: r=0,51; r^2=0,26; p=0,041) in salt-sensitive patients during the high-salt intake regime. No significant correlations were found between these parameters during the normal and low-salt intake regimes.

A negative correlation between PRA and urinary calcium was found in the high-salt intake regime in salt-sensitive patients (r=-0,41; r^2=0,17; p=0,049). Aldosterone was not significantly correlated with urinary calcium.

Total blood calcium was not significantly correlated with PRA and aldosterone during all three regimes. We also found negative correlations of PRA (r=0,53, r^2=0,28, p=0,02) and aldosterone (r=-0,47, r^2=0,22, p=0,035) values with mean arterial pressure regarding salt sensitivity during the high-salt intake regime.

DISSCUSION

Kawasaki and co-workers first divided essential hypertension into salt-sensitive and salt-resistant types according to the response of blood pressure to salt loading[10]. Data presented in the literature showed that salt sensitivity in established essential hypertension occurs in between 30 and 60% of cases[11]. In borderline hypertension, salt sensitivity occurs in 29% of cases, while in the normotensive population, salt sensitivity occurs in 16-25% of cases. The prevalence of salt-sensitive hypertension depends on the defining criteria. For the definition of salt sensitivity, some authors use changes in salt intake, and others use the response of blood pressure to the ratio of the increase in volume due to sodium intake and the decrease due to diuretic administration[12, 13]. Different sodium intake protocols are also used (20 and 220 mmol/d or 70 and 370 mmol/d). It is important to emphasize that changes in blood pressure in response to sodium intake follow a normal distribution curve; therefore, the division is arbitrary.

In several studies, Resnick and co-workers showed correlations between calcium metabolism disturbances, salt sensitivity, PRA and aldosterone system and calcium-regulating hormones in hypertensive patients[14,15]. The results of these studies showed the characteristic metabolic and

hormonal profiles of salt-sensitive patients (low basal PRA values, higher PTH and 1,25-$(OH)_2$-D values, lower calcitonin values, low ionized calcium and higher serum magnesium values), while the salt-resistant group was characterized by reversed metabolic and hormonal profiles. The first studies that investigated the pathogenesis of hypertension explained the increase in the intracellular calcium concentration (and the increase in vascular resistance) by the primary disturbance in membrane ion transport or the actions of some circulating factors on membrane transport[16]. Resnick showed that PRA and calcium-regulated hormones co-ordinate the modulation of sodium's and calcium's effects on blood pressure by influencing membrane ion transport and intracellular ion concentrations. The authors stated that salt and calcium sensitivities could be partially explained by disturbances in metabolic and hormonal parameters[17]. Other authors confirmed the presence of low PRA values in salt-sensitive normotensive and hypertensive individuals[18]. with the salt-resistant group during different regimes of salt intake. Salt loading in the salt-sensitive group caused significant decreases in PRA values, both in rest and effort, in comparison with those values during low sodium intake. Aldosterone values in our study followed the pattern of PRA values during all diet regimes. We also investigated the correlations of different parameters. We found positive correlations between PRA values, aldosterone and ionized calcium and a negative correlation between PRA values and urinary calcium during the high-salt intake regime. Our study also revealed negative correlations between PRA and aldosterone values and mean arterial pressure regarding salt sensitivity during the high-salt intake regime. These results are similar to those of Resnick's group and some other authors, who found significantly low PRA values in salt-sensitive hypertensive and normotensive persons and higher PRA values in salt-resistant individuals[19, 20]. Resnick especially emphasized that low PRA values and ionized calcium could be excellent predictors of the hypotensive effect of calcium supplementation in hypertensive patients.

Some studies have shown that salt-resistant hypertensive patients have higher PRA and aldosterone serum values in comparison with salt-sensitive persons during a low-salt intake regime[21, 22]. Our study confirmed these findings, although we did not detect significant correlations. Significant decreases in these parameters in the salt-sensitive group during salt loading could partially explain better possibilities for the excretion of loaded sodium. Other authors did not find significant differences in basal PRA and aldosterone values in normotensive, salt-sensitive and salt-resistant hypertensive persons during different salt intake regimes[23,24].

Numerous authors found negative correlations between decreased blood pressure during salt restriction and increased PRA values[25]. The degree of renin system reactivity could predict the response of blood pressure to salt restriction. Cappuccio administered saralasin (a competitive AII inhibitor) to hypertensive patients on the 5th day of a low-salt intake regime. The decrease in blood pressure caused by saralasin administration was negatively correlated with the decreased blood pressure caused by sodium restriction. Patients with the most prominent decrease in blood pressure during salt restriction had the smallest decrease of blood pressure during saralasin administration, demonstrating the significance of the renin-angiotensin-aldosterone response to salt restriction. A special subgroup involves patients with heart failure, where more liberal sodium intake can achieve an adequate suppression of plasma renin levels[26]. Paterna et al., in a randomized clinical trial, showed that sodium restriction to 80 mmol/day significantly increased hospitalization and mortality compared with a sodium intake of 120 mmol/day in patients with compensated heart failure and aggressive diuretic therapy[27].

CONCLUSION

It is necessary to distinguish investigations on the effects of salt intake on the incidence and values of blood pressure from investigations on salt restriction's effects on blood pressure levels (i.e., a non-pharmacological therapy for hypertension). Research on salt-sensitive parameters seeks details to quantify the already-established correlation. Different factors could play significant roles in the salt sensitivity phenomenon: i.e., higher sodium retention, abnormal supressibility of the RAAS system, abnormal responses of the sympathetic nervous system, differences in vascular reactivity and abnormality in Na-K-ATP enzymes.

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ORTHOSTATIC HYPOTENSION AND THERAPY WITH AN ACE INHIBITOR IN HYPERTENSIVE PATIENTS

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ORTOSTATSKA HIPOTENZIJA KOD PACIJENATA SA HIPERTENZIJOM NA TERAPIJI ACE INHIBITORIMA

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ABSTRACT

Orthostatic hypotension (OH) is defined as a drop in the systolic blood pressure greater than 20 mmHg and that of the diastolic blood pressure greater than 10 mmHg within 3 minutes from the change of the body's position from lying or sitting down to standing up. The objective of this study is to analyse the incidence and severity of orthostatic hypertension when taking one of the generic representatives of the ACE inhibitor group (trandolapril) as a monotherapy in patients with essential hypertension. The study involved 314 patients (medium age of 54±4 years; 52.5% men) with poorly regulated hypertension for whom trandolapril was introduced as monotherapy. The incidence rates of patients with and without orthostatic hypotension between the first and second examination were not statistically significantly different. At the second control examination, 7 patients (2,3%) still had orthostatic hypotension, as was the case at the first examination. Between the third and fourth controls, a statistically significant decrease in the number of patients with orthostatic hypotension was recorded. No statistically significant difference in the incidence of orthostatic hypotension between patients with normal body mass and those who were overweight was observed. Our study has shown that certain ACE inhibitors, such as Trandolapril, do not have a pronounced adverse effect with regard to orthostatic hypotension and that in long-term application, they can have a positive role in the prevention of hypotensive episodes and improving patient compliance.

Keywords: *Hypertension, orthostatic hypotension, ACE inhibitors*

SAŽETAK

Ortostatska hipotenzija (OH) se definiše kao pad sistolnog krvnog pritiska za više od 20 mmHg i dijastolnog krvnog pritiska za više od 10 mmHg unutar 3 minute od promene položaja tela iz ležećeg ili sedećeg u uspravni. Cilj rada je ispitivanje učestalosti i težine ortostatske hipotenzije pri upotrebi ACE inhibitora kao monoterapije kod bolesnika sa esencijalnom hipertenzijom.. U studiju je uključeno 314 pacijenata (srednje starosti 54±4 godina.; 52.5% muškaraca) sa loše regulisanom hipertenzijom kojima je trandolapril uveden kao monoterapija. Učestalost ispitanika sa i bez ortostatske hipotenzije, između prve i druge kontrole nije se statistički značajno razlikovao 4. Na drugoj kontroli 7 ispitanika (2,3%) i dalje je imalo ortostatsku hipotenziju kao i na prvoj kontroli. Između treće i četvrte kontrole zabeležen je statistički značajan pad broja ispitanika sa ortostatskom hipotenzijom. Nije uočena statistički značajna razlika u učestalosti ispitanika sa ortostatskom hipotenzijom između normalno uhranjenih i gojaznih ispitanika. Naša studija je pokazala da neki ACE inhibitori poput trandolaprila nemaju izraženo nepovoljan efekat u smislu ortostatske hipotenzije i da u dugotrajnoj primeni mogu imati pozitivnu ulogu u smislu prevencije hipotenzivnih epizoda.

