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Vojnosanitetski pregled

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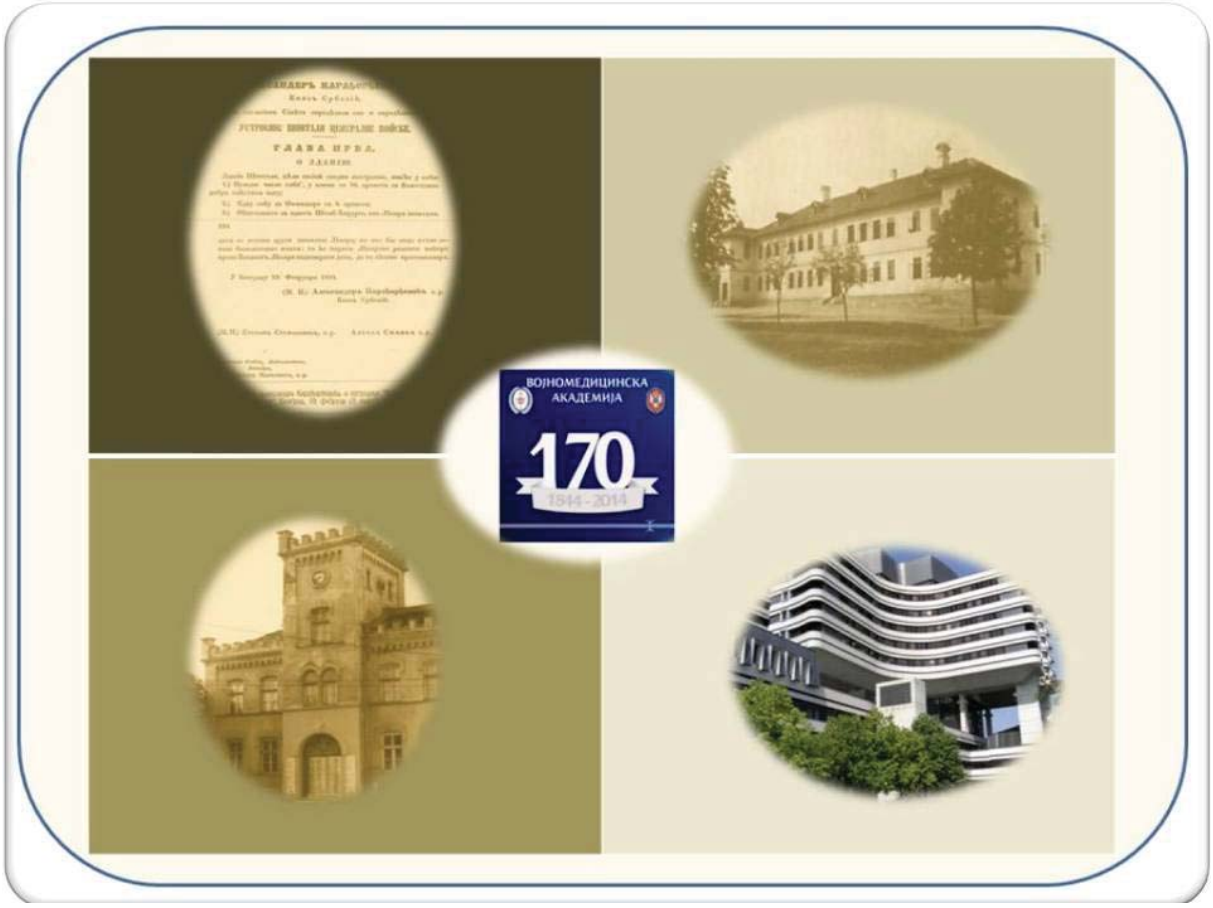

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Uprava za vojno zdravstvo MO Srbije

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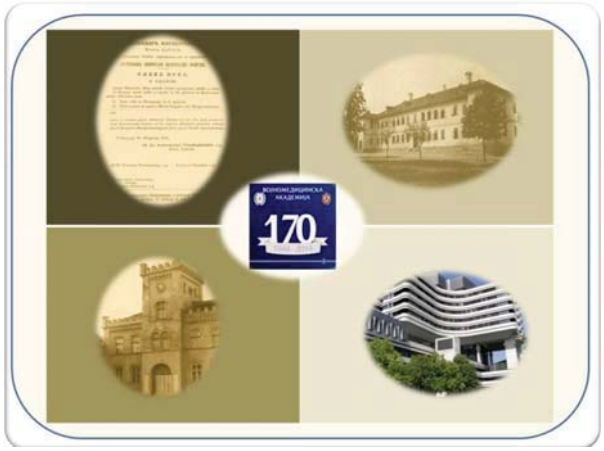

Ove godine, 2. marta, Vojnomedicinska akademija (VMA) u Beogradu, najviša stručna, naučna i obrazovna institucija sanitetske službe Vojske Srbije, proslavlja svoj veliki jubilej – 170 godina postojanja. Tog dana 1844. godine, srpski knez Aleksandar Karađorđević doneo je ukaz o osnivanju centralne vojne bolnice (gore levo – naslovna strana Ukaza iz 1844. godine o formiranju centralne vojne bolnice; gore desno – kasarna u Beogradu u kojoj je 1844. godine bila smeštena Vojna bolnica; dole levo – zgrada Vojne bolnice u Beogradu, kasnije preimenovana u VMA, sagrađena 1909. godine; dole desno – zgrada VMA danas, sagrađena 1981. godine; centar – jubilarni grb VMA, simbol tradicije duge 170 godina).

This year, on March 2, Military Medical Academy (MMA) in Belgrade, the highest professional, scientific and educational institution of the Armed Forces Medical Services of Serbia, celebrates a big anniversary – 170 years of existence. On that day, 1844, the Serbian Prince Alexander Karađorđević issued a Decree establishing the Central Military Hospital (above left – front page of the Decree from 1844 on the Central Military Hospital establishing; above right – barracks in Belgrade in which during 1844 Military Hospital was housed; bottom left – Military Hospital in Belgrade, later renamed the MMA, built in 1909; bottom right – building of the MMA today, built in 1981; center – the MMA jubilee coat of arms, a symbol of its 170-year-long tradition).

E D I T O R I A L / U V O D N I K

The Author and the Reviewer of the Year 2013 Award by *Vojnosanitetski pregled*

Priznanje časopisa „Vojnosanitetski pregled“ najplodnijem autoru i recenzentu u 2013. godini

Silva Dobrić

Institute for Scientific Information, Military Medical Academy, Belgrade, Serbia

The results and information obtained by researches are nowadays considered invisible if not published and made accessible for practical use, and as a guide for further studies. The basic role of scholarly publications so is to transfer the results of investigations to the widest scale of users, and constantly increase the overall knowledge of the humankind. That is the reason not only in the scientific community, but in the wider human society to especially appreciate the authors of scientific publications. It should not be forgotten, however, that the significant role of final touch in making the final version of a scientific report is played by reviewers, the experts for particular scientific branches who by their critical analyses might significantly improve the quality of papers prepared for publishing.

The quality of scholarly and professional publications has a special significance in ranking scientific and professional journals, since publishing of as many as possible high quality papers increases the impact of a journal on its scientific field. Considering this aspect, the Editorial Board and the Publisher of the *Vojnosanitetski Pregled* (VSP) has long before established the Author and the Reviewer of the Year Award. Thus, the Author of the Year by the VSP is the author who, applying reviewing procedures, is shown to publish the highest number of papers on the pages of VSP in the previous year, all in compliance with the criteria regarding the number and the category of the published paper, as well as the order of the authors. That is to say that the original article and the first place among the authors (or the only one) score the highest number in ranking (Table 1). Regarding the Reviewer of the Year by the VSP, apart from the number of peer reviewing done in the previous year, its quality (a detailed review to each article segment) also matters, and, of course, observing time limit set for peer-reviewed article submitting.

Traditionally, The Author and The Reviewer of the Year Award is announced on the celebration party on the Day of the Military Medical Academy (MMA) – March 2, knowing that the Editorial Office of the VSP ever since 1961 has been situated in the Institute for Scientific Information of this high medical, scientific and educational institution.

Prema savremnom shvatanju nauke rezultati naučnoistraživačkog rada i naučne informacije proistekle iz njih praktično ne postoje ako se ne objave, čime se omogućava njihovo neposredno korišćenje u praksi, odnosno korišćenje kao putokaza za dalja istraživanja. Osnovna uloga naučnih publikacija, dakle, jeste prenos rezultata naučnih istraživanja što širem krugu korisnika i neprestano obogaćivanje sveukupnog ljudskog znanja. Zbog toga se, ne samo u naučnoj, već i u široj društvenoj zajednici, posebno cene autori naučnih publikacija. Međutim, treba imati u vidu da u oblikovanju konačne verzije svakog naučnog saopštenja značajnu ulogu igraju i recenzenti, eksperti iz određene naučne oblasti, koji svojom kritičkom analizom rada pripremljenog za publikovanje, mogu značajno da poboljšanju njegov kvalitet.

Kvalitet naučne i stručne publikacije ima posebnu vrednost za status naučnih i stručnih časopisa jer objavljivanje što većeg broja kvalitetnih članaka povećava uticaj koji određeni časopis ima u svojoj naučnoj oblasti. Imajući ovo u vidu, Uredništvo i Izdavač Vojnosanitetskog Pregleda (VSP) već duže vreme dodeljuju priznanje Autor godine i Recenzent godine VSP. Autor godine VSP je autor kome je, nakon sprovedenog recenzentskog postupka, u prethodnoj godini objavljeno najviše radova na stranicama ovog časopisa prema kriterijumima koji uzimaju u obzir broj i vrstu objavljenog članka, kao i redosled autora, pri čemu originalni članak i prvo mesto među autorima (ili jedino) donosi najveći broj bodova (Tabela 1). Prilikom izbora Recenzenta godine, pored broja urađenih recenzija u prethodnoj godini, u obzir se uzima i njihov kvalitet (detaljan osvrt na svaki segment rada) i poštovanje zadatog roka za dostavljanje recenzije.

Tradicionalno, proglašenje Autora i Recenzenta godine VSP vrši se na proslavi obeležavanja Dana Vojnomedicinske akademije (VMA), 2. marta, budući da se Redakcija časopisa još od 1961. godine nalazi u Institutu za naučne informacije ove vrhunske zdravstvene, naučne i obrazovne ustanove.

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Table 1
Tabela 1

Criteria for author and article scoring in the *Vojnosanitetski Pregled* / Kriterijumi za bodovanje autora i članaka u Vojnosanitetskom pregledu

Article category / Kategorija rada	Score / Broj bodova		
	first author / prvi autor	second author / drugi autor	third author / treći autor
Original article / Originalni članak	12	6	3.6
Preliminary report / Prethodno saopštenje	5	2.5	1.5
General review / Pregledni članak	10	5	3
Current topic or Practical advice for physicians / Aktuelna tema ili Seminar praktičnog lekara	8	4	2.4
Case report / Kazuistika	4	2	1.2
History of medicine / Istorija medicine	5	2.5	1.5
Editorial / Uvodnik	5	2.5	1.5

On this year's jubilee celebration of 170 years of existence of the MMA, The Author of the Year 2013 Award will be presented to Prof. Dr. Zoran Slavković, Head of the Clinic for Anasthesiology and Intensive Care, MMA, Full Professor of the Faculty of Medicine, Military Medical Academy, University of Defence in Belgrade, while The Reviewer of the Year 2013 Award will be presented to Prof. Dr. Branka Nikolić, Head of the Conservative Gynecology, Clinic for Gynecology and Obstetrics "Narodni front", Belgrade, Full Professor of the Faculty of Medicine, University of Belgrade, Belgrade.

Within 2013 the VSP published 5 papers by Prof. Dr. Slavković, out of which 3 were scored, 2 in the category of Original article, and 1 in the category of Current topic (Table 2) in accordance with the abovementioned criteria that broth to him the highest score and the position of the First Author among the authors publishing their articles in the VSP within the previous year.

Na ovogodišnjoj proslavi jubilarne 170. godišnjice postojanja VMA, priznanje Autor godine VSP za 2013. godinu biće uručeno prof. dr Zorano Slavkoviću, načelniku Klinike za anesteziologiju i intenzivno lečenje VMA, redovnom profesoru Medicinskog fakulteta VMA Univerziteta odbrane u Beogradu, dok će priznanje Recenzent godine VSP za 2013. godinu biti uručeno prof. dr Branki Nikolić, načelnici Odeljenja konzervativne ginekologije u Ginekološko-akušerskoj klinici „Narodni front" u Beogradu i redovnom profesoru Medicinskog fakulteta Univerziteta u Beogradu.

Profesoru Slavkoviću u 2013. godini objavljeno je pet radova u VSP, od kojih su tri, dva iz kategorije Originalni članci i jedan iz kategorije Aktuelna tema (Tabela 2), prema napred pomenutim kriterijumima uzeta u obzir za bodovonje. Zahvaljujući njima on je ostvario najveći broj bodova i prvo mesto među prošlogodišnjim autorima VSP.

Table 2
Tabela 2

Articles of Prof. Zoran Slavkovića, MD, PhD, published in the *Vojnosanitetski Pregled* in 2013
Radovi prof. dr Zorana Slavkovića u Vojnosanitetskom pregledu u 2013.

Number / Broj	Article category / Kategorija rada	Authors and title of article / Autori i naziv rada
1	Original article / Originalni članak	*Zoran Slavković, Dušica M. Stamenković, Veselin Gerić, Milić Veljović, Nebojša Ivanović, Aleksandar Tomić, Tomislav Randjelović, Jelena Rašković, Menelaos Karanikolas.* Comparison of analgesic effect of intrathecal morphine alone or in combination with bupivacaine and fentanyl in patients undergoing total gastrectomy: A prospective randomized, double blind clinical trial. Vojnosanit pregl 2013; 70(6):541-48.
2	Originalni članak/ Original article	*Zoran Slavković, Dušica M. Stamenković, Veselin Gerić, Milić Veljović, Nebojša Ivanović, Slobodan Todorović, Predrag Marić, Menelaos Karanikolas.* Combined spinal-epidural technique: single-space *vs* double distant space technique. Vojnosanit pregl 2013; 70(10):953-59.
3	Current topic or Practical Advice for Physicians / Aktuelna tema ili Seminar praktičnog lekara	*Zoran Slavković, Dušica M. Stamenković, Predrag Romić, Aleksandar Tomić, Novak Milović, Mirko Jovanović, Menelaos Karanikolas.* The present and future of fiberoptic intubation. Vojnosanit pregl 2013; 70(1):61-8.

Within 2013 Prof. Dr. Branka Nikolić peer reviewed the highest number of articles, totally 15, thus winning The Reviewer of the Year 2013 Award by the VSP. Prof. Dr. Branka Nikolić anyhow befalls the most engaged reviewers of the VSP.

Prof. dr Branka Nikolić je u toku 2013. godine bila recenzent za najveći broj radova, ukupno 15, zbog čega joj je i pripalo priznanje Recenzent godine VSP za prethodnu godinu. Ona je, inače, već nekoliko godina jedan od najangažovanijih recenzenata našeg časopisa.

I am very much honoured and pleased to be in the position to in the names of the Publisher and Editorial Board congratulate to our laureates, Prof. Dr. Zoran Slavković and Prof. Dr. Branka Nikolić for winning these awards, wishing them to go on with such success.

I am, also, pleased to take this occasion to thank them for many years of excellent cooperation which I hope to last.

The Author of the Year 2013 by the VSP – Prof. Dr. Zoran Slavković

Prof. Zoran Slavkovic MD, PhD, was born on March 13, 1950, in the town of Guča, Serbia. He graduated from the Faculty of Medicine, University of Belgrade in 1975 and became Anesthesiology and Intensive Therapy specialist in 1981, at the Military Medical Academy (MMA), Belgrade.

He successfully defended his PhD thesis "Application of amrinone and its combination with dopamine in right myocardial ventricular insufficiency" in 1999, MMA, Belgrade.

He started to work at the Clinic of Anesthesiology and Intensive Therapy, MMA, in 1978, and from 2005 he has been a Head of the Anesthesiology Department. Prof. Dr. Slavković was chosen to be Head of the Clinic of Anesthesiology and Intensive Therapy, MMA, in 2012

From 2004 to 2008 Prof. Slavković was a member of Presidency of the Section of Anesthesiology, Intensive Therapy and Pain Treatment, Serbian Medical Society. He has been contributing the GENOSEPT Project, organized by European Society of Intensive Care Medicine since 2006.

Prof. Dr. Slavković published more than 100 scientific articles in international and domestic scientific journals, 9 of which were published in journals from the SCI list, and also participated in numerous congresses in Serbia and abroad. He is the author of monograph "Anesthesia for Ambulatory Surgery" (Belgrade: IP Glosarijum d.o.o; 2012), and the Author of the Year 2013 by the VSP. Congratulations!

The Reviewer of the Year 2013 by the VSP - Prof. Dr. Branka Nikolić

Prof. Dr. Branka Nikolić (Figure 2), born in 1956 in Sarajevo, then Bosnia and Hertzegovina, graduated from the Faculty of Medicine, University of Belgrade, Belgrade, in

Velika mi je čast i zadovoljstvo što sam prilici da u ime Izdavača, Uređivačkog odbora i Redakcije VSP čestitam našim laureatima, prof. dr Zoranu Slavkovići u prof. dr Branki Nikolić na ovim priznanjima, sa željom da nastave sa ovakvim uspesima i ubuduće.

Ujedno, želim da im se zahvalim na dugogodišnjoj izuzetnoj saradanji uz nadu da će ona potrajati još dugi niz godina.

Autor godine VSP za 2013. godinu – prof. dr Zoran Slavković

Prof. dr Zoran Slavković (Slika 1) rođen je 13.3.1950. u Guči, Republika Srbija. Medicinski fakultet Univerziteta u Beogradu završio je 1975. godine, a specijalizaciju iz anesteziologije sa intenzivnom terapijom 1981. godine na VMA u Beogradu.

Doktorsku disertaciju pod nazivnom „Primena amrinona i njegove kombinacije sa dopaminom u lečenju insuficijencije desne komore srca" uspešno je odbranio 1999. godine na VMA.

Od 1978. godine stalno je zaposlen na Klinici za anesteziologiju i intenzivnu terapiju VMA. U preiodu 2005-2012. bio je načelnik Odeljenja za anesteziologiju Klinike za anesteziologiju i intenzivnu terapiju VMA, a od 2012. godine nalazi se na mestu načelnika Klinike.

Fig. 1 – Prof. Zoran Slavković, MD, PhD – The Author of the Year 2013 by the *Vojnosanitetski pregled.*
Sl. 1 – Prof. dr Zoran Slavković – Autor godine Vojnosanitetskog pregleda za 2013.

Prof. Slavković je od 2004. do 2008. godine bio član predsedništva Sekcije za anesteziologiju, intenzivno lečenje i terapiju bola SLD, a od 2006. godine aktivni je učesnik međunarodnog projekta GENOSEPT, u organizaciji Evropskog udruženja za intenzivnu medicinu.

Do sada je objavio preko 100 naučnih i stručnih u međunarodnim i domaćim časopisima, od kojih je 9 u časopisima sa tzv. *Science Citation Index* (SCI) liste. Učestvovao je na brojnim kongresima u zemlji i inostranstvu. Autor je monografije Anestezija u ambulantnoj hirurgiji (Beograd: IP Glosarijum d.o.o.; 2012) i Autor godine VSP za 2013. godinu. Čestitamo!

Recenzent VSP za 2013. godinu – prof. dr Branka Nikolić

Prof. dr Branka Nikolić (Slika 2) je rođena 1956. godine u Sarajevu, Bosna i Hercegovina. Diplomirala je 1981. godine na Medicinskom fakultetu Univerziteta u Beogradu, na

1981, and in 1991 defended her dissertation "Significance of early prenatal ultrasound detection of pathoanatomical changes in the central nervous system of the fetus for early attitude and treatment in pregnancy" at the same Faculty. Specialisation in gynecology and obstetrics Prof. Dr. Nikolić finished in 1988, and ever since 1983 has been working in the Clinic for Gynecology and Obstetrics "Narodni front", Belgrade, where currently is a Head of the Department for Conservative Gynecology. Starting from 1993, Prof. Nikolić has been engaged in teaching at the Faculty of Medicine, University Belgrade, on the subject Gynecology and Obstetrics, first as an Assistant (2001–2007), Associate (2007–2012), and Full Professor (from 2012).

kome je i odbranila doktorski rad 1991. godine pod nazivom „Značaj rane prenatalne ultrasonografske detekcije patoanatomskih promena centralnog nervnog sistema ploda radi ranog stava i tretmana u trudnoći. Specijalizaciju iz ginekologije i akušerstva završila je 1988. godine. Od 1983. godine stalno je zaposlena u Ginekološko-akušerskoj klinici „Narodni front" u Beogradu, gde trenutno obavlja dužnost načelnice Odeljenja konzervativne ginekologije. Od 1993. godine angažovana je u nastavi na Medicionskom fakultetu Univerziteta u Beogradu, na predmetu Ginekologija i akušerstvo, najpre kao asistent (1993–2001), potom docent (2001–2007), pa vanredni profesor (2007–2012), a od 2012. godina kao redovni profesor.

Fig. 2 – Prof. Branka Nikolić, MD, PhD – the Reviewer of the Year 2013 by the *Vojnosanitetski pregled.*
Sl. 2 – Prof. dr Branka Nikolić – Recenzent godine Vojnosanitetskog pregleda za 2013.

In her rich professional and scientific engagement, Prof. Nikolić has published, as first author or coauthor, numerous monographs, over 166 papers on gynecology and obstetrics, participated in the numerous domestic and foreign scientific meetings, and also been inviting lecturer. In a period 2004–2005 she was a of Head of the School for Improvement of Reproductive Health and Family Planning in the Center for Continual Medical Education, Faculty of Medicine, University of Belgrade, delivering a total of 11 educative seminars.

Prof. Nikolić is a member of numerous Serbian and foreign associations for gynecology and obstetrics, as well as a foreign expert of European Union (EU) for evaluating numerous projects on medicine financed by the members of the EU.

Due to a wide field of scientific interest on gynecology (malignant gestational trophoblastic diseases, gynecilogical endocraniology, upper gynecologic tract inflammations, Doppler ultrasonography in pathologic conditions), Prof. Nikolić took part in numerous Serbian and foreign projects. The two of them, supported financially by the Ministry for Education, Science and Technological Development of the Republic of Serbia, are under their way (Project No 175082 Noninvasive and invasivediagnostics and percutaneous treatment of bifurcation lesions, and Project No 4102 Cellular and molecular pathogenetic mechanisms of reproduction disorders and genital organ diseases in prevention, dignosis and therapy).

Tokom dosadašnjeg bogatog stručnog i naučnog rada u oblasti ginekologije i akušerstva, kao prvi autor i koautor, objavila je više monografskih publikacija, preko 166 stručnih i naučnih radova i učestvovala sa saopštenjima na brojnim domaćim i međunarodnim stručnim i naučnim skupovima, često kao predavač po pozivu. U periodu 2004-2005. godina bila je rukovodilac Škole za unapređenje reproduktivnog zdravlja i planiranje porodice u Centru za kontinuiranu medicinsku edukaciju na Medicinskom fakultetu Univerziteta u Beogradu, tokom koga je održano 11 edukativnih seminara.

Bila je, a i trenutno je član mnogih domaćih i međunarodnih stručnih i naučnih udruženja u oblasti ginekologije i akušerstva, kao i spoljni ekspert Evropske unije (EU) za evaluaciju niza projekata u oblasti zdravstva koje su finansirale zemlje članice EU.

Zahvaljujući širokoj lepezi naučnog interesovanja u oblasti ginekologije (maligne gestacijske trofoblastne bolesti, ginekološka endokrinologija, inflamacije gornjeg genitalnog trakta, Doppler ultrasonografija u patološkim ginekološkim stanjima) do sada je učestvovala u realizaciji više naučnih projekata, uključujući i međunarodne, od kojih su dva, koje finansira Ministarstvo za obrazovanje, nauku i tehnološki razvoj Republike Srbije, trenutno u toku (Projekat br. 175082: *Noninvasive and invasive diagnostics and percutaneous treatment of bifurcation lesions* i Projekat br. 4102: *Cellular and molecular pathogenetic mechanisms of reproduction disorders and genital organ diseases in prevention, diagnosis and therapy*).

In addition to the VSP, Prof. Nikolić peer reviews papers in other journal, of which the following ones are on the SCI list: International Journal of Gynecological Cancer, Cancer Therapy, Central European journal of Medicine, and Srpski arhiv za celokupno lekarstvo.

Considering her enormous scientific engagement, The Reviewer of the Year 2013 by the VSP award won by Prof. Dr. Branka Nikolić is quite reasonable and justified. It is our honor to know that this high award makes a part of such a rich biography.

Osim VSP, recenzent je mnogih domaćih i inostranih medicinskih časopisa, od kojih treba izdovojiti one sa SCI liste kao što su "International Journal of Gynecological Cancer", "Cancer Therapy", "Central European Journal of Medicine" i "Srpski arhiv za celokupno lekarstvo".

Uzimajući u obzir ovaj impozantan stručni i naučni opus prof. dr Branke Nikolić, sasvim je razumljivo što je priznanje Recenzent godine VSP, pripalo upravo njoj. Velika nam je čast što će to priznanje ubuduće biti deo ovako bogate biografije.

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Poziv za reklamiranje u 2014. godini

U prilici smo da vam ponudimo mogućnost oglašavanja i reklamiranja proizvoda i usluga u časopisu „**Vojnosanitetski pregled**“ (VSP). To je sigurno najbolji vid i najzastupljeniji način upoznavanja eventualnih korisnika sa vašim uslugama i proizvodima.

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ORIGINAL ARTICLES

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Particularities of the therapeutic procedures and success in treatment of combat-related lower extremities injuries

Osobenosti terapeutskih postupaka i uspešnog lečenja povreda donjih ekstremiteta nastalih u borbi

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Abstract

Background/Aim. In a combat environment the extremities continue to be the most common sites of injury with associated high rates of infectious complications due to initial contamination. The aim of this observational study was to determine therapeutic procedures effective in a combat environment and to assess functional outcomes of definitive care. **Methods.** A total of 44 casualties with combat-related lower extremities fractures sustained during combat operations in former Yugoslavia in a 2-year period (1993–1994) were enrolled. Initial management of these injuries was performed at battlefield (echelon I), surgical treatment was provided in the hospital in Trebinje (echelon II) and definitive care was provided in the Orthopedic Ward of General Hospital in Nikšić (echelon III). **Results.** All combat casualties received surgical treatment within 6–48 hours. Antibiotics were administered during hospitalization in 37 (84%) of all the patients. In all the cases fractures healed, while 15 (38.59%) of them developed complications (most notably osteomyelitis in 3 of the cases, dysfunction in adjacent joints in 3 of the cases and infection of the soft tissue around pins in 3 of the cases). Follow-up period was a little bit over 2 years and reliable conclusions regarding the therapy and the outcomes could be made. Good functional outcomes were prevalent (63.63%), satisfactory were present in one fifth and inadequate in 13.63% of all the cases. There were no amputations or fatalities. Internal fixation was shown to be the method of definitive surgical care of combat-related lower extremity fractures. **Conclusion.** The management of combat-related lower extremity fractures is complex, multidisciplinary approach through echelons is necessary and internal fixation as the method of definitive surgical care is essential.

Key words:
wounds, penetrating; war; tibial fractures; fractures comminuted; surgicenters; survival; montenegro.

Apstrakt

Uvod/Cilj. Ekstremiteti i dalje predstavljaju najčešće mesto povreda u borbenim uslovima i to sa visokim stopama komplikacija zbog infekcija usled početne kontaminacije. Cilj ove opservativne studije bio je da se utvrde delotvorni terapeutski postupci u borbenom okruženju i procene funkcionalni ishodi završnog lečenja. **Metode.** U ovu studiju bile su uključene ukupno 44 osobe sa prelomima donjih ekstremiteta nastalim u borbi tokom ratnih sukoba u bivšoj Jugoslaviji u 2-godišnjem periodu (1993–1994). Početno zbrinjavanje povreda izvršeno je na terenu (ešelon I), hirurško lečenje u bolnici u Trebinju (ešelon II), dok je završno lečenje sprovedeno u Odeljenju za ortopediju, Opšte bolnice u Nikšiću (ešelon III). **Rezultati.** Svi povređeni u borbi lečeni su hirurški tokom prvih 6–48 sati. Tokom hospitalizacije dati su antibiotici kod 37 (84%) od ukupnog broja povređenih. Prelomi su zarasli kod svih povređenih, kod 15 (38,59%) došlo je do komplikacija (najčešće do osteomijelitisa, kod 3 povređena, disfunkcije okolnih zglobova, takođe kod 3 povređena, i infekcije mekog tkiva oko igala, kod 3 povređena). Period praćenja trajao je nešto duže od 2 godine, te je bilo moguće napraviti pouzdane zaključke o terapiji i ishodima. Dobri funkcionalni ishodi postignuti su kod 63,63% povređenih, zadovoljavajući kod 20%, a neodgovarajući kod 13,63% povređenih. Nije bilo ni amputiranja, niti smrtnih ishoda. Prema našem iskustvu, interno fiksiranje predstavlja metodu potpunog hirurškog zbrinjavanja preloma donjih ekstremiteta nastalih u borbenom okruženju. **Zaključak.** Zbrinjavanje preloma donjih ekstremiteta nastalih u borbenim uslovima veoma je složeno, zahteva multidisciplinarni pristup u ešelonima, dok je metoda internog fiksiranja suštinska za potpuno hirurško izlečenje.

Ključne reči:
rana, penetrantna; rat; potkolenica, prelomi; prelomi, kominutivni; bolnice, hirurške, pokretne; preživljavanje, crna gora.

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Introduction

Modern attitudes in treatment of combat-related lower extremities injuries are not oriented only towards life saving, saving of extremities, avoiding infections and allowing fracture recovery, but also towards the idea to achieve a total recovery of all functions of the injured extremity. It is well-know that the treatment of combat-related injuries differs from the treatment applied in peaceful conditions [1]. Also, it is well-known that combat-related injuries are initially contaminated [2, 3] and that missiles can cause mass destruction of soft tissue, bones and other structures [4].

Methods

A total of 44 injured with combat-related lower extremities fractures sustained during combat operations in former Yugoslavia in a 2-year period (1993–1994) were enrolled, and treated in the Orthopedic Ward of General Hospital in Nikšić. The treatment and care of the injured was managed through echelons. Initial management of these injuries was performed at battlefield, surgical treatment was provided in a hospital in Trebinje and definite surgical care of the injured was provided in a hospital in Nikšić.