Ključne reči: *hipertenzija, ortostatska hipotenzija, ACE inhibitori*

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INTRODUCTION

Hypertension is not just a disease but also a risk factor for developing cardiovascular and cerebrovascular diseases. Poor control and inadequate treatment of hypertension have resulted in sharp increases in the incidence and prevalence of this disease in Serbia in the past half century. ACE inhibitors are a widespread group of drugs most commonly utilized to treat arterial hypertension, heart failure, conditions occurring post-acute myocardial infarction, diabetes, diabetic and non-diabetic renal disease, left ventricular hypertrophy, and microalbuminuria (1). The mechanism of action for these drugs is based on blocking the angiotensin-converting enzyme (ACE), which, in turn, blocks the conversion of angiotensin I into angiotensin II. The advantage of using ACE inhibitors is evident not only because they decrease the activity of angiotensin II but also because they decrease catecholamine levels and influence vascular remodelling (2). Trandolapril is one of the so-called non-sulfhydryl-containing ACE inhibitors. Trandolapril is a prodrug; to exert its effects, it needs to be de-estrified into its active metabolite, trandolaprilat. Trandolaprilat has a high affinity for binding to the ACE; the required concentration for blocking 50% of ACE is lower than those of enalaprilat and captoprilat and is similar to that of ramiprilat (3). When rising from a horizontal position, a small drop in the systolic and a small rise in the diastolic blood pressure normally occur. Orthostatic hypotension (OH) is defined as a drop in the systolic blood pressure greater than 20 mmHg and that of the diastolic blood pressure greater than 10 mmHg within 3 minutes from the change of the body's position from lying or sitting down to standing up (4).

OH can occur in any age and in both sexes, and its prevalence increases with age; its occurrence within the population over 65 years of age is estimated at 5-30% (5). Orthostatic hypotension is a consequence of dysautonomia, which changes the reflex response of the body to postural stress. It can be asymptomatic or accompanied by a range of symptoms. The most common symptoms are dizziness, blurry vision, headache, weakness, palpitations, nausea, and neck pain. It is advised to occasionally measure blood pressure both when lying down and sitting up in all patients above 50 years of age and to gradually introduce hypertension medication (6). Aetiologically, OH is neurogenic or non-neurogenic, while in terms of the timing of the symptoms, it is initial, classic and delayed. Orthostatic hypotension is a significant side effect of some hypertension drugs, including beta-blockers, calcium blockers, ACE inhibitors, and diuretics (7). Keeping in mind the heterogeneous and individual responses of patients suffering from essential hypertension to certain groups of drugs, it is necessary to determine the characteristics of the patients' responses after taking ACE inhibitors in terms of the occurrence of orthostatic hypotension. Analysing the incidence of orthostatic hypotension in certain groups of patients can help with selecting specific drug groups for treating essential hypertension. The objective of this study is to analyse the incidence and severity of orthostatic hypertension when taking one of the generic representatives of the ACE inhibitor group (trandolapril) as a monotherapy in patients with essential hypertension.

METHODS

This research is part of a multicentric, prospective study conducted in over a 24-week period. The study involved 314 patients (medium age of 54±4 years; 52.5% men) with poorly regulated hypertension for whom trandolapril was introduced as monotherapy.

The definition of poorly regulated hypertension included values of systolic blood pressure ≥ 140 and of diastolic blood pressure ≥ 90 mmHg, measured in two control examinations. The patients were divided into two groups. The first group included patients with stage I arterial hypertension (140/90–149/109 mmHg). The second group included patients with stage II arterial hypertension (> 150/110 mmHg).

The study did not include patients younger than 18 years of age, pregnant women (positive β-hCG test), nursing mothers, women of reproductive age with inadequate contraception and the possibility of conception, patients with orthostatic hypotension, patients with serious renal failure, anaemia (haemoglobin < 100 g/L), electrolytic imbalance, heart rhythm disorders, transaminase values 1.5 times higher than reference values, and patients with microalbuminuria > 300 mg/24 h.

All patients were initially given a physical examination: their body weight and height were recorded, their body mass index calculated, a 12-channel EKG conducted, and their heart rate was calculated. Control visits of these patients were conducted after 6, 12 and 24 weeks upon their inclusion in the study. All patient examinations included measurements of blood pressure while sitting and standing and determinations of heart rate. Blood pressure was measured using a mercury sphygmomanometer, placing the cuff to cover 2/3 of the patient's upper arm and including at least 80% of its circumference. Measurements were conducted three times on both arms with one-minute breaks, followed by calculation of the mean value. Each patient's trandolapril dose was corrected at control visits to achieve adequate blood pressure regulation (≤ 120/80 mmHg). All patients signed an informed consent before they were included in the study. The study was approved by the Ethics Review Board of the Cardiovascular Institute Dedinje.

Data are described through descriptive statistical methods and were analysed using repeated measures ANOVA calculations. The descriptive statistical methods used in the research included central tendencies measures (arithmetic mean value, median), structure indicators (expressed in percentages) and variability measures (standard deviation, minimal and maximal value).

RESULTS

The study included 314 patients. The average age of the study subjects was 54,41±11,875 years. The youngest patient was 28, and the oldest was 88. There were 165 men (52,5%) and 149 women (47,5%) in the test group. No statistically significant difference was observed regarding the incidence of patients of either sex (chart 1). The average BMI value in patients in this group was 26,91±3,80, with a range of 16,94 to 37,64. Statistically significant differences in incidence were observed for patients with BMIs both lower and higher than 25. There was a statistically more significant incidence of patients with BMIs equal to or greater than 25 (chart 2). A total of 32,5% patients had BMIs lower than 25, while 67,5% patients had BMIs equal to or greater than 25. Patients were randomized according to hypertension severity into two groups. No statistically relevant differences in the incidence rates of patients with varying degrees of hypertension were observed. In the study group, 152 patients had hypertension of the first degree (48,4%), while 162 patients (51,6%) had hypertension of the second degree (chart 3). At the first control examination, the number of patients with orthostatic hypotension was not statistically significantly different than the number of patients who had orthostatic hypotension before introducing the Trandolapril treatment (chart 4). At the first doctor's appointment, 32 (10,3%) patients had orthostatic hypotension, while 280 patients (89,7%) were without orthostatic hypotension. At the first control examination after the treatment had been introduced (the second doctor's appointment), out of 32 patients who had orthostatic hypotension before Trandolapril treatment, 11 patients (2,3% of the total number of patients) still had orthostatic hypotension, while 31 patients (9,9%) who did not have orthostatic hypotension before the treatment was initiated now had orthostatic hypertension 4-6 weeks into treatment. The incidence rates of patients with and without orthostatic hypotension between the first and second examinations were not statistically significantly different. At the second control examination, 7 patients (2,3%) still had orthostatic hypotension, as was the case at the first examination, while 28 patients who did not have orthostatic hypotension at the first examination now had it at the second control. Between the third and fourth controls, a statistically significant decrease in the number of patients with orthostatic hypotension was recorded (chart 4). Namely, 24-26 weeks into the treatment, orthostatic hypotension was observed only in 6,4% of patients. Seven patients (2,2%) with orthostatic hypotension at the third control examination also had it at the fourth examination, while orthostatic hypotension was observed in 13 patients (4,2%) who did not previously have it. No statistically significant difference in the incidence of orthostatic hypotension in patients with normal body mass and those who were overweight was observed. Upon introducing Trandolapril treatment, a somewhat higher incidence of orthostatic hypotension was observed in patients with BMIs greater than 25, but until the end of the monitoring period, the incidence rates of orthostatic hypotension in both groups of patients were less than 10% (chart 5). At the end of the study, 2% of patients suffered from side effects. During the study, there were no deaths among the tested patients (table 1).