Results

Demographic characteristics of the injured are presented in Table 1.

Table 2 shows the percentage of fractures localizations according to the anatomic level of the lower extremities and distribution of fractures depending on the level of comminution.

Table 1

Distribution of the injured according to gender and age

Age (years)	Male		Female		Total	
	n	%	n	%	n	%
21–30	12	27.27	1	2.27	13	29.54
31–40	15	34.09	1	2.27	16	36.36
41–50	10	22.72	0		10	22.72
51–60	4	9.09	0		4	9.09
61–70	0	0	0		0	0
Over 70	1	2.27	0		1	2.27
Total	42	95.45	2	4.54	44	100

Table 2

Fractures localization according to lower extremities anatomic level and fractures distribution regarding the level of comminution

Anatomic level of fracture	n	%	Type of fracture	n	%
Upper third	3	6.81	Without or with small comminution	16	36.36
Middle third	32	72.72	Medium comminution	18	40.90
Lower third	9	20.45	Big comminution	10	22.72
Total	44	100	Total	44	100.00

Complications present in combat-related injuries are a current problem in military medicine, while in the literature there is a very small amount of dates and facts about the treatment of combat-related injuries. The aim of this study was to contribute through a detailed retrospective analysis of injured patients in the period from 1993 to 1994, to success in treatment of this category of injuries and to compare the treatment that was once used with the modern doctrine of military medicine.

In spite of the fact that 20 years passed from that period, our aim was to compare our experience gathered in the treatment of combat-related injuries in that period, and to determine if our experience was different from modern doctrine used in treatment of combat-related injured patients, in order to contribute to the whole consideration of this matter.

In the study, shrapnel caused injuries in 27 (61.36%) and bullet in 17 (38.63%) of the cases. There were statistically significant differences in the instruments that caused injuries ($\chi^2 = 23.24$; $p < 0.01$). In 7 (15.90%) injured were also registered joined injuries as follows: 3 of them had other fractures, and other 4 cases had injuries of the head, chests, urinary tract and blood vessels (*arteria tibialis anterior*).

All the injured received surgical treatment within 6–48 hours. Most of them, 19 (43.18%) injured, received surgical treatment in the first 24 hours. Up to 12 hours were necessary for 17 (38.63%) injured to be surgically treated, and 48 hours for the rest (11.38%). Only 6.81% of the injured were surgically treated in the first 6 hours from wounding.

Antibiotics were administrated during hospitalization in 37 (84.09%) of all the patients. In the first 6 hours following wounding, antibiotics were administrated only to one (2.27%) patient. In 18 (40.90%) cases of all the patients, 24 hours passed from wounding to administration of antibiotics. Twelve hours after wounding, 13 (29.54%) of the injured received antibiotics, while 5 (11.36 %) of the injured received antibiotics after 48 hours.

Sixteen (36.36%) of the injured that received antibiotic therapy (n = 37) during hospitalization had moderately comminuted fractures, 11 (25%) had small comminuted fractures and 10 (22.72%) had big comminuted fracture. The relation between the level of fracture and the antibiotic treatment is showed in the Table 3.

3 (6.81%) had small comminution. Duration of hospitalization in relation to the type of fracture is shown in Table 5. There was a highly statistically significant difference in a relation between the duration of hospitalization and the type of fracture ($\chi^2 = 23.56$; $p < 0.01$).

Table 3

Administration of anitbiotics during the treatment regarding the level of comminution

Type of fracture	Antibioticscs				Total	
	yes		no			
	n	(%)	n	(%)	n	(%)
Small comminution	11	(25.00)	5	(11.36)	16	(36.36)
Medium	16	(36.36)	2	(4.54)	18	(40.90)
Big	10	(22.72)	0		10	(22.72)
Total	37	(84.09)	7	(15.90)	44	(100)

Intraoperatively, during hospitalization, smear was taken from all the injured. Bacterial analysis showed the positive results in half of the cases. The positive results were found in 23 (52.25%) of the patients, while the negative one were present in 21 (47.72%) of the cases. In the group of patients with the positive results different bacteria were found, (Table 4).

Table 4

Bacteria isolated at the injury site

Isolated bacteria	Microbiologic result, n (%)	
	positive	negative
Staphilococcus aureus	9 (20.45)	21 (47.72)
Pseudomonas aeruginosa	7 (15.90)	
Proteus species	4 (9.09)	
Acinetobacter baumannii	3 (6.81)	

In all the cases fracures healed, while 15 (38.59%) of them developed complications. The highest number of complications was present in fractures with big comminution (8; 18.16%). Osteomyelitis developed in 3 (6.81%) of the patients. It is also important to mention other complications like 2 (4.54%) cases of dysfunction in adjacent joints. There was soft tissue infection around pins in 3 (6.81%) cases and in one case unequality was bigger than 3%. The level of comminution was highly statistically significant for the appearance of complications ($\chi^2 = 14.32$; $p < 0.01$).

Regarding functional therapeutic results, the period of monitoring of the patients lasted 8.3– 38.4 months, so the average period was 25.7 months long. The mentioned period provided good and reliable conclusions related to the results of the treatment. Good results of the treatment were noticed in 23 (63.63%) of all the injured, satisfactory results of the treatment in 10 (22.72%), and inadequate in 6 (13.63%) of the cases.

Table 5

Lenght of hospitalization in relation to the type of fractures

Type of fracture	Lenght of hospitalization										Average lenght of hospitalization (days)
	15 days		up to 20 days		up to 30 days		over 30 days		total		
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
Small	6	(13.63)	8	(18.18)	2	(4.54)	0		16	(36.36)	19.3
Medium	1	(2.27)	4	(9.09)	10	(22.72)	3	(6.81)	18	(40.90)	28.6
Big	0		0		3	(6.81)	7	(15.90)	10	(22.72)	36.00
Total	7	(15.90)	12	(27.27)	15	(34.09)	10	(22.72)	44	(100)	27.96

Injured patients were treated in hospital from 15 to 30 and more days. The average period spent in hospital for all the injured was 27.96 days. The average period of hospitalization for the injured with small comminution was 19.3 days, with moderate comminution 28.6 days, and with big comminution 36 days. Most of the injured (15; 34.09%) were hospitalized up to 30 days. From that number, 10 (22.72%) injured had moderate comminuton, and 3 (6.81%) patients had big comminution. For 12 (27.27%) injured the period of hospitalization took up to 20 days, where 8 (18.18%) of them had small comminution and 4 of them (9.09%) had big comminution. Ten injured (22.72%) were hospitalized more than 30 days, 7 (15.90%) of them had big comminution, and

Discussion

It is well-know that the treatment of combat-related injuries differs from the treatment applied in peaceful conditions [1]. Also, it is well-known that combat-related injuries are initially contaminated [2, 3] and that missiles can cause mass destruction of the soft tissue, bones and other structures [4, 5]. These facts imply different approachs than those the surgeons meet in everyday procedures. Instruments that cause combat-related injuries are different, therefore injuries differ, too. Missiles often move very fast, and they are fragmented in the moment of crash. Surgeons sometimes do not know the weapon that causes injury. Therefore, it is very important

for a surgeon to know the mechanisms that can cause injuries and possible types of damages in order to make an appropriate evaluation of each patient's condition and to apply optimal methods in management of injuries. There are principles of surgical treatment of tibia fractures that are common for combat-related injuries and for injures in peaceful conditions.

Our experience shown in this study is related to the elements of definitive operative management of lower extremities fractures applied as it was imposed by medical doctrine 20 years ago. In the echelons of combat-related injuries management, internal fixation was in the last place of the treatment procedure. Meanwhile, new studies show that there is a trend of temporal and spatial approaching of external and internal fixation to the war environment, so it starts from the hypothesis that the performance of these surgical procedures is possible even at battlefield. Possley et al. [6] made a study based on the analysis of 55 consecutive tibia fractures inflicted in war environment, that were initially managed by external fixation. They especially paid attention to complications related to the procedure. They concluded that important complications as neurovascular damages, mechanical dysfunctions and osteomyelitis were not present. External fixation was successful in 77% of the cases, so they concluded that this procedure was safe and efficient in war environment. Rigid external fixation allows aggressive and simultaneous treatment of bones and soft tissues. Bandaging of injuries is easier, and it is possible to put a skin graft on injury, to install irrigation without any fear that bone fragments will be moved. External fixation is very suitable in the treatment of infections.

Stinner et al. [7] analyzed the results in fractures treatment in patients with injuries managed by internal fixation at battlefield. The authors point out that internal fixation at battlefield is rarely performed because there is a limited availability of instruments and radiological support, as well as impossibility to confirm the sterility in the first line at battlefield. Because of the lack of facts, the authors made analysis of 47 injured with internal fixation on 50 fractures in the operating room in the zone of battlefield. The most common were hip fractures forearm and ankle joint and open fractures. The average value of the Injury Severity Score (ISS) was 11.4. Thirty nine of all fractures healed without any complications. There was one case of infection and one case of acute surgical complications. In 10 cases of fractures, including the one with infection, it was necessary to perform additional procedures. Internal fixation at battlefield was managed efficiently, therefore the level of complications did not exceed the usual number.

All the injured in our study received surgical treatment in 6–48 hours. Surgical treatment was provided for the most of the injured in the first 24 hours. In the first 12 hours, the surgical treatment was necessary for 17 of the injured, and in the 48 hours for the 8 of the injured. The treatment was provided in the first 6 hours only for 6.81% of the injured. The percentage is that low because of the conditions at battlefield, the lack of adequate equipment and trained staff .

In our study, fractures healed in all the cases, and 15 of them developed complications. The most of complications were developed in the cases of big comminution. Osteomyelitis was developed in 3 of the cases and it is important to mention other complications like dysfunction in adjacent joints in 2 of the cases. There was soft tissue infection around pins in 3 of the cases, and one patient presented inequality more than 3 cm. The level of fractures had important statistical significance for the presence of complications. Comminution cannot be easily estimated by simple clinical examination, even after radiography. Comminuted fractures are at a high risk for the aspect of osteogenesis, because it is slow and uncertain. And if there is a case of initial contamination, osteogenesis is even more endangered. From the above-written, it can be concluded that it is better when fixation is made earlier during the echelons in the treatment of patients, but we did not have any conditions for it.

As far as the functional results of therapeutic procedures are concerned, the period of monitoring of the injured patients was in the range 8.3–38.4 months, so the average period was 25.7 months. The quoted period gave the possibility to reliably conclude on the results of treatment. Good results of the treatment were achieved in 23 of the cases, satisfactory results in 10 of the cases, while inadequate ones were present in 6 of the cases. In the majority of cases (86%), good or satisfactory results of definitive reconstruction were accomplished. We think that it is a direct result of the fact that we, as far as we could, followed the principles and aims of good clinical practice, like covering and closing of injuries, prevention of infection, reestablishment of the length, alignment, rotation and stability, injury healing and functions regaining [8, 9].

Soft tissues defects of different intensities often follow fractures of other bones, especially in the combat-related injuries. Therefore, infected injury can be present in the moment of wounding, and it can be connected to the longer period of hospitalization that can expose the patients to nosocomial pathogens. All this can contribute to infective complications in the patients. Historically, etiology of infection of combat-related injuries has changed from the clostridium that provoked infections, registered before World War I, to polimicrob infections registered in the Vietnam War, when an increase in the frequency of pathogens resistant to antibiotics was also noticed. New experiences from battlefields indicate gram-negative pathogens that are resistant to more antibiotics, like *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia* that provoke infections of combat-related injuries. Johnson et al. [10] in their research focused on infectious complications present in tibia fractures. Meanwhile, there were registered recurrent infections provoked by staphylococcus. New studies show that infectious complications and injuries of soft tissues are risk factors that contribute to late amputation after severe lower extremities trauma [11].

Within combat processes, extremities are most commonly the location of injuries connected to the high risk of infectious complications. In about 15% of the injured patients with injuries of extremities, osteomyelitis was pres-

ent, while 17% of present infections were recurrent which in addition makes more complicated the procedure of definitive management of injuries. Bacterial spectrum that provokes these infections involves, apart from the mentioned ones (*Acinetobacter baumannii, Pseudomonas aeruginosa* and *Klebsiella species* that produces ß-laktamase), *Escherichia coli*, as well as methicillin – resistant *Staphylococcus aureus* – MRSA. Surgical debridement [12] and early use of proper antibiotics [13] are the key elements in prevention of infections together with combat-related extremity injuries.

In our study, antibiotic therapy was applied during hospitalization in 37 of all the patients. In the first 6 hours after wounding, only one injured received antibiotic therapy, in 18 of the cases 24 hours passed from the moment of wounding to the moment of antibiotics administration. Twelve hours after wounding, 13 patients received antibiotics, and 5 received them after 48 hours. At first glance it seems that the percentage of those who received appropriate antibiotic therapy in 6–12 hours is not satisfying, however, it should be taken into consideration that new studies on the appropriate use of antibiotic therapy in cases of difficult sepsis and septic shock for example, show that only 50% of them got appropriate antibiotic in the first 6 hours, in the elite units of intensive therapy in peaceful conditions in America and Canada [14, 15]. Even in circumstances of appropriate antibiotics use on time, the rate of mortality in cases of difficult sepsis and septic shock is unacceptably high [16].

Intraoperatively, during surgical hospitalization, smear was taken from injuries of any patients. Bacterial analysis showed the positive result in half of the cases. In the group of the patients with the positive results different bacteria were found, and the results, in part, match with the similar studies [12, 13]. (*Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter baumannii*).

The outcomes of combat-related injury depends on the type and character of the instrument that caused injury. The bigger amount of kinetic energy is used, the bigger will be the destruction of tissues, and fractures will be multifragmented with bigger bone destruction. Injury contamination is also significant. Different wounding factors influence specific processes present in an injury. The loss of blood causes the beginning of pathophysiological reactions that lead to ischemic-reperfusion damages. In injury of arterial blood vessels that feed muscle mass, damages of soft tissue are even more expressed.

The injured patients were monitored during 25 months following the treatment, which allowed us to make reliable conclusions on the methods and quality of treatment. Good functional results were confirmed in most of the cases, satisfactory results in one fifth of the patients, while inadequate results in 13.63%. The key element in the analysis of the functional capacity of the injured, meaning the restoration of the functions of the bone and joint system of the lower extremities is the fact that there was no need for amputation in any of the cases. A big study on 569 injured in peaceful conditions, was focused on the results of severe trauma of the lower extremities. The two results were present – reconstruction or amputation, and the functional capacity of the injured was evaluated after two years [17, 18]. The period of monitoring was almost identical to our period, our sample, indeed, was smaller, but there were involved primary infected combat-related injuries and there was no amputation of any height. One of the new studies that analyzed the return to active military service of 395 American injured patients who had their extremities amputated, showed that from the quoted number 65 patients returned to active military service [19]. The authors concluded that compared to the period 1980–1990 when out of 469 injured with amputation, 11 returned to active military service, this percentage increased by over 16% as a direct consequence of improvement in the management of the injured. Lately, there are lots of analysis of risk factors for delayed amputation [20]. In our study, none of our patients, among those with the inadequate functional results, was at risk of amputation. Today, it is considered that the functional result between those who had primary amputation and those who had their lower extremities saved is not very different [21] and that the quality of life depends more on the height of amputation in cases of the lower extremities (below knees and thighs) [22]. Of course, there are complications directly related to the trauma and amputation in cases of combat-related injuries, for example heterotopic ossification [23].