SEX

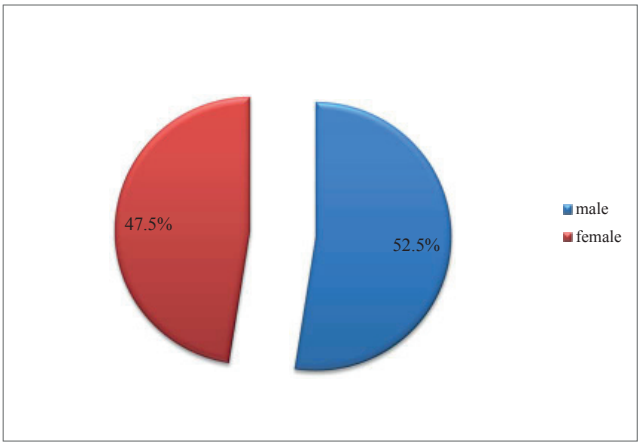

Chart 1. Distribution of subjects by gender

BMI

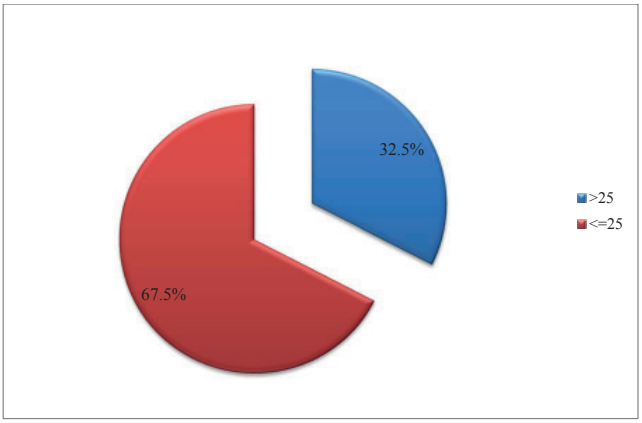

Chart 2. Distribution of subjects according to BMI

Severity of hypertension

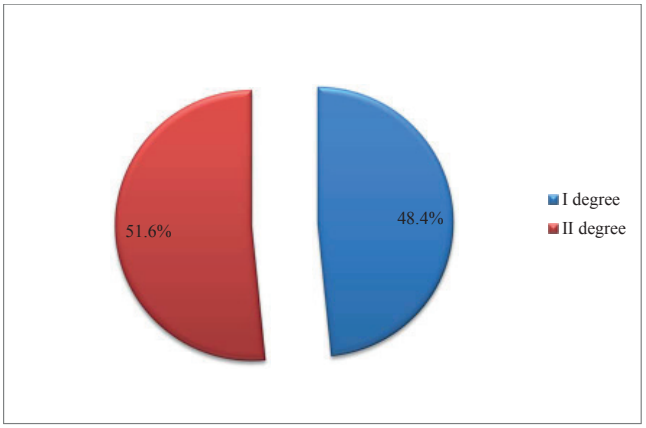

Chart 3. Distribution of subjects according to severity of hypertension

DISCUSSION

Our study illustrates the excellent efficiency and safety of Trandolapril use in patients with unregulated hypertension and cardiovascular complications of hypertension. Over 24 weeks, Trandolapril caused significant decreases in systolic, diastolic and mean blood pressure in all patients. The anti-hypertensive effect of Trandolapril was strong and continuous throughout the study period. Our study showed a very low percentage of side effects, with a particularly low incidence of dry cough (0.3%). Our study also revealed a statistically significant decrease in the number of subjects with orthostatic hypotension in the second half of the study period, between the third and fourth control examinations. After 24-26 weeks of treatment, only 6,4% of study subjects had orthostatic hypotension. No statistically significant difference in the incidence of orthostatic hypotension in patients with normal body mass and those who were overweight was observed. Upon introducing Trandolapril treatment, a somewhat higher incidence of orthostatic hypotension was observed in patients with BMIs greater than 25, but until the end of the monitoring period, the incidence rates of orthostatic hypotension in both groups of patients were less than 10%. Several studies have shown that there are differences in the hypotensive effects of different ACE inhibitors, keeping in mind the differences in their pharmacokinetics.

Orthostatic hypotension is more frequent in patients with diabetes mellitus and is accompanied by higher incidence rates of falls, fractures and early death (8). Orthostatic hypotension can occur occasionally depending on the time of day and other medications being taken. The condition is more frequent in the morning and requires taking several measurements to achieve an accurate diagnosis. New diagnostic methods, such as the "table-tilt" test and "beat-to-beat" blood pressure monitoring, enable better quantification of orthostatic hypotension (9). Numerous studies have demonstrated the clinical efficiency and safety of the use of Trandolapril in hypertension treatment. The drug-induced orthostatic hypotension mechanism is connected to the drug's interference with reflexes that limit vasoconstriction, heart rate frequency or the determination of the minute volume (10). Several studies have shown that orthostatic hypotension is coupled with cardiovascular and cerebrovascular mortality (heart attack, stroke, heart failure) (11). However, the mechanisms of origin

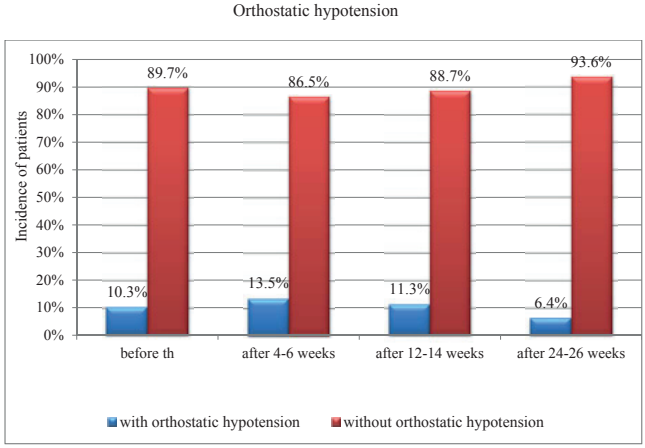

Chart 4 Incidence of orthostatic hypotension in patients during trandolapril therapy

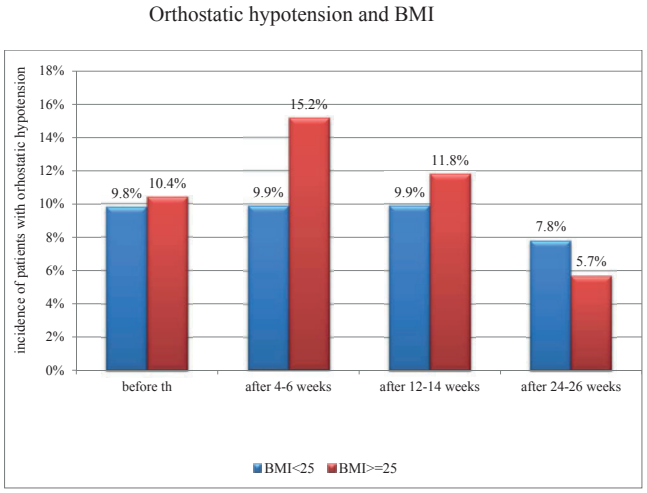

Chart 5. Incidence of orthostatic hypotension in patients with normal BMI and obese patients during trandolapril therapy

Table 1. Adverse effects

Incidence of adverse effects

Incidence of adverse effects n (%)	Time		
	After 4-6 weeks	After 12-14 weeks	After 24-26 weeks
No adverse effectsa	299 (98,7%)	296 (98,3%)	299 (98,0 %)
Mild fatigue	1 (0,3%)	0 (0%)	0 (0%)
Mild occasional a	1 (0,3%)	0 (0%)	0 (0%)
Rare episodes of dry cough	1 (0,3%)	1 (0,3%)	1 (0,3%)
Mild nausea	1 (0,3%)	0 (0%)	0 (0%)
Mild vertigo	0 (0%)	2 (0,7%)	1 (0,3%)
Occasional haedache	0 (0%)	2 (0,7%)	0 (0%)
Occasional moderate vertigo	0 (0%)	0 (0%)	4 (1,3%)

#Fridman-ov test

for orthostatic hypotension in patients with hypertension and diabetics have not yet been fully explained (12). The Malmö Study on prevention has especially looked into the connection between the risk factors and the occurrence of orthostatic hypotension (13). The study determined that, apart from hypertension and diabetes, other factors, such as smoking, age and positive patient history for cardiovascular disease, were coupled with an increased incidence of orthostatic hypotension. The ARIC Study showed that orthostatic hypotension was coupled with a considerable risk of ischaemic stroke in all age categories (14). The analysis of a large "British Women's Heart and Health Study" showed that there is a considerable prevalence of orthostatic hypotension in patients with hypertension (15). The prevalence of orthostatic hypotension in women between 60 to 80 years of age is 28%; systolic orthostatic hypotension was more frequent than diastolic orthostatic hypotension (20.4% vs. 12.4%). A higher correlation between the use of ACE inhibitors and the prevalence of orthostatic hypotension in women over 65 years of age has been shown. A large study by Irish authors looked into the effects of monotherapy for hypertension (ACE inhibitors, beta-blockers, calcium blockers and diuretics) on the prevalence of orthostatic hypotension in older patients with hypertension. The research showed that only monotherapy with beta-blockers was coupled with long-term and persistent orthostatic hypotension (16). A group of French authors demonstrated a higher occurrence of orthostatic hypotension with the use of diuretics and calcium blockers, while ACE inhibitors were not connected to a significant postural drop in blood pressure (17). In differential diagnosis, we have to discern persistent orthostatic hypotension from the condition called initial orthostatic hypotension, which can occur at both young and old ages. Affected individuals are persons who suffer from a transitory (up to 15 seconds) drop in blood pressure when moving from lying down to an upright position (18). The pathophysiological cause for this condition is a temporary imbalance between the minute volume and the peripheral vascular resistance. Finally, it is important to note that in both short- and long-term use, Trandolapril is characterized by a low incidence of orthostatic hypotension, unlike other ACE inhibitors. Several other studies have also shown the absence of orthostatic hypotension with the use of Trandolapril (19, 20).

CONCLUSION

Although treatment for hypertension is an important step in reducing cardiovascular risk, orthostatic hypotension and its symptoms are important causes of poor compliance and inadequate treatment. Careful diagnosis of orthostatic hypotension in patients with hypertension is necessary, as is the adequate application of both non-pharmacological and pharmacological measures with the aim of both mitigating and treating the condition. Our study has shown that certain ACE inhibitors, such as Trandolapril, do not have a pronounced adverse effect with regard to orthostatic hypotension and that in long-term application, they can have positive roles in the prevention of hypotensive episodes and improving patient compliance.

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THE ASSOCIATION BETWEEN OBESITY AND VISIT-TO-VISIT VARIABILITY IN SYSTOLIC BLOOD PRESSURE: A PROSPECTIVE STUDY

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POVEZANOST GOJAZNOSTI I VARIJABILNOSTI SISTOLNOG KRVNOG PRITISKA PRILIKOM POSETA: PROSPEKTIVNA STUDIJA

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ABSTRACT

With the prevalence of obesity and all accompanying health risks, both prevention and health education, as well as identifying predictors for the development of obesity-related diseases are primary. The pathophysiological relationship between obesity and visit-to-visit variability in systolic blood pressure (SBPV) has not been completely resolved.