Regarding complications of difficult lower extremities injures, in our study osteomyelitis developed in 3 of the patients. It is important to mention other complications, like 2 patients with dysfunction in adjacent joints. In 3 of the cases there was soft tissues infection around pins, and in one case unequality was higher than 3 cm. These percentages are visibly lower than the ones mentioned by other authors. Harris et al. [24] reported the following complications in the injured that had their extremities saved after severe injuries in peaceful conditions: infections (23.2%), osteomyelitis (8.6%) and dysfunctions (31%) of the cases.

During the 25-month monitoring period of the injured in our study, there were no cases of fatalities. Numerous studies have ascertained that 10% of soldiers killed in battle bleed to death from extremity wounds. In the study of Dorlac et al. [25] authors examined the treatment course and outcomes of civilian patients who exsanguinated from isolated penetrating extremity injuries. In this study all the patients died (n = 14), and 93% succumbing within 12 hours.

Conclusion

The treatment of lower extremities combat-related injuries presents a very complex therapeutic problem that requires management in echelons and team work of different fields. Stabilization of bone elements has special importance in the treatment of lower extremities combat-related injuries and presents the key element that substantially influences the success of treatment.

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Prevalence of hypertension in adults in the Šumadija District, Serbia – A cross-sectional study

Prevalencija hipertenzije kod odraslih u Šumadiji – unakrsno istraživanje

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Abstract

Background/Aim. World Health Organization (WHO) studies on the global level have shown that one of the major problems of the public health is hypertension. Blood pressure level greater than 140/90 mmHg is directly and predictively linked to other cardiovascular diseases. The aim of this research was to determine the prevalence of hypertension and the risk groups among the adult population in the Šumadija District, Serbia. **Methods.** This cross-sectional study included 1.669 elderly population of the Šumadija District, aged 25–74. The study was performed according to the protocol of the Countrywide Integrated Noncommunicable Disease Intervention (CINDI) international program. **Results.** In the Šumadija District more than a half of the population aged 25–74 suffers from hypertension (53%). In the Šumadija District 9% of population has undiagnosed hypertension. In the group of people familiar with their high blood pressure problems, good disease control is achieved in only 46% of them. Statistically, hypertension occurs more frequently in males aged 45–74, of lower education, and in rural population. This is the target group for implementation of the high risk strategy. Statistically, there is a higher prevalence of hypertension in people suffering from myocardial infarction ($p = 0.04$), angina pectoris ($p = 0.00$), other cardiac diseases (cardiac insufficiency) ($p = 0.00$) and cerebrovascular crises ($p = 0.04$). **Conclusion.** A continuous increase of patients with hypertension, coupled with the developed complications and increase in cardiovascular diseases as a cause of death, points to the lack of effective access to prevention and early detection of these diseases in the primary health care among the risk groups in Šumadija.

Key words:
hypertension; serbia; prevalence; incidence; risk factors.

Apstrakt

Uvod/Cilj. Istraživanja Svetske zdravstvene organizacije na globalnom nivou pokazala su da je hipertenzija jedan od najvećih problema narodnog zdravlja. Visina krvnog pritiska iznad 140/90 mmHg direktno ukazuje na povezanost sa drugim kardiovaskularnim bolestima (KVD). Bolesti srca i krvnih sudova u Srbiji u 2006. godini su u strukturi mortaliteta činile više od polovine svih smrtnih ishoda. Cilj ovog istraživanja bio je da se utvrdi prevalencija hipertenzije, kao i rizične grupe kod odraslih stanovnika Šumadije. **Metode.** Ova studija preseka obuhvatala je reprezentativni uzorak od 1 669 odraslih u Šumadiji, starosti 25–74 godine, koji je formiran u skladu sa protokolom međunarodnog programa *Countrywide Integrated Noncommunicable Diseases Intervention* (CINDI). **Rezultati.** U Šumadiji više od polovine stanovništva (53%), starosti 25–74 godine ima hipertenziju. Novootkrivenu hipertenziju ima 9% stanovnika Šumadijskog okruga. U grupi osoba koje su znale da imaju povišen krvni pritisak dobra kontrola bolesti postignuta je samo kod 46%. Hipertenzija se statistički češće javljala kod ispitanika muškog pola, starosti 45–74 godine, kod ispitanika nižeg obrazovanja i seoskog stanovništva. Ovo su ciljne grupe za primenu strategije visokog rizika. Postoji statistički značajno veća učestalost hipertenzije kod osoba koje boluju od infarkta miokarda ($p = 0,04$), angine pektoris ($p = 0,00$), drugih bolesti srca (srčana insuficijencija) ($p = 0,00$) i cerebrovaskularnih kriza ($p = 0,04$). **Zaključak.** Neprekidan porast obolevanja od hipertenzije, skopčano s razvojem komplikacija i porastom udela kardiovaskularnih bolesti u strukturi uzroka smrti, ukazuje na nedovoljno efikasan pristup prevenciji i njihovom ranom otkrivanju na nivou primarne zdravstvene zaštite kod rizične grupe u Šumadiji.

Ključne reči:
hipertenzija; srbija; prevalenca; incidenca; faktori rizika.

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Introduction

The epidemic of cardiovascular diseases (CVDs) in the world marked the 20th century with a clear tendency to keep the trend of increasing prevalence in many countries as well as in the 21st century. The increasing prevalence of CVD, primarily linked to aging population, and the population in Serbia is among the oldest in Europe [1, 2].

In the world, according to the World Health Organization (WHO), in 2006 from heart and vascular diseases died 17.5 million people, accounting for 30% of all deaths. In European countries, in the same year there were 5.1 million deaths, representing 52% of all deaths [3]. Deaths from heart and blood vessels diseases in Serbia in 2006 were more than half of all deaths (57.3%). The standardized heart and vascular mortality rate diseases in Serbia in 2006 was 567.0 deaths *per* 100,000 population (in Central Serbia, 544.2). Compared to the average mortality rate in Europe of 479.4 *per* 100,000 population, Serbia was in that year in a group of countries with a high risk of daying from cardiovascular diseases [4, 5].

Hypertension is a major risk of damaging blood vessels and consequent organ damage, especially heart, kidney and brain [6]. Studies on risks of mortality and morbidity, conducted by the WHO at the global level, have shown that hypertension is one of the biggest public health problems. It is shown that this disease is a higher risk factor of all the identified factors, such as consumption of tobacco smoke, hypercholesterolemia and obesity, even in developing countries [7, 9]. Hypertension is attributed to 9.7% of total years of life lost (YLL) due to premature death for males and 13.3% for women [10].

Hypertension is defined as the value of blood pressure which causes a higher risk of adverse consequences in the form of organ damage. That results in the increased cost of treatment of hypertension [6]. According to the definition of hypertension, based on criteria adopted by consensus JNC 7 (Joint Committee on Detection, Evaluation and Treatmant of High Blood Pressure) [11], hypertension is a permanent increase in arterial blood pressure to the values above 140 mmHg in systole and 90 mmHg in diastole. Elevation of blood pressure above 140/90 mmHg [11, 12] is a continuous, gradual, consistent, independent and directly predictive, associated with apoplexy, coronary artery disease, chronic renal disease progression [13, 14], thus with that value of blood pressure it is necessary to start treatment urgently for all applicable protocols [11].

The aim of this study was to determine the prevalence of hypertension in the population of adults in the Šumadija District, Serbia, and risk groups for the diseases such as hypertension and its association with other cardiovascular diseases.

Methods

This research was a part of the project "Capacity building of primary health care for the primary prevention of chronic disease-development model" implemented at the Institute of Public Health, Kragujevac, in 2011. Epidemiological studies in a type-sectional study was conducted on a representative sample of the Šumadija District population, aged 25–74 years. The study was conducted in 7 municipalities of Šumadija: Kragujevac, Aranđelovac, Topola, Rača, Lapovo, Batočina and Knić. The study of each municipality included the number of patients proportional to the number of inhabitants *per* municipality in Šumadija, aged 25–74 years. The sample consisted of 1,850 respondents, but 181 subjects were excluded from the study. Exclusion criteria were: incomplete survey data relevant to this research and irregular blood pressure. The sample was divided, by the age of respondents, into 5 groups: 25–34, 35–44, 45–54, 55–64, 65–74. Within these defined groups, the same number of males and females was randomly included according to the list received from the Serbian Ministry of Internal Affairs. The final sample consisted of 1,669 respondents, 50.8% males and 49.2% females.

The investigation protocol was developed in accordance with the protocol of the international Countrywide Integrated Noncommunicable Diseases Intervention (CINDI) program [15]. The data surveyed were collected, systemic examination of subjects, other anthropometric measurements and laboratory analyzes were performed.

The survey respondents were conducted by the physicians (respondents in the households or in the office of the Health Center), "face to face." A systematic review of the subjects was done by the physician at the Health Center. Blood pressure was measured during systematic examination 3 times at 1-minute intervals. Blood pressure elevation was obtained as the mean value of systolic and diastolic blood pressures of the second and third measurements.

We defined 4 categories of hypertension as follows: no hypertension, newly identified, controlled and uncontrolled hypertension, based on the values of blood pressure measured at examination by a physician, and on the answers given by the examinees to 2 questions: 1) Did a doctor or other health worker tell you that you have high blood pressure during last year (12 months)?, and 2) Do you regularly take drugs that your doctor has prescribed you to lower blood pressure?

Based on measurement data and the answers to these questions they were classified into 4 subgroups: no hypertension (doctor found no hypertension, it was under control amounting to < 140/90 mmHg; newly identified hypertension (≥ 140/90 mmHg); controlled hypertension (< 140/90 mmHg); uncontrolled hypertension (≥ 140/90 mmHg).

According to the analysis of associated diseases and conditions the subjects were classified into 2 categories: no hypertension; yes hypertension (uncontrolled hypertension).

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki 1975, revised in 1983. The study was approved by the Ethics Committee of the Institute of Public Health in Kragujevac, and each respondent was familiar with the aims and methods of the study, and in connection with the information sheet and signed consent to participate in the survey.

For statistical analysis we used SPSS Kall and software packages. For examination of dependence of categorical

variables the χ^2 test used. Hypertension was considered dependent, all other variables were independent.

Results

At the time of the study we measured high blood pressure in 32.4% of the representative sample. Another 20.1% of them knew to have hypertension but and regularly took medication, which and their blood pressure was normal at the time of blood pressure testing.

The results of measurements at the time of study were classified on the basis of the ESH/ ESC 2007 (ESH – European Society of Hypertension, ESC – European Society of Cardiology) [12]. The majority of people with hypertension had mild hypertension, 22.3% (grade I). High-normal pressure (130/85 to 139/89 mmHg) had 17.7% of the population. Moderate hypertension (grade II) was established in 7.9%, and severe (grade III) in 2.2% of respondents. Blood pressure > 160/100 mmHg had as many as 10% of the Šumadija population (Figure 1).

In Šumadija more than half of the population aged 25–74 had hypertension. One out of 5 people with hypertension did not previously know to have this disease. This study also found that 9% of the Šumadija population had a newly discovered hypertension (incidence). In addition, good disease control was achieved in 46% of people be awaring to have high blood pressure, and the disease was not well controlled in more than half of cases previously diagnosed with hypertension (Figure 2).

The categories of hypertension in relation to socioeconomic characteristics are shown in Table 1.

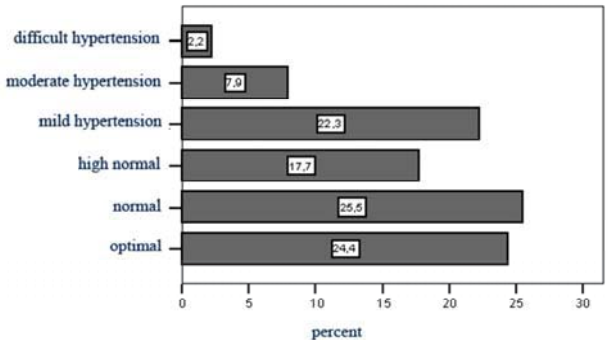

Fig. 1 – Frequency of blood pressure values in the classified groups (ESH/ESC 2007) in the Šumadija District, Serbia, during the research.

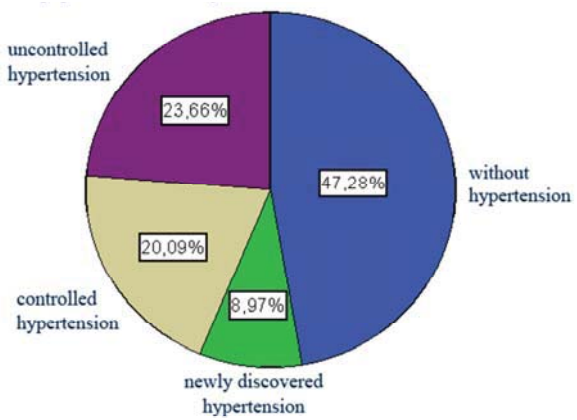

Fig. 2 – Prevalence of hypertension subgrups among the population of the Šumadija District, Serbia.

Table 1

Categories of hypertension in relation to some sociodemographic characteristics

Characteristics of populations (n = 1669)	Hypertension (% of patients)			
	no	controlled	uncontrolled	newly discovered
Patients	47.3	20.1	23.6	9.0
Sex				
male	44.2	19.1	25.2	11.5*
female	50.4	21.0	22.1	6.5*
Age groups, (years)				
25–34	80.8**	6.9**	7.0**	5.3*
35–44	67.4**	10.5**	11.1**	11.0
45–54	45.1	23.6	20.9	10.4
55–64	24.1**	31.9**	34.7**	9.3
65–74	15.0**	27.1*	49.3**	8.6
Education				
primary	27.4**	22.1	41.1**	9.2
secondary	50.6	21.1	19.1**	9.3
high	60.3**	15.2*	16.6**	7.9
The percentage of income for food	43.1	22.0	28.1	6.8
< 30	49.6	19.0	21.6	9.8
31–50	44.5	21.2	25.1	9.2
51–70	49.6	20.1	23.6	6.7
> 71				
Type of settlement				
city	52.2	21.7	18.8**	7.3
suburb	45.4	20.9	26.1	7.6
village	42.1	17.5	28.4*	12.0*

Values given as percentages of the hypertension variables by the category within the examined sociodemographic characteristics, and expressed as percentages of sequence (the sum of the percent in the line is 100%); n = total number of patients; *$p < 0.05$; **$p < 0.01$.

The males were more likely to suffer from hypertension than the females (55% *vs* 50%), and there were no significant intergroup differences among categories with respect to sex ($p = 0.000$). A significant deviation from the average was in the population of newly discovered hypertension (9.0%) by sex, $p < 0.05$, while women had a lower frequency (6.6%), and men had a higher incidence of newly detected hypertension (11.5%). The males were more likely to have uncontrolled hypertension (25.2%) than the females (22.1%), but with no statistical significance compared to the average frequency.

Hypertension is a disease of the elderly and its incidence increases in proportion to age. In the age groups 55–64 and 65–74 the incidence of hypertension was 76–85%. It was significant that in the age group 45–54 the percentage of people with hypertension exceeded 50%. Also, one out of 5 people aged 25–34, and one out of 3 people aged 35 to 44 years had hypertension. Analysis of categories of hypertension by age groups showed the expected results, namely statistically significantly higher incidence of controlled and uncontrolled hypertension in people older than 55 years. The incidence of uncontrolled hypertension was highest among the oldest respondents, 65–74 (49.3%). Surprisingly, a high prevalence of newly detected hypertension was in the age group 35–44 (11.0%), and 45–54 (10.4%), showing that every 10th person in these age groups did not know to have hypertension.

No significant incidence of hypertension was found in relation to the socioeconomic status of the respondents ($p = 0.40$).

Hypertension was more common in people living in rural areas compared to the suburbs and the cities (58% *vs* 55% of village *vs* suburban city 48% $p = 0.00$). The incidence of uncontrolled (28.4%) and newly discovered (12.0%) hypertension among residents of villages in Šumadija was significantly higher than the average frequency of these categories of hypertension in the city population ($p < 0.05$), while city dwellers had less frequent uncontrolled hypertension, 18.8% ($p = 0.01$).

The incidence of the other cardiovascular diseases, which are also complications of hypertension, is shown in Table 2.

Table 2

Cardiovascular disease (CVD) association with hypertension

Type of CDV (n = 1669)	Hypertension (% of patients)	
	without	with
All comorbidities	47.3	52.7
Myocardial infarction		
without	47	53
with	29	71
Angina pectoris		
without	48	52
with	15*	85*
Other heart related issues		
without	49	51
with	27*	73*
Stroke		
without	47	53
with	38	62
Cerebrovascular crisis		
without	47	53
with	25	75

Values in the table are given as percentages of the hypertension variables by categories of variables in the CVD, and expressed as percentages of sequence (the sum of the percent in the line is 100%); n = total number of patients; *$p < 0.01$.

There were a statistically significant intergroup differences in the incidence of myocardial infarction, angina pectoris, other heart diseases (heart failure) and cerebrovascular crises in people with hypertension.

Of all the people with heart attack, 71% had hypertension, and 73% had other heart diseases (heart failure). People with angina pectoris had hypertension in 85%, cases, which was significantly more likely than the average ($p < 0.01$). There were no significant differences in the incidence of diseases such as stroke ($p = 0.97$).

Discussion

Analysis of data on the prevalence of hypertension at the global level indicates that the increase in prevalence was expected. In 2000 the prevalence of hypertension was 26.4%; in 2010 we had the planned increase by 50% [16], and by the 2025 will be it more than 60% [7].

The first health survey conducted on a representative sample in 2000 in Central Serbia, showed hypertension in 43.3% aged 19 and over, in 2006 it was 46.0% [5]. Our results showing the incidence of hypertension of 53% in Šumadija indicate further increase in the prevalence of hypertension in this area, with an increase of 10% in 10 years, the greater increase trend than in developed countries. In the United States an increasing prevalence of 8.3% was found between studies in 1988–94 and 1999–2000 [17]. The Canadian study showed that hypertension was increased from 153.1 *per* 1,000 adults in 1995, to 244.8 *per* 1,000 adults in 2005, an increase in the relative risk of > 60% [18]. Increasing age of Serbian popula-

tion [2] is definitely one of the important factors, but can not be crucial for such a dramatic increase in the prevalence of hypertension. Education as an independent factor was associated with hypertension in several studies [19, 20]. In our study it was shown that subpopulations of lower educated persons represent a risk group for increased morbidity from hypertension, with particularly high prevalence of uncontrolled hypertension and newly discovered. People with lower education generally live in villages and in old age groups. There is evidence that communities with predominant population engaged in agriculture and lower level of education is directly associated with age and disappears as an independent factor for the onset of hypertension [21]. Although there are studies that indicate that lower socioeconomic status is associated with a higher incidence of hypertension [20], in our study it was not the case. In the studied area hypertension includes both rich and poor groups of population.

Despite improving knowledge and treatment options for controlling hypertension, the prevalence of patients with uncontrolled hypertension remains high in developed countries [22, 23]. Our research shows that with ¼ of the total population, or even 54% of the population known to have hypertension does not establish control over the height of arterial pressure, indicating the ineffectiveness of treatment. Research conducted in the United States indicated that pharmacological therapy provides control of hypertension in only 39% of patients treated in primary care, which coincides with our findings [16]. Also, many prospective studies have demonstrated the ineffectiveness of drugs in preventing complications of hypertension [24]. Medications maintenance of blood pressure < 135/85 mmHg in hypertensive individuals does not provide additional benefits in extending life and reducing heart attack, angina or heart failure [25, 26]. Unfortunately, there is a well-known problem of the influence of pharmaceutical industry at all levels of care, in Serbia and in our circumstances the problem of hypertension is solved in curative rather than preventive level. On the other hand, the development capacity of secondary health care level in the field of gerontology, and emergency services in urgent care situation in the field over the past decade were the key reasons for the comforting fact that in the Šumadija District in a 1998–2008 period revealed decline in mortality from hypertension-derived diseases (ICD 10: I10 - I15) [10].

Our results suggest that other cardiovascular diseases such as myocardial infarction, angina pectoris, heart failure and cerebrovascular stroke in ¾ patients were associated with hypertension. Literature data indicate that the absolute individual risk of developing complications of hypertension and organ damage depends not only on the amount of blood pressure, but also on other risks for cardiovascular disease and associated clinical disorders. Therefore, it is necesary to divert the struggle against hypertension from diagnosis and treatment, to programs of prevention of hypertension and its complications [6, 27].

The results indicating that 53% of population suffers from hypertension, 9% of the population do not know to have hypertension, the incidence of hypertension exceeds 50% of population already in the age group of 45–54 years, and that the incidence of other cardiovascular diseases is significantly higher in patients with hypertension, may be considered alarming. Therefore, the focus of hypertension problem solving in Šumadija is just at the primary level of care and implementation of effective intervention projects on prevention and early detection of heart and blood vessels diseases.

In Serbia there are no data on socio-economic impact of diseases such as hypertension and development of its complications. According to economic analysis of the American Heart Association (AHA) in the U.S.A. in 2006 more than 430 billion dollars was spent for the diagnosis, outpatient and inpatient care of patients with CVD, including the cost of lost work capacity [28]. It is scientifically proven that the technique of detecting and reducing risk factors is very efficient and cost-effective [15, 29].

Our research shows that the target groups for preventive action and early detection are: male sex, age of 25–44 years, persons with lower education and rural population. Prevention and early detection activities should focus precisely on these risk groups in order to investigate the risk factors, their prevention or modification, in order to prevent the start or progress of the disease and to prevent disability and premature death.

The potential for improving population health in Šumadija lies in a comprehensive strategy to prevent and control hypertension, which would also improve promoting health at population level, programs to prevent the disease actively targeted to individuals and groups at high risk, and maximum population coverage with systematic preventive reviews.

Conclusion

Hypertension is present in 53% of population and its prevalence in Šumadija increased in comparison to previous studies in Serbia, which in some way indicates the inefficiency of primary health care level. About 54% of respondents who know they have hypertension do not regulate blood pressure levels, although they take medications. We found 9% of new cases of hypertension, which indicates the quality of primary care activities in the early detection.

The prevalence of hypertension is significantly higher in males, in older age groups, in less educated people and inhabitants of rural environment, so they should be the target group for the application of the so-called high-risk strategy.

Newly discovered hypertension is more common in men, middle aged, in the countryside, and they should be a target for interventions to early detect the disease.

Using these strategies we can expected to reduce comorbidity caused by hypertension, as confirmed by the association of hypertension with myocardial infarction, angina pectoris, other heart diseases and cerebrovascular crises.

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The effect of disinfectants on dimensional stability of addition and condensation silicone impressions

Uticaj dezinficijenasa na dimenzionalnu stabilnost otisaka izrađenih od adicionih i kondenzacionih silikona

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Abstract

Background/Aim. Dimensional stability and accuracy of an impression after chemical disinfection by immersion in disinfectants are crucial for the accuracy of final prosthetic restorations. The aim of this study was to assess the deformation of addition and condensation silicone impressions after disinfection in antimicrobial solutions. **Methods.** A total of 120 impressions were made on the model of the upper arch representing three full metal-ceramic crown preparations. Four impression materials were used: two condensation silicones (Oranwash L – Zhermack and Xantopren L Blue – Heraeus Kulzer) and two addition silicones (Elite H-D + regular body – Zhermack and Flexitime correct flow – Heraeus Kulzer). After removal from the model the impressions were immediately immersed in appropriate disinfectant (glutaraldehyde, benzalkonium chloride – Sterigum and 5.25% NaOCl) for a period of 10 min. The control group consisted of samples that were not treated with disinfectant solution. Consecutive measurements of identical impressions were realized with a Canon G9 (12 megapixels, 2 fps, 6x/24x), and automated with a computer Asus Lamborghini VX-2R Intel C2D 2.4 GHz, by using Remote Capture software package, so that time-depending series of images of the same impression were obtained. **Results.** The dimensional changes of all the samples were significant both as a function of time and the applied disinfectant. The results show significant differences of the obtained dimensional changes between the group of condensation silicones and the group of addition silicones for the same time, and the same applied disinfectant (p = 0.026, F = 3.95). **Conclusion.** The greatest dimensional changes of addition and condensation silicone impressions appear in the first hour after their separation from the model.

Key words:
dental impression materials; silicones; disinfectans; dental prosthesis.

Apstrakt

Uvod/Cilj. Dimenzionalna stabilnost i preciznost otiska posle hemijske dezinfekcije potapanjem u dezinficijens predstavljaju osnovu za preciznost definitivnih zubnih nadoknada. Cilj ovog istraživanja bio je da se proceni dimenzionalna stabilnost otisaka izrađenih od adicionih i kondenzacionih silikona posle dezinfekcije u antimikrobnim rastvorima. **Metode.** Napravljen je uzorak od 120 otisaka, dobijenih otiskivanjem modela gornje vilice sa ispreparisanim zubima za metalokeramičke krune. Od otisnih materijala korišćena su dva kondenzaciona silikona (Oranwash L – Zhermack i Xantopren L Blue – Heraeus Kulzer) i dva adiciona silikona (Elite H-D + *regular body* – Zhermack i Flexitime *correct flow* – Heraeus Kulzer). Odmah po odvajanju od modela, otisci su potopljeni u odgovarajući dezinficijens (glutaraldehid, benzalkonijum-hlorid – Sterigum i 5,25% NaOCl) u trajanju od 10 min. Kontrolnu grupu činili su uzorci koji nisu tretirani dezinficijensom. Uzastopna merenja istovetnih otisaka vršena su pomoću fotoaparata Canon G9 (12 megapiksela, 2 fps, 6 × / 24 ×), a automatizovana sa računara Asus VX 2R Lamborghini-Intel C2D 2,4 GHz, korišćenjem opcija softverskog paketa *Remote Capture* tako da su dobijene vremenske serije fotografija istog otiska. **Rezultati.** Utvrđene su izražene dimenzionalne promene svih uzoraka kako u funkciji vremena tako i u funkciji primenjenog dezinficijensa. Rezultati pokazuju postojanje značajnih razlika dimenzionalnih promena između grupe kondenzacionih silikona i grupe adicionih silikona za isto vreme i isti primenjeni dezinficijens (p = 0,026, F = 3,95). **Zaključak.** Najveće dimenzionalne promene otisaka uzetih adicionim i kondenzacionim silikonima beleže se u prvom satu po odvajanju sa modela.

Ključne reči:
stomatološki materijali za otiske; silikoni; dezinfekcija; zubna proteza.

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Introduction

Impression materials are used in dentistry to reproduce the form and relations of the teeth and surrounding oral tissues. Impressions are used for fabricating diagnostic and master casts. Silicone impression materials are widely used thanks to their excellent physical properties, favorable handling properties and good patient acceptance. Dimensional stability and accuracy of impressions under various conditions are crucial for the accuracy of the final prosthetic restoration. Accuracy of impressions also depends on the correct choice of impression material [1, 2].

In order to prevent transmission of infectious diseases such are hepatitis B virus (HBV) infection, AIDS, herpes infection and tuberculosis, disinfection of the entire dental equipment, including dental impressions, is mandatory. Dental impressions, contaminated with the patient's blood and saliva are a potential route of transmission of infection. Unfortunately, disinfection of dental impressions was not a routine procedure until the outbreak of AIDS in the late 20th century. Although the number of microorganisms decreases after rinsing impressions under water, a measurable bacterial load remains on the impressions and can be transferred to the casts [3]. Even though various disinfection treatments are being proposed, chemical disinfection of impressions by immersion in disinfectants is the most reliable and practical method. Immersion will disinfect both internal and external surfaces of an impression, including a tray and will minimize the risk of inhalation of disinfectant [4–6].

Two main concerns for disinfectant evaluation are: the efficiency of disinfecting solutions in eliminating pathogens, and the influence of disinfection treatment on the dimensional stability of dental impression materials.

The guidelines for the proper disinfection protocols in dental offices and laboratories are continuously issued by American Dental Association (ADA), Centers for Disease Control and Prevention, textbooks on dental materials, scientists, manufacturers of impression materials and others [7, 8].

A considerable number of articles has reported on dimensional stability of disinfected impressions [2–6]. Glutaraldehyde, used to be a commonly used disinfectant but iodophors, chlorine, alcohol and phenolic compounds were also tested. The most frequently used were elastomeric impression materials. Specimens were disinfected by spraying or immersing in disinfectant solution for the period to 60 min or longer. Control specimens were left in water, air or poured immediately. In estimating dimensional changes of impressions, measurements were taken either on the impressions or on the casts poured from those impressions. Because of the numerous variables and the above differences, direct comparison of the results of numerous researchers is difficult. The recommended exposure time for the most surface disinfectants is 10–15 min. However, repeated disinfection of an already disinfected impression is often done in a dental laboratory. The results of a research conducted by the ADA and British Dental Association (BDA) showed no good communication between dental offices and laboratories in terms of weather and which disinfection procedure was carried out [9]. The research of Giammanco et al. [10] shows that impressions must be disinfected immediately because the efficiency of certain disinfectants is reduced if disinfection is delayed for 6 h from the time of impression taking. Lepe and Johnson [11] state a significant effect of 2% glutaraldehyde on dimensional stability of A-silicones and polyethers if they are exposed to disinfectant for long (18 h). They advise disinfection of impressions in the recommended period of time that is necessary for disinfection of elastomers.

Since dimensional stability and accuracy of impression materials after removal from the mouth and disinfection are important factors in obtaining an accurate final restoration, the aim of this study was to assess the deformation of elastomeric materials after disinfection in antimicrobial solutions.

In this study it was assumed that impression disinfectants significantly affect the dimensional stability of these impressions.

Methods

This research was carried out *in vitro* in the Laboratory for Condensed Matter Physics, Faculty of Physics, University of Belgrade and in the Dental Laboratory, Clinic of Prosthodontics, Faculty of Dental Medicine, University of Belgrade.