To investigate the association between obesity and SBPV in hypertensive patients.

The prospective study comprised three visits was performed at the hypertension outpatient clinic during the follow up period of 22-months between March 2014 and January 2016.

This study included 300 randomly selected hypertensive patients (average 67.76±9.84 years), who were divided in groups of obese/non-obese examinees. SBPV was defined as the standard deviation (SD) from three values of SBP.

The values of SBP and SBP-SD were significantly higher in the group of obese hypertensive patients than in the group of non-obese patients (126.67±8.22 vs 120.45±7.79 mmHg, 11.00±5.64 vs 7.34±3.96; p<0.01). The highest SBPV was recorded in the 4th quartile in obese patients (43.13±7.50 mmHg). There was statistically stronger correlation between SBPV and BMI/Waist cirumferences (WC) (ρo=0.425/ ρo=0.356, p<0.01). During 22-months follow up there was a significant decrease of SBPV for 8.2 mmHg, BP for 31/8 mmHg, BMI for 3.8 kg/m², WC for 10 cm and body weight for 8.24 kg.

During 22-months follow-up, reduction of body weight was associated with reduction of blood pressure variability in hypertensive patients. Persistently decrease both body weight and long term visit-to-visit variability may explain lower cardiovascular risk in obese-related disease.

Key words: *Obesity, hypertension, visit-to-visit systolic blood pressure variability.*

SAŽETAK

Sa prevalencijom gojaznosti i svih pratećih zdravstvenih rizika, primarna je preventivna i zdravstvena edukacija, kao i identifikovanje prediktora za razvoj bolesti povezanih sa gojaznošću. Patofiziološki odnos između gojaznosti i varijabilnosti sistolnog krvnog pritiska prilikom poseta pacijenta (SBPV) nije u potpunosti jasan.

Istražiti povezanost između gojaznosti i SBPV kod hipertenzivnih pacijenata.

Prospektivna studija je obuhvatila tri posete u ambulanti za hipertenziju tokom perioda praćenja od 22 meseca u period od marta 2014 i januara 2016 godine.

U ovoj randomiziranoj studiji uključeno je 300 hipertenzivnih pacijenata (prosečne starosti 67,76 ± 9,84 godina), koji su podeljeni u grupu gojaznih i negojaznih ispitanika. SBPV je definisan kao standardna devijacija (SD) tri vrednosti SBP.

Vrednosti SBP i SBP-SD bile su znatno veće u grupi gojaznih hipertenzivnih pacijenata nego u grupi ne-gojaznih pacijenata (126.67 ± 8.22 vs. 120.45 ± 7.79 mmHg, 11.00 ± 5.64 vs 7.34 ± 3.96, p <0.01). Najveći SBPV zabeležen je u četvrtom kvartilu kod gojaznih pacijenata (43,13 ± 7,50 mmHg). Dokazana je statistički jaka korelacija između SBPV i BMI / obim struka (OS) (ro = 0,425 / ro = 0,356, p <0,01). Tokom 22-mesečnog praćenja došlo je do značajnog smanjenja SBPV za 8,2 mmHg, BP za 31/8 mmHg, BMI za 3,8 kg / m2, OS za 10 cm i telesne težine za 8,24 kg.

Tokom 22-mesečnog praćenja pacijenata, smanjenje telesne težine bilo je povezano sa smanjenjem varijabiliteta krvnog pritiska kod hipertenzivnih pacijenata. Konstatno smanjenje i telesne težine i dugotrajna varijabilnost sistolnog krvnog pritiska prilikom poseta moze se objasniti nižim kardiovaskularnim rizikom kod gojaznih bolesti.

Ključne reči: *gojaznost, hipertenzija, varijabilnost sistolnog krvnog pritiska prilikom poseta*

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INTRODUCTION

Obesity and hypertension (HT) are health and economic problems that pandemically spread and increase the risk of cardiovascular events. Worldwide, prevalence of arterial hypertension is about 25-40% in the adult population, which is over 1 billion people (1). As per World Health Organization report, more than 1.9 billion adults aged 18 years and older were overweight in 2015. (2) In Serbia 56.3% of people are overweight in 2014. The more and more concerning fact is that younger population in Serbia is obese (3).

Through human evolution adipose tissue have been a number of protective roles: energetic, metabolic and immunological. In modern society, hypercaloric diets, physical inactivity, make adipocytes show their other side, which means they secrete different bioactive molecules. Researchers have documented that the disorder of immunometabolic regulatory mechanisms, altered levels of proinflammatory adipokines, and "state of low-grade inflammation", oxidative stress in adipose tissue, activation of the sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS) are the pathogenetic link between central fat accumulation, insulin resistance, hyperlipidemia, and hypertension, which precedes the development of metabolic and vascular disorders (4-6). Obesity, especially visceral adiposity is associated with 65–75% increased risk of the primary (essential) hypertension in overal population It is well know that blood pressure (BP) increases with the body mass index (BMI) on every kilogram of the body mass increase, the BP increases for 2-3 mmHg (7).

On the other hand, recent data indicate that not all obese patients have hypertension and that approximately 10-30% of obese people are not affected by metabolic abnormalities. Recent researchers show that there are 6 different phenotypes of body composition, with different degree of nutrition and metabolic functions, out of which the fifth phenotype is metabolically 'healthy' obesity (MHO). (8,9,10)

Many studies have shown that visit-to-visit variability in systolic blood pressure (SBPV) is independant predictor of clinical events and independant risk factor in hypertensive patients and in overall population (11-13). There are very few studies which examined the correlation between obesity and variability of blood pressure in hypertensive patients (14,15). The questions whether body fat mass, central or peripheral, is harmful for the metabolic status has not been completely resolved, neither has the pathophysiological relationship between blood pressure variability (BPV) and cardiovascular disease.

According to recent reports which indicate that SBPV is independent cardiovascular risk factor and high prevalence of obesity-related diseases, the objective of this study is to investigate the association between obesity and visit-to-visit variability in systolic blood pressure in hypertensive patients.

MATERIALS AND METHODS

Prospective study included 300 randomly selected hypertensive patients (147 men and 153 women, average age 67.76±9.84), who were divided, according to BMI≥30 kg/m^2, to subgroups of obese (n=153) and non-obese examinees (n=147). The study comprised three visits during the follow up period of 22-months. High and unregulated or inadequately regulated blood pressure was included as criteria in the study. The criteria for non-inclusion were: patients with associated diseases of the digestive and renal systems, acute infections in the past three months, neoplastic diseases, diabetes mellitus, surgery in the previous year, weight changes >5 kg within the previous 6 months. BP values were defined by the arithmetic mean of three measurements each of the study visits.

All participants were included in this study at the Institute for Treatment and Rehabilitation "Niska Banja", Niska Banja, Serbia from March 2014 to February 2016. Ethics Committee of Institute for Treatment and Rehabilitation "Niska Banja" approved the study and fully informed written consent was obtained from each patient prior to the investigation.

All participants signed epidemiological questionnaire which were divaded general information, health information, medication situation, family health information and diet and lifestyle.

Hypertension was defined as BP≥140/90 mmHg and/or antihypertensive drug therapy according to the European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines (16). In order to estimate detailed evaluation of distribution SBPV quartiles of SBP-SD were formed. SBPV for each participant was defined using the standard deviation from 3 values of SBP. High SBPV was defined as SBP-SD in the 4th quartile.

Obesity was evaluated through body weight (BW), body mass index BMI≥30 kg/m^2 and waist cirumferences WC≥94 cm for males and WC≥80 cm for females. BW measurement (kg) was performed using a digital scale with the accuracy of measuring up to 0.1 kg. Body height measurement (cm) was performed using anthropometer (altimeter), with the accuracy of measurement to the nearest 0.5 cm. We used the most recent weight to calculate BMI, which was calculated as weight in kilograms divided by the square of height in meters. The measurement of WC was performed in a standing position, with heels apart, arms relaxed besides the body, and was measured in the middle distance between the rib cage and the iliac bone on the middle axillary line (at the level of the umbilicus). WC was used as an index of central obesity (17).

STATISTICAL ANALYSIS

All analysis were performed using IBM SPSS Statistics 20.0 software using descriptive and analytical methods. All the data were presented as means ± standard deviations

(SD), as absolute numbers and percentages, dependent on the statistical method used. The chi-square test was used to analyze differences between categorical data. To analyze continuous data distribution and to compare the means of the two examinee groups was applied the Student T-test. The comparison of mean parameters of obesity, BP and visit-to-visit SBPV was achieved using analysis of variance (ANOVA). The 25th, 50th and 75th percentiles were calculated in order to determine the 4 quartiles of the SBP-SD distribution. Bivariate correlation analysis (Spearman's correlation coefficient) was used to estimate the association between parameters of obesity, BP and SBPV. All statistical analysis were two-tailed, performed for the statistical significance level of $p<0.05$.

RESULTS AND DISCUSSION

Table 1. presents baseline and anthropometric characteristics and visit-to-visit variability in sistolic blood pressure of the study group across visits.