For the purpose of this study individual custom resin trays [12] were designed (L-Palavit acrylic resin, Galenika, Serbia) for making impressions of teeth preparations on the model of epoxy resin. A model was obtained by duplicating the Kavo (Germany) master model of the upper arch representing three full metal-ceramic crown preparations (central incisor, first premolar and first molar). The tray was lined by an uniform thickness of wax spacer in order to mantain the uniform thickness of impression material. For adequate retention of the impression material the appropriate adhesive was applied to the tray (universal tray adhesive for impression silicones – Zhermack, Italy; universal adhesive for silicone impression materials – Heraeus Kulzer, Germany) according to the manufacturer's directions and allowed to air dry for 15 min in order to achieve maximum bond strength. A total of 120 impressions were obtained from the model of epoxy resin (40 impressions per each parameter, 10 impressions per each impression material). Four impression materials were used: two C-silicones (Oranwash L – Zhermack + Indurent-gel catalyst for C-silicone – Zhermack and Xantopren L Blue – Heraeus Kulzer + Activator universal – Heraeus Kulzer) and two A-silicones (Elite H-D + regular body – Zhermack and Flexitime correct flow – Heraeus Kulzer). All impression materials were mixed and used according to the manufacturer's instructions. The whole equipment and materials used in this study were kept at room temperature ($23 \pm 2^{\circ}C$) and relative humidity of $50 \pm 10\%$ before being used [13].

The effect of each disinfectant (glutaraldehyde, benzalkonium chloride – Sterigum and 5.25% NaOCl) was examined on 40 samples made of these impression materials. The

control group included 40 samples not treated with disinfectant solution.

According to the ISO 4823 [13] recommendations, the models were pre-heated in a water bath at 35 ± 1ºC.

The appropriate impression material was mixed and manipulated according to the manufacturer's instructions at room temperature, 23 ± 2ºC, and with a custom tray placed on a master model within the working time recommended by the manufacturer. The finger pressure was done over the tray until the stopers reached the teeth on the model. The model with the tray and impression material was placed in a special container and transfered to the water bath to maintain the temperature of 35 ± 1ºC, simulating open oral cavity temperature [14]. After 10 min from starting to mix, the tray with impression material was moved from the model.

The disinfectants used according to the manufacturer's directions, were: 5.25% NaOCl and disinfectant and detergent on the base of glutaraldehyde and benzalkonium chloride (Sterigum – Zhermack, Italy) that is virocidal [human immunodeficiency virus (HIV), HBV, hepatitis C virus (HCV)], bactericidal, fungicidal and tuberculocidal. Sterigum contains disinfectant glutaraldehyde 0.50 g / benzalkonium chloride 0.50 g in 100 g, and solvent (purified water to 100 g).

After removal from the model the impressions were immediately immersed in a container with the appropriate disinfectant for 10 min. Following disinfection, impressions were removed from the container, thoroughly rinsed under running water and air dried.

The whole measurement procedure was performed with a Canon G9 (12 megapixels, 2 fps, 6x/24x), and automated with a computer Asus Lamborghini VX-2R Intel C2D 2.4 GHz, by using software package Remote Capture. With the usage of the adapter – tube (Canon) and close up lenses (up to 10D, Hama), applied to the Canon G9 camera, highly reproducible macro photographies of the surface of impression material were obtained (Figure 1).

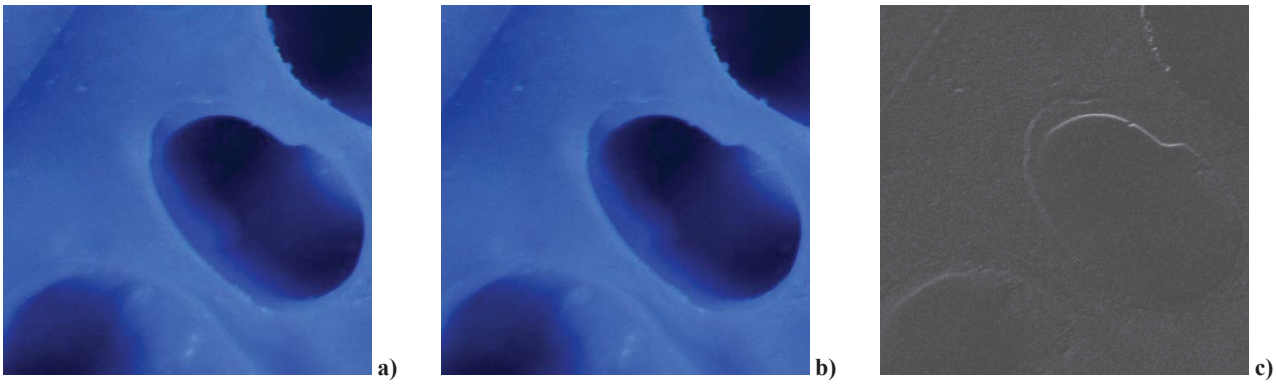
In our study the exact position of the camera to the sample was secured in two ways – experimentally and by using software. Experimentally, the camera was positioned by using laboratory cathetometers, which are commonly used in physical measurements. This means that at any time, the distance and orientation of the camera and the sample were

Fig. 1 – Measurement – taking photos after impressions disinfection.

determined with the limit of estimated error of 0.1 mm. The distance from the camera to the sample, in the macro mode, was more than 100 mm by using close-up lens, and therefore the relative error of distance was 0.1%. Additionally, camera was used in the manual focus mode, by using fixed focal lengths. Canon allows setting the focal length of lens at several fixed values, whose reproducibility are extremely accurate. In our software, the image analysis was performed after geometric transformation of recorded samples which is in accordance with predefined movements of the marked positions. This transformation is also used in geodesy for obtained photos processing in post-production of aero-photo images into ortho-photo.

Identical impressions consecutive measurements were realized, and time-depending series of images of the same impression were initially received. Measurements serials were divided in subgroups of 60 shots in 30 min and were repeated several times during the day, after 24 h and after 7 days at the temperature of 23ºC. Measurements were realized within 10 min of the disinfectant treatment, within 30 min after removal of the impressions from the disinfectant, and later within 30 min after 1h, 24 h and 7 days.

The measures of dissimilarities of identical images in comparison to their modified forms with statistically distributed single pixel noise were obtained by the initial calibration procedure. This procedure allowed determination of the mean values of dissimilarities which were taken as a nominal shift in producing a pixel in a given series of images (Figure 2).



a) b) c)

Fig. 2 – The same cut of the two photographies of an elastomeric impression: a) immediately after the removal, b) 30 min after the removal, and c) the differences.

The methods based on spectral Fourier analysis and approximations in the form of efficient fast fourier transform (FFT) solutions enable obtaining of the spectra of vectors and matrices of red, green and blue (RGB) values for each pixel, which are assigned values in each field. The identical numerical procedure determines the measure of dissimilarities of images whether in the native form or its FFT spectrum [15–19] (Figure 3).

The dimensional changes of the control samples, which were not exposed to disinfection treatment, were measured in function of time at the temperature of 23 ºC. Their mean accumulated values of dimensional changes were 0.178% after 30 min, 0.198% after 1 h, 0.440% after 1 day and 0.548% after 7 days.

In the first 30 minutes of measurements the mean accumulated value of dimensional changes for all samples after

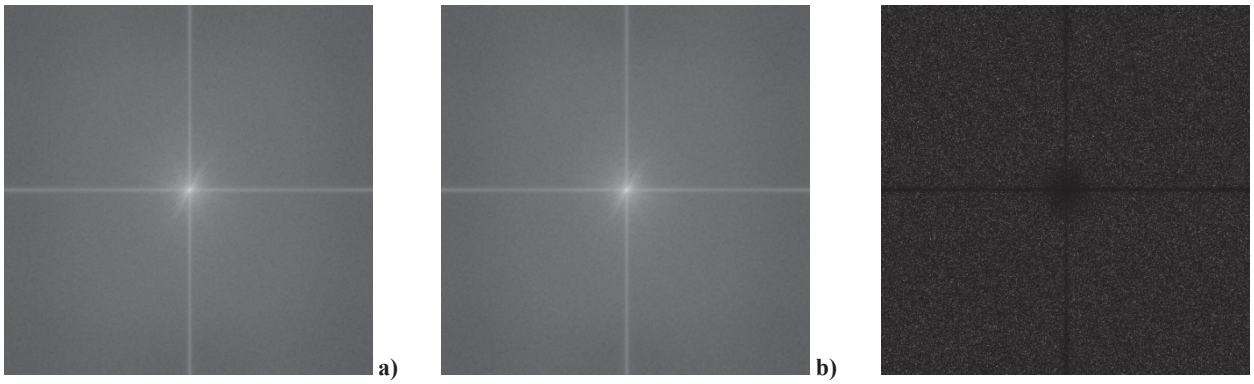


Fig. 3 – Fast Fourier transform power spectra of identical cut of the two photographies of an elastomeric impression: a) immediately after the removal, b) 30 min after the removal, and c) the differences.

For the purpose of calibration study we developed software for calibration of measurements by using dissimilarity analysis.

Comparison of variables was performed by the Student's *t*-test and analysis of variance by ANOVA test.

A statistically significant difference between the groups or correlations of values of different parameters was accepted in accordance with the significance level criteria, $p < 0.1$.

Results

Table 1 shows the accumulated values of dimensional changes for the control samples and for the samples after disinfection in 5.25% NaOCl and Sterigum by the time of sample evolution in the first: 30 min, 1 h, 24 h, and 7 days.

disinfection in 5.25% NaOCl was 0.220%, and for those disinfected in Sterigum 0.140%.

Within 1 hour mean accumulated value of dimensional changes of the impressions after disinfection in 5.25% NaOCl was 0.613% and for those disinfected in Sterigum 0.373%.

After 1 day evolution of all the samples treated with 5.25% NaOCl was 1.053%, and after disinfection in Sterigum 0.598%.

After 7 days the mean accumulated value of dimensional changes of the samples treated with 5.25% NaOCl was 1.505%, and for the impressions disinfected in Sterigum 0.988%.

The dimensional changes of all the samples were significant both as the function of time and the applied disinfectant (Figure 4).

Table 1

Relative dimensional changes of the tested materials as the function of the applied disinfectant and the time from the moment of impressions removal

Material	Relative dimensional changes of elastomers – silicones (%) – estimated error limits = 0.025%											
	30 min			1 h			24 h			7 days		
	Control	NaOCl	Sterigum	Control	NaOCl	Sterigum	Control	NaOCl	Sterigum	Control	NaOCl	Sterigum
1 CS	0.19	0.23	0.14	0.21	0.65	0.44	0.49	1.22	0.65	0.58	1.89	1.11
2 CS	0.19	0.28	0.20	0.20	0.70	0.42	0.47	1.18	0.67	0.58	1.70	1.21
3 AS	0.16	0.20	0.12	0.19	0.55	0.33	0.40	0.93	0.58	0.52	1.20	0.85
4 AS	0.17	0.17	0.10	0.19	0.55	0.30	0.40	0.88	0.49	0.51	1.23	0.78
Statistics												
$\bar{x}$	0.178	0.220	0.140	0.198	0.613	0.373	0.440	1.053	0.598	0.548	1.505	0.988
p	0.073	0.068	0.065	0.066	0.070	0.067	0.060	0.047	0.083	0.043	0.040	0.040
Test value (F)	2.38	2.42	2.55	2.45	2.41	2.42	2.72	2.85	2.25	2.95	3.07	3.12

NaOCl – 5.25% sodium hypochlorite; Sterigum – disinfectant glutaraldehyde and benzalkonium chloride (Zhermack); 1CS – condensation silicone Oranwash L (Zhermack); 2CS – condensation silicone Xantopren L Blue (Heraeus Kulzer); 3AS – addition silicone Elite H-D+ regular body (Zhermack); 4AS – addition silicone Flexitime correct flow (Heraeus Kulzer); $\bar{x}$ – the average values of the obtained mean values of samples dimensional changes.
***p* – the level of significance of the applied test hypotheses compared to the grouped samples for the same applied disinfectant and the same time; test value – F-value one way ANOVA.**

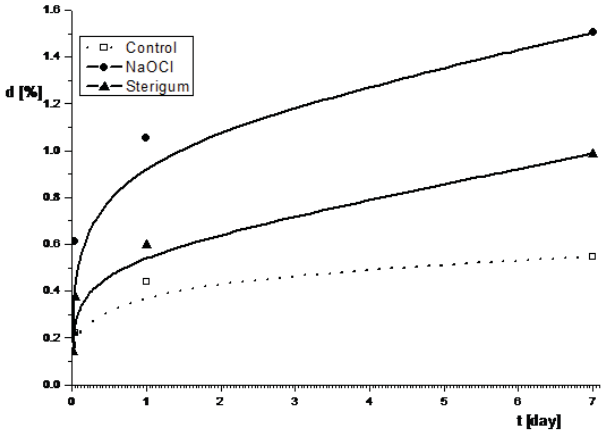


Fig. 4 – Average relative dimensional changes of all the samples as a function of time and the applied disinfectant.

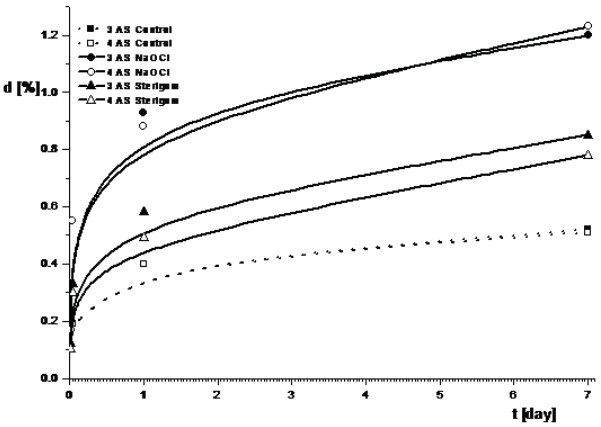


Fig. 6 – Average relative dimensional changes of addition silicones as a function of time and the applied disinfectant.

Statistical parameters which complement the above statement (Figure 4) are based on hypotheses about the presence of significant differences in the grouped results of the obtained dimensional changes of the tested impression materials without disinfecting treatment (control) as the function of time (p = 0.021, F = 42.1), then of the tested impression materials disinfected in 5.25% NaOCl as the function of time (p = 0.036, F = 393.2) and of those after the treatment in Sterigum as the function of time (p = 0.090, F = 35.1).

The values of statistical significances and associated F-values depending on the applied disinfectant for the same disinfecting treatment time intervals for different samples were p = 0.072, F = 2.44, (Figure 4).

Figures 5 and 6 show the differences in dimensional changes of condensation silicones compared to the addition silicones for the same time and the same applied disinfectant.

Statistical parameters that complement the above statement are based on the test of hypotheses about the existence of significant differences of the obtained dimensional changes between the group of condensation silicones and the group of addition silicones for the same time, and the same applied disinfectant (p = 0.026, F = 3.95) (Figures 5 and 6).

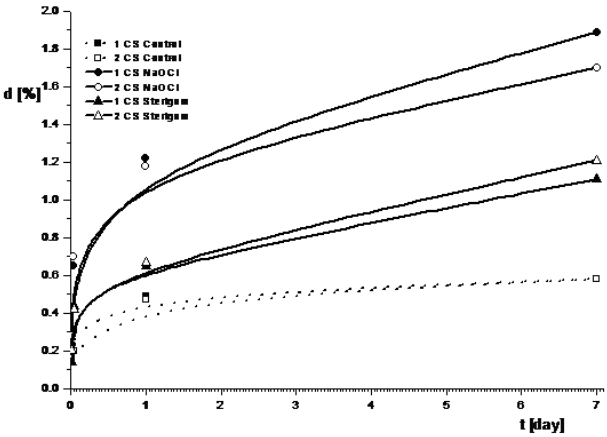


Fig. 5 – Average relative dimensional changes of condensation silicones as a function of time and the applied disinfectant.

Discussion

In numerous studies on impression materials tested for their dimensional stability depending on various factors, many different methods were used. In a certain number of studies dimensional stability of elastomeric impression materials was tested according to ISO 4823 (which corresponds to ADA Spec. No 19) and consisted of measuring the profiled grooves on elastomeric impressions made of the machined cylindrical mold, using a measuring microscope with the accuracy of 0.005 mm [13, 20].

The accuracy of that method dependes on the skill of the operator who carries out such measurements and on a translation screw of the microscope. Another drawback is that the tested elastomeric samples do not represent clinically relevant form. This means that in impression making and their removal, deformations of elastomers are not the same as in real impressions in clinical practice. A third limitation is that the prescribed measurements were recorded on a flat surface, disregarding the possibility of dimensional changes in three dimensions. Some studies have used this method [4, 21, 22], while the other authors [23–25] have introduced different modifications.

Modified techniques did not offer any significant advantages as they require fabrication of a test block out of an impression, introducing errors related to dimensional changes that could occur in the cast and measurements still depend on the microscope and micrometer.

Stober et al. [5] made impressions on the modified typodont master model containing simulated stainless steel crown preparations and measured the distance between the referent points on the master model and the gypsum cast obtained from elastomeric impressions of a master model after they had been disinfected. Dimensional changes of these materials were expressed in three dimensions. Their technique also required fabrication of a gypsum die from an impression and measurements were performed using a microscope.

Thouati et al. [26], for example, used a test block specimens as described in Normes Françaises specification which is in compliance with ADA Spec. No. 19 and ISO 4823.

Each test specimen was immersed in a disinfectant solution, rinsed in running water and the die stone was casted. The measurements of the referent lines were carried out on impression plaster reproduction in order to assess the dimensional stability of elastomeric impression materials.

In a 1983, Clancy et al. [27] examined the dimensional stability of three elastomers as the function of time using specimens from the stainless steel test block and a mold recommended by ADA spec. No.19 (ISO 4823). Impressions were placed under the reflecting microscope and the images were projected on the screen of the image analyzing computer. Measurements were performed on the referent lines on the specimens.

In one of the referent studies specimens were measured using the two methods, one using micrometers, and the other using a scanning laser digitizer with an automatic data processing in order to evaluate the dimensional stability and accuracy of impression materials. Measurements were performed on the casts made from the impressions. The study found that more precise measurements were achieved by using a scanning laser [28].

DeLong et al. [29] in 2001 examined the factors influencing optical 3D scanning of polyvinyl siloxane impression materials. They pointed the importance of the surface angle of digitizing and surface texture of these materials.

The inability to scan impressions due to the difference in reflectivity of these impression materials has led to the need to use the replication technique, stone casting. Assessment of dimensional stability was based on the analysis of the images of the scanned stone casts. Except for these disadvantages that have to be overcome by the appropriate adjustments to the scanner, it should be noted that this method is very expensive [30].

In the present study an epoxy resin master model was used that resembled the upper arch containing three teeth preparations for complete metal-ceramic crowns. Measurements were performed directly on the elastomeric impressions, without the need to use the replication technique (stone casting).

According to the authors' knowledge, none of the studies has used this method for analysis of digital images of elastomeric impressions of the complete dental arch in order to evaluate the dimensional stability of impression materials, depending on various factors. The method was developped at the Faculty of Physics, University of Belgrade, as a fully original method for investigation the evolution of polimers. Up to this study, this method has not been used in the field of dentistry.

The advantages of the methods applied in the present study compared to other methods described in a number of references, are based on the use of the originally two-dimensional analysis of changes in the whole visual field and on the three-dimensional analysis that was obtained by fine analysis of colors and tones in the shadow areas.

Another advantage comes from measuring at numerous points. The accuracy of the obtained values of dimensional changes was increased due to high reproducibility and mutual comparison of all images.

The disadvantage of the methods applied in this study was that it could not be clearly detected whether contraction or expansion of the tested materials occured, although detection of dimensional changes was precise.

Another problem is that in terms of surface reactions or in the conditions in which the specimen changes color during maturation, this method shows slightly higher values of dimensional changes than those stated by other authors [21, 31]. However, even with such lacks of the used methods, the results are in accordance with the ISO standardization.

There are many factors that affect the dimensional stability of elastomeric impression materials. Among them are contraction during polymerization as a result of volume reduction due to the cross linking and alcohol evaporation, which is typical for C-silicones. Another factor that may change the dimensional stability of elastomers is expansion that may occure after immersion in disinfectant solutions. The incomplete elastic recovery of these materials may also lead to dimensional changes.

Elastomeric impression materials dimensional changes after immersion in various disinfecting solutions are complex and relate to their individual chemical composition. Although the major ingredients of each material are known, the specific amount of these components is the secret of each manufacturer. Certain ingredients, may be present in ample quantity or may be absent. Therefore, the behavior of a certain material is difficult to relate to its chemical composition [23].

Some publications on the effect of disinfectants on the dimensional stability of elastomers state that the disinfecting process does not have an adverse effect on the dimensional stability of impressions [24, 32–35]. Others, however, point to the negative effect of disinfecting agents on elastomers [6, 26, 35].

Dimensional changes of impression materials occur in three dimensions. The methods depending on measuring microscope are one dimensional and neglect dimensional changes that exist in all three dimensions [21, 26, 27]. The studies of Saleh Saber et al. [23] and Kronström et al. [24] illustrate the reference points and distances for measurements of three-dimensional objects which confirm the existence of three-dimensional changes, that is in accordance with the results of the present study.

The results of Jagger et al. [36] demonstrate that even though the dimensional changes of addition silicones after disinfection are small, in the order of microns, they may be of clinical significance for further procedures.

Evaluating the influence of immersion period in disinfectant solutions on dimensional change of elastomers, Carvalhal et al. [22] note that there are time limits within disinfection which must be performed, because of the reactivity of disinfecting agents. They also emphasize that in shorter immersion periods, sodium hypochlorite solution lead to greater dimensional change of condensation silicone (Xantopren) compared with glutaraldehyde, which is in accordance with the results of the present study.

Thouati et al. [26], in assessing the dimensional stability of addition and condensation silicones after disinfection in

5.25% NaOCl for 30 min, point out the changes up to 0.46%, which corresponds to the values obtained in this study for the same disinfectant. This disinfectant has affordable price, but is unstable over time and has to be made fresh daily to ensure the necessary efficiency. The authors underline that chlorine is a highly reactive element and in the concentration of 5.25% could react and fix on the impression material. When condensation silicones are used, these authors suggest that impressions should be poured as soon as possible. This is in agreement with the results of Saleh Saber et al. [23].

The beginning of disinfecting treatment strongly affects the stability of impression materials and critical changes occur in the first few minutes. In fact, the half of all the changes occures in the first 4 min. These results agree with the results of Melilli et al. [21]. Their findings suggest that immediate disinfection by immersion always induces a significant expansion of the impression material, while the second disinfection, repeated 6 h after the first one, does not cause any significant dimensional change, probably due to chemical stabilization of the material that occurs in the first hours after the impression taking.

The mean value of accumulated dimensional changes obtained in this study for A-silicones after disinfection in glutaraldehyde is in accordance with the results of Wadhwani et al. [37] and amounted to 0.10–0.12% for a 30-minute period, and after one hour the change was 0.30–0.33%.

In the present research, the values obtained within 30 min of disinfection of addition silicones in glutaraldehyde (0.12%) correspond to the results of Melilli et al. [21]. They show that immediately after immersion of addition silicone specimens in glutaraldehyde for 5 min, dimensional changes of A-silicones are significant (0.13%), compared to the initial measurement prior to disinfection.

For glutaraldehyde (Sterigum) the change, accumulated after a day for all the specimens in the present study was 0.598%. Therefore, pouring casts from impressions may be postponed for a day.

Generally, A-silicones in the current study were more stable than C-silicones. However, the two tested materials Xantopren L Blue (Heraeus Kulzer C-silicone) and Flexitime correct Flow (Heraeus Kulzer A-silicone) showed better stability than the other two tested materials.

Some of chemical immersion disinfectants in higher concentrations could cause the adverse surface changes of an impression material [38]. This should not be neglected in evaluation impression material dimensional stability. The photometric method is so precise to detect the discoloration caused by that minor surface changes, as well as the significant dimensional changes of the impression material.

Conclusion

According to the results of this research we can conclude that, generally, A-silicones are more stable than the C-silicones for the same time and the same applied disinfectant. The greatest dimensional changes of both addition and condensation silicone impressions are reported in the first hour after their separation from the model. The beginning of activity of disinfectants strongly influences the stability of these impression materials and critical changes occur in the first few minutes. Disinfection of addition and condensation silicone impressions with 5.25% NaOCl leads to great dimensional changes. In the mandatory disinfection of the addition and condensation silicone impressions the usage of NaOCl of the concentration of 5.25% should be avoided. Condensation silicones exposed to 5.25% NaOCl after the second day show dimensional changes more than 1%. Addition silicones are stable, with the dimensional changes less than 1%. The use of disinfectants that contain benzalkonium chloride and glutaraldehyde (Sterigum) does not significantly change dimensional stability of the tested elastomeric materials.

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Physiological tolerance to uncompensated heat stress in soldiers: effects of various types of body cooling systems

Uticaj sistema za hlađenje tela na toleranciju nekompenzovanog toplotnog stresa kod vojnika u uslovima nošenja nepropusne zaštitne odeće

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Abstract

Background/Aim. In military services, emergency situations when soldiers are exposed to a combination of nuclear, biological and chemical (NBC) contamination combined with heat stress, are frequent and complex. In these specific conditions, usage of personal body cooling systems may be effective in reducing heat stress. The present study was conducted in order to evaluate the efficiency of four various types of contemporary personal body cooling systems based on the "Phase Change Material" (PCM), and its effects on soldiers' subjective comfort and physiological performance during exertional heat stress in hot environments. **Methods.** Ten male soldiers were voluntarily subjected to exertional heat stress tests (EHSTs) consisted of walking on a treadmill (5.5 km/h) in hot conditions (40ºC) in climatic chamber, wearing NBC isolating impermeable protective suits. One of the tests was performed without any additional cooling solution (NOCOOL), and four tests were performed while using different types of cooling systems: three in a form of vests and one as underwear. Physiological strain was determined by the mean skin temperature (Tsk), tympanic temperature (Tty), and heart rate values (HR), while sweat rates (SwR) indicated changes in hydration status. **Results**. In all the cases EHST induced physiological response manifested through increasing Tty, HR and SwR. Compared to NOCOOL tests, when using cooling vests, Tty and Tsk were significantly lower (on 35th min, for 0.44 ± 0.03 and 0.49 ± 0.05ºC, respectively; $p < 0.05$), as well as the average SwR (0.17 ± 0.03 L/m²/h). When using underwear, the values of given parameters were not significantly different compared to NOCOOL tests. **Conclusions**. Using a body cooling system based on PCM in the form of vest under NBC protective clothes during physical activity in hot conditions, reduces sweating and alleviates heat stress manifested by increased core and skin temperatures and heart rate values. These effects directly improve heat tolerance, hydration state, decrease in the risk of heat illness, and extends the duration of soldiers' exposure to extreme conditions.

Key words:
heat stress disorders; protective clothing; physical exertion, military personnel.

Apstrakt

Uvod/Cilj. Izloženost vojnika toplotnom stresu pri vanrednim situacijama gde postoji kombinacija nuklearne, biološke ili hemijske (NBH) kontaminacije i visoke spoljašnje temperature, uz nošenje nepropusnog zaštitnog odela, predstavlja veoma složen problem. U takvim situacijama, primena individualnih sistema za hlađenje tela može biti efikasna za smanjenju toplotnog stresa korisnika. Ovaj rad iznosi rezultate istraživanja na polju efikasnosti nekoliko savremenih tipova sistema za hlađenje tela izrađenih na bazi „materijala koji menjaju fazno stanje" i njihovog uticaja na fiziološku podobnost u uslovima izloženosti fizičkom naporu i ekstremno visokim temperaturama. **Metode.** Deset vojnika muškog pola, odevenih u NBH zaštitnu odeću izolujućeg tipa od nepropusnog materijala, izlagano je visokoj temperaturi (40ºC) uz istovremeni fizički napor submaksimalnog intenziteta (hodanje na pokretnoj traci, brzinom od 5.5 km/h). Jedan test je izveden bez ikakvog rashladnog sistema (NOCOOL), a naredna četiri uz upotrebu tri tipa rashladnih prsluka i jednog rashladnog pododela. Intenzitet fiziološkog opterećenja određivan je preko sledećih pokazatelja: srednje temperature kože (Tsk), timpanične temperature (Tty) i frekvencije srčanog rada (HR), dok je vodeno-elektrolitski status određivan preko intenziteta znojenja (SwR). **Rezultati.** U svim slučajevima fizički napor u toploj sredini izazvao je fiziološki odgovor manifestovan kroz povećanje Tty, HR i SwR. U varijantama primene tri tipa rashladnih prsluka

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izmerene su značajno niže vrednosti Tty, Tsk i SwR u odnosu na NOCOOL varijantu. Vrednosti prilikom nošenja pododela nisu se statistički značajno razlikovale u odnosu na NOCOOL varijantu. **Zaključak.** Primena ispitivanih sistema za hlađenje tela na bazi PCM, u formi prsluka koji se nose ispod nepropusne NBH zaštitne odeće, ublažava povišenje unutrašnje temperature tela i srednje temperature kože, a takođe ublažava povećanje frekvencije srčanog rada i znojenje, čime se poboljšava fiziološka podobnost zaštitne odeće, umanjuje rizik od toplotnog stresa i istovremeno produžava vreme boravka i rada vojnika u ekstremnim temperaturnim uslovima.

Ključne reči:
stres, toplotni, poremećaji; odeća, zaštitna; fizički napor; kadar, vojni.

Introduction

Accumulation of heat, reflecting peripheral and internal body temperatures, occurs during heavy physical exertion or exposure to warm and human environment. Long-term accumulation of heat in a quantity of about 0.5 W/kg during 2 h leads to increase in body temperature that some people cannot tolerate. Heat stress can occur in compensated and uncompensated forms. The ability to compensate heat load is primarily determined by biophysical factors (environmental conditions, clothing, the intensity of physical exertion), but also moderately under influence of biological factors such as acclimatization to heat and hydration status [1].

Physiological thermoregulation involves activation of mechanisms for disclosure of excessive heat and increase blood flow through the skin, which is achieved by enhancing stroke volume and heart rate and simultaneous increasing of sweating [2]. During physical activity in hot conditions, sweating rate up to 1–1.5 L/h is not unusual, and may even reach 2 L/h under extreme efforts, providing a potential loss of excess heat by evaporation in the amount of 4500 kJ (14 W/kg, or 1 kW for a person weighted 70 kg). In the absence of proper rehydration, this process leads to the loss of body fluids from all body compartments. In prolonged periods of exposure to hot environment, the major heat dissipation mechanism is sweat evaporation, which is proportional to the effective (exposed) skin area, water vapour pressure gradient between the skin and the environment, and water vapour permeability of clothing. Hence, when protective military clothing is worn, sweat evaporation rates decrease and heat dissipation is reduced [3, 4]. The efficiency of physiological adaptation depends on the heat amount generated in active muscles, the intensity of the workload as well as the level of biophysical heat exchange with environment [5]. Extreme situations involving NBC contamination represent a considerable problem, due to the need for specific protection of engaged personnel. Very often, execution of various operations in contaminated area, such as determination of hazard type, detection, identification, rescue missions or decontamination, request engagement of personnel wearing protective equipment of different level. In practice, it is often necessary to achieve full NBC protection, covering the whole body and respiratory system. Specialized liquid-proof, contamination-resistant clothing covers most of the body's surface area [6]. As a result, the pathways for sweat evaporation and heat exchange by radiation and convection are disrupted, particularly in the torso area, with a number of layers providing insulation between the body and environment.