The prevalence of obesity evaluated through BMI in hypertensive subjects at the beginning of the follow-up was 153 (51%) and it was evaluated as WC 192 (64%). During 22-months follow up (across three visits) there was a significant decrease in prevalences of obesity defined according to BMI (51% vs. 32% vs. 17%, $p<0.05$, respectively) and WC (64% vs. 39% vs. 23%, $p<0.01$, respectively). There was significant decrease in the apsolute and relative values of SBPV across the three study visits (16.20±13.34 vs. 9.91±6.80 vs. 8.04±4.43 mmHg, $p<0.01$, respectively) and (10.66% vs. 7.34% vs. 6.64%, $p<0.01$, respectively). Moreover, the values of SBP were significantly lower (152.42±14.97 vs. 135.18±10.13 vs. 121.51±8.17 mmHg, $p<0.01$, respectively).

All parameters of both blood pressure and obesity are in significant, positive and moderate correlations (Table 2). It is also, statistically stronger correlation between SBP-SD and BMI as parameter of total obesity compared to large correlation with WC as parameter of central obesity ($\rho o=0.425$ vs. $\rho o=0.356$, $p<0.01$).

The baseline parameters of blood pressure and obesity after the first and the third visits in non-obese and obese hypertensive patients are shown in Table 3.

All parameters of blood pressure and obesity were significantly lower in obese patients after the third visit compared to baseline values ($p<0.01$), except DBP. The values of SBP and SBP-SD after the third visit were significantly higher in the group of obese hypertensive patients than in the group of non-obese patients (127.06±8.30 vs 120.37±7.75 mmHg, 11.29±5.67 vs 7.37±3.94; $p<0.01$). The difference between DBP was not statistically significant ($p>0.05$).

Characteristics across quartiles of the SBP-SD in hipertensive obese and non-obese patients after the third visit are presented in Table 4. There was significantly higher

Table 1. Baseline and anthropometric characteristics of the study group

PARAMETERS	VISITES			P value
	1.	2.	3.	
Age (years)	67.02±9.21	67.73±9.78	68.53±9.97	>0.05
Sex (M/W)	147/153	147/153	147/153	>0.05
BMI≥30 kg/m² (N/%)	153 (51%)	96 (32%)	51 (17%)	**<0.05**
WC≥94(80) cm (N/%)	192 (64%)	117 (39%)	69 (23%)	**<0.01**
Weight (kg)	83.34±10.68	78.14±10.35	75.10±10.77	**<0.01**
Absolute value of SBP (mmHg)	152.42±14.97	135.18±10.13	121.51±8.17	**<0.01**
Relative value of SBP - Cv (%)	9.82%	7.49%	6.76%	**<0.01**
SBPV - SBP-SD (mmHg)	16.20±13.34	9.91±6.80	8.04±4.43	**<0.01**
Relative value of SBP-SD - Cv (%)	10.66 %	7.34%	6.64%	**<0.01**
DBP (mmHg)	85.08±10.68	82.78±10.35	80.14±9.71	**<0.05**

BMI = body mass index, **WC** = Waist cirumferences, **BP** = Blood pressure, **SBP** = systolic BP, **BPV** = blood pressure variability - **SBP-SD** = standard deviation of systolic blood pressure, **DBP** = diastolic BP. **Cv** - coefficient of variation = SD/mean*100 (%).

Table 2. Correlation between parameters of blood pressure and parameters of obesity

Spearman correlation coefficient	SBP-SD	Blood pressure		Obesity		
		SBP	DBP	BW	BMI	WC
SBP-SD	-	0.633**	0.467**	0.428**	0.425**	0.356**
SBP	0.633**	-	0.777**	0.321**	0.359**	0.360**
DBP	0.467**	0.777**	-	0.170	0.262*	0.313**
Body weight	0.428**	0.321**	0.170	-	0.749**	0.743**
BMI	0.425**	0.359**	0.262*	0.749**	-	0.663**
WC	0.356**	0.360**	0.313**	0.743**	0.663**	-

** P<0.01* P<0.05

SBP-SD = standard deviation of systolic blood pressure, **SBP** = systolic blood pressure, **DBP** = diastolic blood pressure, **BW** = Body weight, **BMI** = body mass index, **WC** = Waist cirumferences.

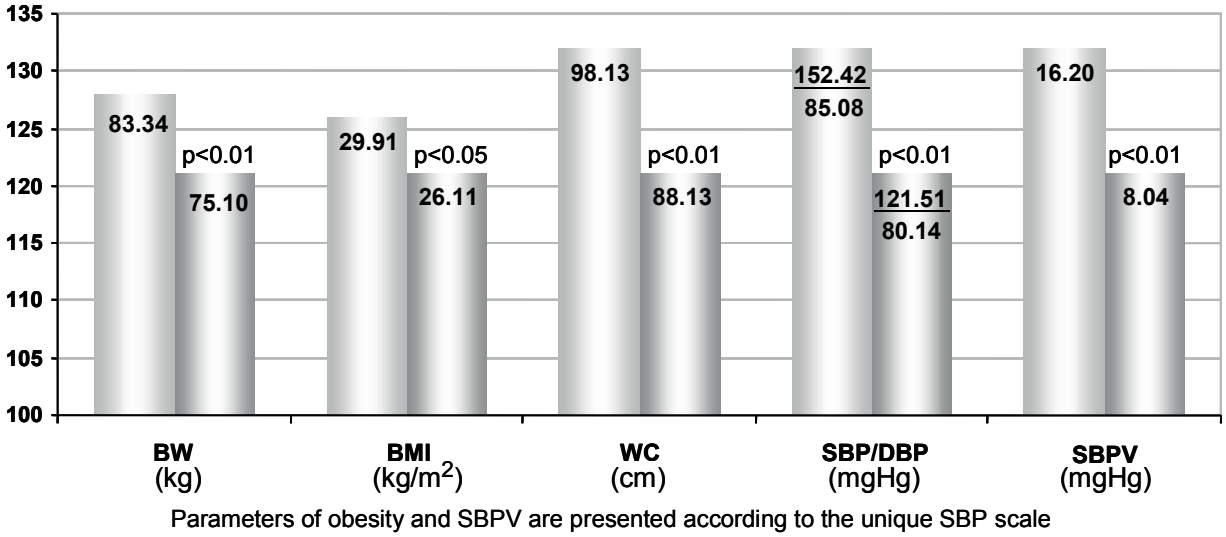
Table 3. Mean values of parameters of blood pressure and obesity after the first and the third visits

PARAMETERS	**Obese patients** (BMI>30)		**Non-obese patients** (BMI≤30)		P value
	N=153	N=51	N=147	N=249	
	1. visit	3. visit	1. visit	3. visit	
SBP-SD (mmHg)	16.52±9.41	11.29±5.67	15.87±17.05	7.37±3.94	0.001
SBP (mmHg)	154.21±15.20	127.06±8.30	150.56±14.59	120.37±7.75	0.007
DBP (mmHg)	87.04±9.18	81.18±7.40	83.03±8.75	79.93±5.22	0.058
Body weight (kg)	91.78±9.45	86.11±8.50	74.56±8.49	72.85±8.24	0.001
BMI (kg/m^2)	33.46±2.21	32.05±1.90	26.21±2.45	24.89±2.85	0.001
WC (cm)	106.12±11.17	101.82±11.07	89.81±10.16	85.33±8.86	0.001

SBP-SD = standard deviation of systolic blood pressure, **SBP** = systolic blood pressure, **DBP** = diastolic blood pressure, **BW** = Body weight, **BMI** = body mass index, **WC** = Waist cirumferences

Table 4. Characteristics across quartiles of the SBP-SD after the third visit

GROUPS	QUARTILES				P value
	1	2	3	4	
OBESE PATIENTS	6.67±2.13	11.67±3.56	25.08±4.35	43.13±7.50	p<0.001
NON-OBESE PATIENS	5.52±1.68	8.12±3.25	20.15±4.21	34.29±5.40	p<0.001



Graph 1. Change of values of obesity and blood pressure parameters at the beginninig and the end of the study

value of SBP-SD in hipertensive obese and non-obese patients in the fourth quartile compared to the values recorded in the other three quartiles. The highest SBPV was recorded in the 4th quartile in obese patients compared to SBPV in the 4th quartile of non-obese patients (43.13±7.50 mmHg vs. 34.29±5.40, p<0.001).

Graph 1. presents the change of values of obesity and blood pressure parameters**.** Comparative analysis of the follow-up data of all hypertensive subjects showed statistically significant average reduction of SBP-SD for 8.2 mmHg, BP for 31/5 mmHg, BW for 8.24 kg, BMI for 3.8 kg/m^2 and WC for 10 cm, at the end of study compared to baseline values.

DISCUSSION:

With the prevalence of obesity in the young, which should already be considered as a pandemic phenomenon (with all accompanying health risks), both prevention and health education, as well as identifying predictors for the development of obesity-related diseases are primary. Etiopathophysiology of development obesity and hypertension is very complicated including a great variety of factors (socio-economic factors, age, sex, menopause) and biological mechanisms (insulin resistance, chronic proinflammatory state, stimulation of the sympathetic nervous system as well as the RAAS, renal and heart dysfunction) which lead to abnormal circardial rhythm of blood pressure. On

the other hand, the role of fat tissue distribution, adipocyte characteristics and products had been involved in the attempt to explain the occurrence of hypertension in the presence of obesity.

Result of famous The Framingham Heart Study during 44-years, showed that obesity as an independent risk factor for cardiovascular disease and prevalence of obesity (evaluated throught body weihgt, including overweight and obesity) in 5209 hypertensive subjects, was approximately 26% in men and 28% in women (18,19). We have found higher prevalence of obesity, particularly abdominal obesity compared to total obesity in hypertensive patients (64% vs. 51%). During 22-months follow up there was a significant decrease in prevalences of obesity (23% vs. 17%). Our results showed significant differences in prevalence of central obesity in women, probably caused by both mutual up-regulation of protective hormones and **fat storage** and redistribution. Large adipocytes of visceral fat are dysfunctional due to the increased secretion of pro-inflammatory factors, reduced secretion of the insulin, estrogen and adiponectin, which increases the presence of chronic subclinical inflammation, the degree of insulin resistance, and metabolic disorders.

Due to frequent spontaneous variation of the blood pressure values during 24 hours, one month or one years, as well as the significance of obesity-related hypertension disease, is important for successful therapy and adequate control BP, without target organ damage. The greatest disadvantages of the classic measurement of BP are the inadequate insight in circardial rhythm and the phenomenon of peripheral resistance. On the other hand, hour 24-hours ambulatory blood pressure monitoring on healthy population has shown technical problems - significant variation on single measurements, compared with the values achived applying classic measurements (20).

The majority of studies (21,22) have analysed sensitivity of many different parameters of visit-to-visit BPV concerning the estimation of prediction of cardiovascular events (CVE): standard deviation, standard deviation independent of the mean (SDIM), coefficient of variation (CV), successive variation (SV), average real variability (ARV), range. We followed the standard deviation of SBP, as it was the simplest and the best indicator of future CVE due to the fact that other parameters of BPV were closely correlated and give similar reflections of BPV.

Just in the past decade, results from research groups (23-25) have documented a relationship between the reduced body weight and abdominal obesity and lower valuae of BP.

Understanding the complex relationship between obesity and hypertension these entities are important in clearing of the increasing prevalence of CVE. According to recent results (14,24,25), we have found, that values of visit-to-visit SBPV were significantly lower in non-obese hypertensive patients compared to obese hypertensive patients (7.37±3.94 vs. 11.29±5.67, $p<0.001$).

This is probably caused by the increase in sympathetic activity, insulin and vascular resistence, and the concentrations of proinflammatory cytokines, which leads to the increased heart pumping activity in hypertension accompanied with obesity. In non-obese patients, the possible mechanisms in the decreased baroreceptor sensitivity, as the results of dysfunction of neurohumoral regulation, as well as the structural and funtional changes on heart and blood vessels.

Our results showed in consistent with the several study there was significant, positive and moderate correlations between SBPV and all parameters of obesity ($p<0.01$) and there was average decrease SBPV across visits (16.20 vs 9.91 vs 8.04 mmHg, $p<0.01$), and also, the highest SBPV was recorded in the 4th quartile in obese patients (43.13 mmHg). The results of the recent study (14) similarly designed as our research, which included more participants (14988) beloning to general population showed the positive correlation between both total and central obesity with BPV. BPV was 6.89 mmHg across study visits.

In addition, the recent The Dallas Heart Study (26) *indicate the significance of the correlation between visceral fat mass distribution measured by dual X-ray absorptiometry (the modern advanced way of measuring abdominal obesity) and s*hort-term and long-term BPV during 5-month-period of observing 2595 overweight subjects with mean BP 127/79 mmHg and BMI 29 kg/m^2. Long-term BPV was 9.8 mmHg across overall visits.

Our study included only hypertensive patients with untreated BP values and the registered values of visit-to-visit SBPV was 8.2 mmHg, which was higher compared to general population in the previously mentioned study. Our results indicate the importance of distribution of fat mass, as well as the more significant impact of BMI as indicator total obesity than of WC, as parameter of central obesity on SBPV in hypertensive patients.

The recent study Tadic and all. (15) showed the relationship between parameters of obesity, BPV and remodeling of right ventricle in hypertensive patients with different nutrition degree. The increased body mass leads to the increased metabolic needs of an organism, extracellular fluid volume expansion, faster blood flow through both adipose and non-adipose tissue and organs, especially through heart, kidneys, skeletal muscles, which parallelly leads to the cardial output increase. However, it can later lead to reduction of "reserve" blood flow and damage of flow endothelium-dependent vasodilation. The rapid endothelial dysfunction along with the arterial stiffening and blood-flow variability lead to vascular endothelial dysfunction and the cascade of CVE, which was also proved in the studies (27-29).

Additionally, central fat accumulation contributes to the changes in the serum levels of adipokines, and also contributes to the decrease of insulin sensitivity, as well as the increase of the activity of the sympathetic nervous system. Large adipocytes are dysfunctional due to the in-

creased secretion of pro-inflammatory factors, reduced secretion of the protective hormones (insulin, estrogen and adiponectin), which increases the presence of chronic subclinical inflammation, and dysregulation of metabolic homeostasis. On the other hand, in hypertensive state, the formed "*circulus vitiosus*" is easily maintained by the up-regulated levels of proinflammatory cytokines and adipokines (30).

Finally, during 22-months follow up, the appropriate diet, the increase in physical activity and antihypertensive therapy, resulted in reduced obesity parameters, particularly body weight, and adequate control of BP, which significantly decreased the values of SBPV.

Similarly to the results presented in a recent study (31) our results showed the long-term effect weight loss on BP, statistically significant average decrease of SBPV for 8.2 mmHg, BP for 31/8 mmHg, BMI for 3.8 kg/m^2 and WC for 10 cm.

Reduction of all parameters of obesity is the most important step in reducing hypertension, and adequate control of BP and metabolically 'healthy' obesity. The results of a recent study showed that during a four- year-follou-up of 181 obese hypertensive patients, a 10 percent weight-loss produced an average of a 4.3/3.8 mmHg decrease in BP. The results of this study showed that the of weight loss for 1 kg produced an average of a 2.1 mmHg reduction in SBP, which could be the results of multiple antihypertensive effects and mechanisms: decrease visceral fat of accumulation, lower simpthatectic nerve activity and improved elasticity of blood vessels. Our results showed that reduction weight for 1 kg produced an average of a 3.76/0.61 mmHg reduction in BP and 1 mmHg in SBPV. Also, reduction weight increased the effectiveness of BP treatment.

Significant factor that contribute to the impact of obesity on BPV in hypertensive patients are distribution of body fat, duration of obesity as well as the degree of target organ injury. The additional important factor is how obesity parameters variability during the long period (several years) influences the BPV, because prolonged obesity leads to development of uncontrolled blood pressures and cardiovascular complications (8,32,33).

CONCLUSION

Results of this study, showed that obesity is strongly correlated with higher variability of systolic blood pressure across study visits. During 22-months, reduction of body weight was associated with reduction of blood pressure values, and lower value of blood pressure variability. Persistent decrease of both BP and long term visit-to-visit variability may explain lower cardiovascular risk in obese-related diseases.

Conflict of interest:
All authors declare no conflict of interest.

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SIMILARITIES AND DIFFERENCES IN EPIDEMIOLOGY AND RISK FACTORS OF CEREBRAL AND MYOCARDIAL ISCHEMIC DISEASE

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SLIČNOSTI I RAZLIKE U EPIDEMIOLOGIJI I FAKTORIMA RIZIKA CEREBRALNE I MIOKARDNE ISHEMIJSKE BOLESTI

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ABSTRACT

Ischemic heart disease and cerebral ischemia represent the leading causes of mortality worldwide. Both entities share risk factors, pathophisiology and etiologic aspects by means of a main common mechanism, atherosclerosis.

The autors aimed to investigate differences and similarities in epidemiology and risk factors that could be found between both entities.

In a retrospective sudy 403 patients were included and divided into two groups: group of 289 patients with history of myocardial infarction (AMI), and group of 114 patients with history of ischemic stroke (IS). All patients were evaluated for nonmodifiable risk faktors, which included age and sex, and modifiable, such as hypertension, dyslipidemia, diabetes, obesity, physical activity and smoking. Differences in some epidemiological aspects were also considered: occupation, marital status, alcohol consumption, exposure to stress.

Patients with history of IS were significantly older then AMI patients (64.0 ± 9.9 vs 64.0 ± 9.9, p=0,028), with higher diastolic blood pressure (87,1 ± 10,2 vs 83,6 ± 10,4, p=0,003) and higher Sokolow-Lyon index in ECG, an also index of left ventricular hypertrophy (19,2 ± 9,1 vs 14,7 ± 6,5). There were no significant differences between groups in the estimated body mass index and waist circumference. Differences between groups in stress exposure, occupation, alcohol consumption or physical activity were no significant. Patients in AMI group were more frequently male (199 (69%) vs 59 (52%), p=0,001), married (252 (87%) vs 88 (77%), p=0,037), smokers (162 (56%) vs 50 (44%), p=0,018) and with higher incidence od dyslipidemia (217 (75%) vs 73 (64%), p=0,019) compared with IS group. Incidence of arterial hypertension and diabetes was similar in both groups.

Both entities share similar pathophysiological mechanisms and, consequently, main traditional risk factors. However, incidence of myocardial infarction increases with male sex, dyslipidemia, smoking and marital status, while incidense of ischemic stroke increases with age, higher diastolic blood pressure and also with ECG signs of left ventricular hypertrophy.

Keywords: *Ischemic heart disease, mortality, hypertension*

SAŽETAK

Ishemijska bolest srca i cerebralna ishemija predstavljaju vodeće uzroke smrtnosti u svetu. Oba entiteta dele faktore rizika, patofiziologiju i etiološke aspekte. Cilj rada je bio razmotriti razlike i sličnosti u epidemiologiji i faktorima rizika za oba entiteta.

U retrospektivnu studiju uključena su 403 bolesnika podeljena u dve grupe: grupa od 289 bolesnika sa istorijom akutnog infarkta miokarda (AMI) i grupa od 114 bolesnika sa istorijom ishemijskog moždanog udara (IS). Kod svih bolesnika su praćeni nekorektibilni faktori rizika, kao što su godine i pol kao i korektibilni faktori, kao što su hipertenzija, hiperlipoproteinemija, dijabetes, gojaznost, fizička aktivnost i pušenje. Razmatrane su i razlike u nekim epidemiološkim aspektima; bračni status, upotreba alkohola i izloženost stresu.

Bolesnici sa istorijom IS bili su signifikantno strariji u poređenju sa bolesnicima koji su imali AMI (64.0 ± 9.9 vs 64.0 ± 9.9, p=0,028), sa višim dijastolnim pritiskom (87,1 ± 10,2 vs 83,6±10,4, p=0,003) i imali su veće vrednosti indeksa hipertrofije leve komore (Sokolow-Lyon) u EKG-u (19,2 ± 9,1 vs 14,7 ± 6,5). Nije bilo značajnih razlika između grupa u indeksu telesne mase i obima struka. Takođe, razlike između grupa u izloženosti stresu, konzumaciji alkohola ili fizičkoj aktivnosti nisu bile značajne. Bolesnici sa AMI su češće muškog pola (199 (69%) vs 59 (52%), p=0,001), oženjeni (252 (87%) vs 88 (77%), p=0,037), pušači (162 (56%) vs 50 (44%), p=0,018) i sa većom učestalošću hiperlipoproteinemije (217 (75%) vs 73 (64%), p=0,019) u poređenju sa IS grupom. Učestalost arterijske hipertenzije i dijabetesa bila je slična u obe grupe.

Oba entiteta dele slične patofiziološke mehanizme, a time i glavne tradicionalne faktore rizika. Međutim, učestalost AIM je bila veća kod osoba muškog pola, osoba u braku, pušača i bolesnika sa hiperlipoptoteinemijom, dok je učestalost ishemijskog moždanog udara bila povezana sa godinama starosti, višim dijastolinim krvnim pritiskom i sa znacima hipertrofije leve komore u EKG-u.

Ključne reči: Ishemijska bolest srca, smrtnost, hipertenzija

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INTRODUCTION

Cerebral and myocardial ischemic disease share similar risc factors and pathophysiology and represent the consequence of atherothrombosis as an main etiological factor. About 87% of all strokes are ischemic strokes, in which blood flow to the brain is blocked [1]. Both entities represent the leading causes of mortality worldwide. Coronary artery disease (CAD) is a leading cause of death or disability in both, men and women. According to the World Health Organization (WHO), in 2002 there were 7.22 million deaths from coronary artery disease globally. [2]

Coronary artery disease alone is the most common cause of death in Europe, accounting for nearly 2 million deaths each year. More than 1 in 5 deaths of women (22 percent) and men (21 percent) are from CAD [3].

Stroke is also a major cause of death and a leading cause of serious long-term disability [4, 5].

According to WHO estimates, 15 million people each year suffer from strokes and 5 million people are left permanently disabled. [2] Based on report of American Heart Association in the Heart Disease and Stroke Statistics – 2012 Update, the average age for the incidence of a stroke is>75 years for women, and 71 years for men [4].

Stroke risk increases with age, but strokes can occur at any age. Compared to older people young adults are at a lower risk of stroke, however incidence of stroke in young people ranges from 60 to 200 new cases per year per million inhabitants. By the age of 75, 1 in 5 women and 1 in 6 men will have a stroke [6, 7].

Previous study [8] reported a yearly increase in frequency of stroke from 2.4 per 100,000 for a person aged between 20 and 24 years, to 4.5 per 100,000 for a person aged between 30 and 34 years, and to 32.9 per 100,000 for a person aged 45–49 years. Incidence of stroke was slightly higher in women younger than 30 years and in men older than 35 years.

Although coronary heart disease and stroke share important risk factors, some risk factors appears to have a stronger association with risk of stroke, such as high blood pressure, whereas others, for example total cholesterol, may have a stronger association with risk of coronary heart disease [9-13].

Luckily, although not curable, cardiovascular diseases are largely preventable. Modification of 9 easily measured clinical and laboratory risk factors can prevent up to 90% of first myocardial infarctions [14]. The long-recognized risk factors include age, sex, blood pressure, cholesterol levels, smoking status, diabetes mellitus, obesity, and a sedentary lifestyle. In addition, chronic kidney disease and insulin resistance (pre-diabetes) can be important risk factors for coronary heart disease, such as atrial fibrillation for stroke.

Unfortunately, the previous studies have demonstrated that coronary artery disease increases the risk for stroke, whereas patients with stroke are more likely suffer from coronary artery disease [15-18].

In present study the differences and similarities in epidemiology and risk factors that could be found in between both entities were analyzed and discussed.

MATERIALS AND METHODS

This observational, multicenter, epidemiological study consisted of 403 patients divided into two groups: group of 289 patients with history of myocardial infarction (AMI), and group of 114 patients with history of ischemic stroke (IS).

Patients were recruited from primary care facilities and outpatient cardiology clinics, part of the Hypertension, infarction and stroke prevention association (HISPA).

All subjects involved in the study went through clinical examination, anthropometry and blood pressure measurements, electrocardiography, and laboratory tests, which included parameters of metabolic control and diabetic status.

The body mass index (BMI) was calculated as body weight (in kilograms) divided by height (in meters squared), while systolic and diastolic blood pressure (SBP/DBP) values were meassured in the sitting position. Waist size was meassured too in all patients.

Patients were evaluated for nonmodifiable risk faktors, which included age and sex, and modifiable, such as hypertension, dyslipidemia, diabetes, obesity, physical activity and smoking. Differences in some epidemiological aspects were also considered: marital status, alcohol consumption, exposure to stress.

STATISTICAL ANALYSIS

All statistical analyses were performed by SPSS for Windows (SPSS version 20.0, Inc., Chicago, IL, USA). All statistical tests were two-tailed, in which a p-value of <0.05 was considered significant.

Continuous data are presented as mean±standard deviation when normally distributed (as assessed by the Kolmogorov–Smirnov test) and as a median when non-normally distributed. Categorical data are presented as frequencies and percentages.

The data were compared between groups by an unpaired t-test for continuous variables. Categorical variables were compared by nonparametric tests.

RESULTS

The study population consisted of 403 patents, mean age 64.7±9.8 years; 258 (64%) men and 145 (36%) women.

The general characteristics of the study groups are presented in Table 1.

Patients with history of IS were significantly older then AMI patients. Diastolic office blood pressure (DBP)

Table 1 General characteristics of patients

	Groups		
	AMI (n=289)	IS (n=114)	p
Age (years)	64.0 ± 9.9	66.3 ± 9.3	**0.028**
Sex, male/female (%male)	199/90 (68.9%)	59/55 (51.8%)	**0.001**
SBP (mmHg)	139.2 ± 19.9	142.7 ± 22.6	0.127
DBP (mmHg)	83.6 ± 10.4	87.1 ± 10.2	**0.003**
Heart rate (bit/min)	69.4 ± 9.9	71.3 ± 13.2	**0.231**
Sokolow-Lyon index in ECG	14.7 ± 6.5	19.2 ± 9.1	**0.047**
BMI (kg/m^2)	29.0 ± 4.1	28.1 ± 5.0	0.103
Waist size (cm)	100.2 ± 11.7	100.7 ± 14.1	0.791

Results are shown as a mean ± standard deviation, SBP-systolic blood pressure, DBP-diastolic blood pressure, BMI-body mass index, ECG – electrocardiography, (*) significant at the 0.05 level, (*) at the level 0.01

Table 2 Modifiable risk faktors and epidemiological aspects

	Groups		
	AMI (n=289)	**IS (n=114)**	**p**
Hypertension, n (%)	**270 (93.4%)**	**106 (93.0%)**	**0.513**
Diabetes, n (%) dyslipidemia	**77 (26.6%)**	**29 (25.4%)**	**0.455**
Dyslipidemia, n (%)	**217 (75.1%)**	**73 (64.0%)**	**0.019**
Smoking, n (%)	**162 (56.1%)**	**50 (43.9%)**	**0.018**
Family history, n (%)	**238 (82.4%)**	**98 (86.0%)**	**0.235**
Alcohol consumption, n (%)	**20 (6.9%)**	**7 (6.1%)**	**0.487**
Exposure to stress, n (%)	**168 (58.1%)**	**67 (58.8%)**	**0.499**
Marital status, married n (%)	**252 (87%)**	**88 (77%)**	**0,037**

(*) significant at the 0.05 level, (*) at the level 0.01

was found to be significantly higher in IS patients, and Sokolow-Lyon index in ECG, as a index of left ventricular hypertrophy, also was found to be significantly higher in the same group of patients. There were no significant differences between groups in the estimated body mass index and waist size.

Patients with AMI were more frequently male, while gender distribution in IS group were found to be almost equal.

Table 2 displays comparison of well established modifiable risk faktors and some epidemiological aspects between the groups.

Patients in AMI group were more frequently married, smokers and with higher incidence od dyslipidemia compared to SI group. Incidence of arterial hypertension, diabetes, family history, alcohol consumption and exposure to stress was similar in both groups.

A significant difference in physical activity, which was graded in five levels, was not found ($X^2 = 3.028$, $p = 0.082$).

Table 2 displays general characteristics of patients and nonmodifiable and modifiable cardiovascular risk faktors adjusted by gender.

Men who suffered from AMI were significantly older, more frequent smokers and alcohol users, while men who suffered from IS had higher values of diastolic blood pressure and also were more alcohol users compared to women.

DISCUSSION

Overall, results indicates substantial similarities of modifiable risk factors with coronary heart disease (CHD) and stroke.

Table 3 General caracteristic and cardiovascular risk factors adjusted by gender

	AMI			IS		
	male	female	p	male	female	p
Age (years)	63±9.87	66±9.47	**0.004**	65±11.1	67±6.7	0.262
SBP (mmHg)	138±18.9	141±21.9	0.329	146±22.5	140±22.4	0.156
DBP (mmHg)	84±9.7	83±11.9	0.396	89±10.9	85±9.0	**0.014**
Heart rate (bit/min)	70±10.9	68±7.4	0.245	71±8.7	72±16.8	0.778
Sokolow-Lyon index	14.9±6.8	14.3±6.2	0.812	16±8.4	21±9.4	0.296
BMI (kg/m^2)	29±3.7	29±4.8	0.456	29±4.2	28±5.7	0.264
Waist size (cm)	102±11.2	96±11.6	**<0.001**	106±13.6	96±13.2	**0.007**
Hypertension, n (%)	184(92.5)	86(95.6)	0.239	54(91.5)	52(94.5)	0.398
Diabetes, n (%) dyslipidemia	51(25.6)	26(28.9)	0.329	15(25.4)	14(25.5)	0.583
Dyslipidemia, n (%)	151(75.9)	66(73.3)	0.373	35(59.3)	38(69.1)	0.187
Smoking, n (%)	123(61.8)	39(43.3)	**0.003**	30(50.8)	20(36.4)	0.085
Family history, n (%)	165(82.9)	73(81.1)	0.413	52(88.1)	46(83.6)	0.337
Alcohol consum., n (%)	20(10.1)	0	**<0.001**	7(11.9)	0	**0.008**
Stress, n (%)	117(58.8)	51(56.7)	0.416	31(52.5)	36(65.5)	0.113
Married n (%)	180(90.5)	72(80.0)	**0.013**	47(79.7)	41(74.5)	0.334

Results are shown as a mean ± standard deviation, SBP-systolic blood pressure, DBP-diastolic blood pressure, BMI-body mass index, (*) significant at the 0.05 level, (*) at the level 0.01

MODIFIABLE RISK FAKTORS AND EPIDEMIOLOGICAL ASPECTS

Previous investigations have found that hypertension has a generally stronger association with risk of stroke versus CHD, whereas cholesterol has a generally stronger influence on risk of CHD [19, 20].

Hypertension is a main risk factor not only for hemorraghic stroke but also for IS [21]. According to data from the Sagrat Cor of Barcelona Stroke Registry (2704 patients with ischemic stroke), hypertension was the main risk factor in the different age groups [7].

In a study conducted by Ihle-Hansen et al [23] 60% of patients with stroke (126/210) had hypertension, while in a study conducted by Putaala et al. [24] 39% of patients (389/990) had hypertension.

In our study incidence of hypertension in group of IS patients was significantly higher in comparison to previous investigations, even 93% of patients with IS had hypertension (106/114). Incidence of hypertension was similar in bouth our study groups, but value of diastolic blood pressure was significantly higher in IS group. Men who suffered from IS in our study had higher values of diastolic blood pressure and also were more alcohol users compared to women.

Dyslipidemia is a major risk factor for atherosclerosis and atherosclerotic based diseases [25]. Serum cholesterol has generally strong influence on risk of CHD [19], and is positively related to coronary heart disease morbidity and mortality [26].

In our study dyslipidemia was significantly frequent in group of AMI patients compared to patients who suffered from IS.

Diabetes mellitus is well-established risk factor for cardiovascular disease, but also an independent risk factor of ischemic stroke of atherothrombotic cause [27]. Dyslipidemia, hypertension and obesity are atherogenic risk factors frequently found in type 2 diabetes patients [28, 29]. The combination of hypercholesterolemia and hypertension increases the frequency of vascular complications in patients with diabetes.

Incidence of diabetes in our study was equal in both groups.Abdominal obesity is defined by a waist circumference > 102 cm in men and 88 in women [41]. Unfortunately a lot of our patients were overweight and obese. This is an important finding due to the fact that weight and abdominal fat reduction is associated with a lowering in blood pressure, and may thereby reduce the risk of stroke,

A great deal of evidence over the last few decades has confirmed that cigarette smoking is an independent predictor of cerebrovascular disease in both gender. Smokers have a significantly higher risk of ischemic stroke compared to non-smokers. Finally, there is an indication that passive cigarette smoker have highest risk of stroke. It is known that smoking increases the risk of atherosclerosis, also causing thrombosis in narrow arterial vessels. Smoking have contrabutin in the onset of endothelial dysfunction, increase in blood viscosity, and platelet aggregation [30-32].

Patients who suffered from AMI in our study were more frequently smokers compared to IS group, predominantly men who were significantly older, more frequently smokers and alcohol users compared to women.

Physical activity reduces the risk of cardiovascular disease, premature death and stroke [33].

Based on data from a large population-based case-control study conducted in Stockholm, Sweden, 1992-1994 investigators concluded that aerobic physical activity such as exercise or walking at work seemed to reduce the risk of myocardial infarction, whereas anaerobic activity such as heavy lifting at work were related to increased risk of myocardial infarction.

According to data collected from 23 corresponding studies, there is strong evidence that subjects with high physical activity as compared to those with low physical activity had a lower stroke risk [34].

A significant difference in physical activity, which was graded in five levels, was not found between groups in our study.

The evidence from previous studies suggest that stressful life events, specially acute psychological stress factors contribute independently to the risk of coronary heart disease [35, 36] and have been shown to be independent predictive factors of CHD [37].

Stress may be a trigger for neuroendocrine and platelet activation and directly affect CHD, or may cause adverse health behaviors such as smoking, poor diet, and sedentary lifestyle, which increases the risk of CHD [38].

In our study stress exposure were significant, almost equall in both groups, 58.1% in AMI and 58,8% in IS group.

In the study conducted by Tulio et al. [39], left ventricular hypertrophy and abnormal left geometry were independently associated with increased stroke risk. Left ventricular hypertrophy is strongly associated with ischemic stroke in all age, sex, and race-ethnic subgroups.

In our study left ventricular hypertrophy was estimated with Sokolow-Lyon index by electrocardiography, as an index of left ventricular hypertrophy wich was significantly higher in IS group.

NONMODIFIABLE RISK FAKTORS

Incidence of coronary heart disease in male is well recognised. Cardiovascular disease develops 7 to 10 years later in women than in men [39].

In accordance with previous studies, in our study patients in AMI group were more frequently male and significantly younger compared to female.

The coronary heart disease event rate in women is low and predominantly attributed to smoking before menopause, Smoking increases the risk of a first acute myocardial infarction more pronounced in females compared to male [42].

However, in our study male were more frequent smokers compared to female.

The incidence of stroke increases significantly with age, and is higher in men up to age 75, similar in the 75-84 age group, and higher in women in the age group greater than 85 [43].

Despite the higher risk in men, the lifetime risk of stroke is higher in women. The Framingham study calculated lifetime risk of stroke among middle age men and women and found that the lifetime risk in women age 55 was 21% and in men age 55, 17% [44].

In our sudy IS patients were significantly older compared to AMI group, but without significant difference in age between men and women in IS group. Men who suffered from IS had higher values of diastolic blood pressure and were more alcohol users compared to women.

Hypertension associated with age represents leading risk factors for cerebrovascular disease and also multiply the risk for stroke [45, 46].

CONCLUSION

Both entities share similar pathophysiological mechanisms and, consequently, main traditional risk factors. However, the majority of cardiovascular risk factors show no important differences between the groups. Incidence of myocardial infarction increases with male sex, dyslipidemia, smoking and marital status, while incidence of ischemic stroke increases with age, higher diastolic blood pressure and also with ECG signs of left ventricular hypertrophy.

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