Considering these facts, various body cooling systems have been developed, with the main purpose to increase comfort, as well as to reduce thermal stress. In military services, the additional benefit is increased mission duration, decreased hydration needs, improved mental acuity and physical performance maintenance. Many systems are developed, yet they generally may be classified in five basic groups: evaporative cooling products, products based on phase change materials (PCM), compressed air systems, liquid circulation systems and thermoelectric systems [7].

The aim of this study was to investigate the efficiency of cooling vest type system based on PCM. PCM is a substance with a high heat of fusion which, melting and solidifying at a certain temperature, is capable of storing and releasing large amounts of energy. Heat is absorbed or released when the material changes from solid to liquid and *vice versa*; thus, PCM are classified as latent heat storage units [8].

This study investigated the efficiency of various types of body cooling systems in simulated conditions, similar to possible real extreme situations, using exertional heat stress test protocols previously developed in our laboratory [9, 10]. The main goal was to test the effects of cooling vests worn under NBC protective suit on subjective comfort and physiological strain during physical effort in hot environment. We hypothesized that cooling systems would alleviate soldiers physiological strain and extend previously limited duration of work while wearing isolating protective equipments in extremely hot conditions. It is reasonably assumed that it could increase the ability of military personnel to successfully complete any mission in conditions of possible chemical, biological, or nuclear threat.

Methods

The participants of this study were 10 male professional soldiers aged 25.8 ± 2.4 years, with similar anthropometric and ergometric characteristics. The subjects were briefed on the nature of the experiment, its purpose, conditions, safety measures, and potential risks. Each participant read and signed an informed consent form, in accordance to the standards of medical safety during examination in extreme hot or cold environment [11]. The protocol for investigation was approved by competent Ethical Committee. The procedures performed in the present study corresponded to the standards or thermal strain evaluation by physiological measurements [12].

Extertional heat stress tests (EHSTs) were conducted in a climatic chamber in the Military Medical Academy, Bel-

grade, Institute of Hygiene, during May to September 2011. During EHSTs, participants wore individual isolating protective equipment used by specialized NBC military units of the Serbian Armed Forces. The equipment consists of a protective overall (made of polyester textile with both surfaces rubberized with butyl and caoutchouc-based compound), protective mask (model with phonic unit), double-layer gloves (rubber material, inside lined with cotton), and boots. The protective capacity of unused overall against drops of toxic agents is not less than 150 min, while after five alternative contaminations and decontaminations not less than 105 min. The material does not burn out under the effects of thermal impulse of at least 52 J/cm^2, and sustains nuclear explosion of 30 kT for at least 10 s. In contact with drops of burning napalm compound, the overall does not burn out for at least 10 s.

Each of ten subjects performed five EHSTs in full protective equipment, without any cooling system (the NOCOOL) and with various cooling systems worn under the protective garment. Four different types of PCM cooling systems were tested: a model with crystal balls inside the vest which swell into biodegradable viscose get by initial soaking in water (the model A); a model with cooling packs inserted into specially designed pockets inside the vest, with the ability to freeze at 18.3ºC (the model T); a model with "phase core elements", i.e. salt mixture sealed inside an aluminium wrapper, in a form of 22 cartridges installed into special pockets, with activation point at 28ºC (the model S); cooling underwear made of microcapsules from non-toxic paraffin placed in a durable membrane (3.000.000 microcapluses/cm^2), obtained by polymerization of melamine-formaldehyde (the model O).

All EHSTs were performed under the same air temperature (40ºC, relative humidity 30 ± 3%) by walking on a motorized treadmill (speed 5.5 km/h). Skin temperatures (Tsk) were measured continuously using contact probes with transducers TSD202E and TSD202F (precision ± 0.2ºC, range 0–60ºC, response time 0.9 s; BIOPAC Systems Inc. USA). The thermistors were set at 4 locations (neck, right scapula, left hand, and right shin). The mean Tsk was calculated every 5 minutes from the values obtained and weighted [12]. Core (tympanic) temperatures (Tty) were continuously measured using contact probe TSD202A (precision ± 0.1ºC, range 20–50ºC, response time 0.6 s) with transducer introduced into the auditory canal and placed toward the eardrum. The temperatures were registered every 10 sec. All measurements were automatically monitored and recorded in real-time using a physiological data monitoring system (MP150 SKT100C, BIOPAC Systems Inc. USA). Heart rates (HR) were continuously telemetrically monitored (Q4500 Exercise Test Monitor, Quinton instruments, USA), and recorded every 5 min. Sweat loss was calculated as the difference between pre-test and post-test nude body weight. Sweat rates (SwR) were expressed per hour per square meter of body surface (L/m^2/h).

Considering given temperature conditions and physical exertion level, duration of the test was limited to maximally 45 min, while criteria for early termination were: achieving critical value of Tty (39.5ºC), or HR (190 bpm), or subjecting feeling of unbearable strain [13, 14].

The data are presented as mean ± SD. The normal distribution was tested by the Shapiro-Wilk test. The significance of differences between the parameters obtained during tests without cooling systems (the NOCOOL group) and with cooling systems (the A, S, T, and O groups) at the end of EHST was tested by the Student's *t*-test, with significance level $p < 0.05$.

Results

None of the soldiers during or after EHSTs showed any symptom of heat stroke or severe heat exhaustion. Mean test durations without cooling systems and with cooling systems were 35 minutes and 45 minutes, respectively. In the NOCOOL group, 2 soldiers completed the test, in 7 cases the tests were terminated due to subjective intolerable strain, and in 1 case due to reaching Tty limit. Contrary, when cooling systems were used, in 85% of the cases the 45-minutes test was completed, and the Tty barrier was never reached. The average duration of the test when cooling was used was 10 minutes longer compared to that to the NOCOOL condition. The summary of the results for temperatures and heart rates are displayed in Table 1.

Table 1

Comparison of the means for temperatures and heart rates (HR) during exertional heat stress tests (EHST)

Parameters	NOCOOL, 35th min, 40°C	With cooling, 45th min, 40°C			
		A	S	T	O
Tty (°C)	38.88 ± 0.12	38.6 ± 0.18	38.85 ± 0.14	38.97 ± 0.08	38.9 ± 0,09
Tsk (°C)	38.22 ± 0.26	37.9 ± 0.22	38.20 ± 0.14	37.78 ± 0.18	38.37 ± 0,11
HR (bpm)	170 ± 14	162 ± 12	166 ± 15	160 ± 12	173 ± 10

Data given as $\bar{x}$ ± SD; Tty – tympanic temperature; Tsk – skin temperature; NOCOOL – no cooling system; A, S, T, O – models with cooling systems (for details see Methods)

Comparable reviews of Tty values during EHST are displayed in Figure 1. The mean Tty in the NOCOOL increased from 36.30 ± 0.15ºC at the start to 38.88 ± 0.12ºC at the end of test (35th minute). With cooling systems, after 10th min Tty began to grow slower. Compared to the NOCOOL, in 35th min the mean Tty was lower for 0.59 ± 0.04ºC (model A), 0.35 ± 0.03ºC (S), and 0.38 ± 0.02ºC (T). During entire duration of EHST, the mean values of Tty did not differ between the NOCOOL and the O group; $p > 0.05$.

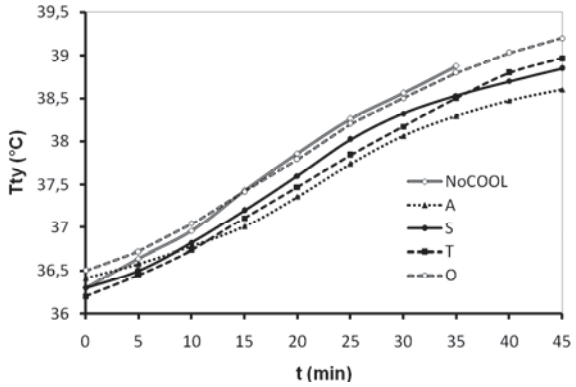

Fig. 1 – The mean tympanic temperatures (Tty) during exertional heat stress tests (EHSTs).

NOCOOL – no cooling system; A, S, T, O – models with cooling systems (for details see Methods).

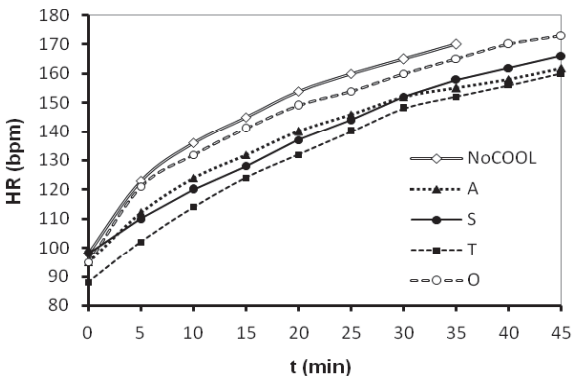

Fig. 3 – The mean heart rates (HR) during the exertional heat stress tests (EHSTs).

NOCOOL – no cooling system; A, S, T, O – models with cooling systems (for details see Methods).

Comparable reviews of Tsk values during EHST are displayed in Figure 2. Body skin temperatures increased in a similar pattern in all the groups, rapidly during the first 15 min (until sweating occurred), and then slowed towards the end of the test. When cooling systems were used, the mean Tsk values were significantly lower. The lowest values were recorded in the T group, with a significant difference as compared to both the S and the O groups (on 35th min: 37.45 ± 0.15ºC (T) *vs* 38.07 ± 0.12ºC (S); and 38.04 ± 0.09ºC (O); $p < 0.05$). At the end of EHST, mean Tsk in the NOCOOL group (35th min) was 38.22 ± 0.26ºC, and with cooling systems mean Tsk values at the end (45th min) were: 37.9 ± 0.22ºC (A), 38.2 ± 0.14ºC (S), 37.78 ± 0.18ºC (T), and 38.37 ± 0.11ºC (O), $p < 0.05$).

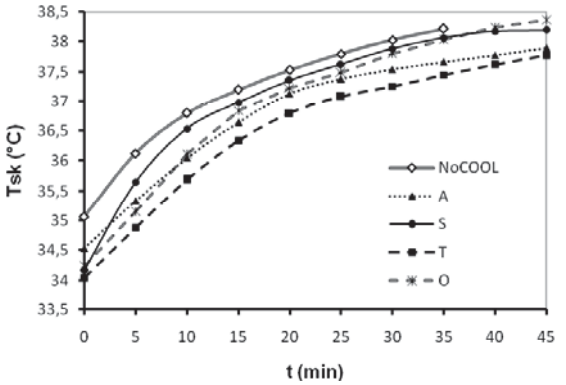

Fig. 2 – The mean skin temperatures (Tsk) during the exertional heat stress tests (EHSTs).

NOCOOL – no cooling system; A, S, T, O – models with cooling systems (for details see Methods).

The dynamics of the average heart rate values are displayed in Figure 3. During entire tests, there were no significant differences in HR values between the groups. Heart rates increased in similar manner in all the groups constantly toward the end of the tests, but the limit of 190 bpm was not reached during any single EHST. Maximum recorded HRs in subjects without cooling and with cooling systems were 179 and 166 bpm, respectively.

In order to minimize the differences regarding EHST durations, SwR was expressed per hour. The average rate of sweating, as expected, was the highest in the NOCOOL group (0.68 ± 0.04 L/m^2/h). In the O group, the mean SwR was similar to the NOCOOL group (0.65 ± 0.08 L/m^2/h). In the other three groups, the recorded values were similar with each other, and significantly lower compared to the NOCOOL and the O groups: 0.52 ± 0.12 L/m^2/h (A), 0.54 ± 0.08 L/m^2/h (S), 0.48 ± 0.14 L/m^2/h (T), $p < 0.01$ (Figure 4).

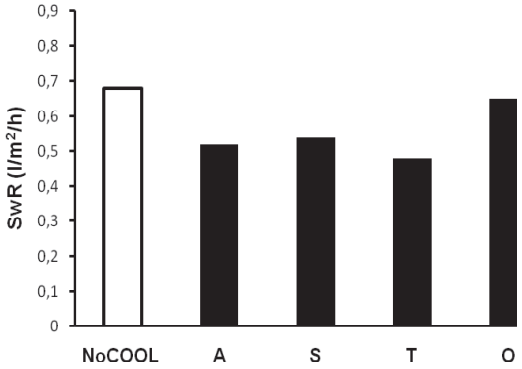

Fig. 4 – The mean sweat rates (SWR) during the exertional heat stress tests (EHSTs).

NOCOOL – no cooling system; A, S, T, O – models with cooling systems (for details see Methods).

Discussion

Impaired physical, cognitive, and working abilities is a well-known consequence of heat strain[9]. This is particularly important for military services. Core temperature (Tc) is considered as a relevant indicator of thermal strain [2], and tympanic thermometry is reliable method for monitoring changes in core temperature during physical activity [15]. While carrying our specific military tasks and missions, military training guidelines tolerate high level of body core temperature, even up to 40ºC [16]. Sawka et al. [17] reported similar Tc (39.4ºC) at exhaustion. Study of Nag et al. [14] with 11 male volunteers who did ergometric work at an intensity of 60% VO_{2max} suggests the tolerable limit of short duration

human exposure in heat (40–45 min) is at Tc 39ºC. Considering the fact that these values of Tc are possible and common during NBC missions, they deserve to be investigated.

In our study a very small number of subjects even without cooling systems, terminated test before 45th min. This relatively good tolerance to heat may be attributed to high fitness level, considering their regular engagement in strenuous physical activity related to professional services. Fit individuals can tolerate higher values of Tc during heat stress before exhaustion (as much as 0.9ºC) compared to unfit and untrained [18].

Protective clothing worn by the participants was made of butyl rubber – a waterproof material, isolated type, which prevents disclosure of excessive heat through evaporation of sweat. Cooling vests covering only the torso area (A, S, and T) showed better results than O underwear. This is confirmed also by the soldiers subjective feeling, because from the total number of subjects who interrupted EHST, 72% were dressed in O. This is in agreement with the results reported by Montain et al. [5]. In their study seven acclimatized men attempted treadmill walks at 43ºC wearing full of partial protective clothing. The authors determined that partial encapsulation results in physiological tolerance similar to that reported for unclothed persons. In situations when full encapsulation in protective clothing is necessary, cooling systems that enable heat dissipation from part of the body surface may be effective solution. Since the torso area has the greatest capacity for heat dissipation (both by evaporative cooling and heat conduction) of all the body surfaces, cooling strategies that put emphasis on the torso area promise the best results.

As the greatest benefit of all cooling systems the subjects cited easier breathing and less strain compared to tests without cooling. Alleviation of physical exertion is a result of less cardiovascular strain, as a consequence of slower increase of Tty. This was reflected on lower values of heart rates while using cooling systems; mean HRs on 35th min in these groups were lower by 15 bpm (A), 12 bpm (S), and 18 bpm (T) compared to the NOCOOL group. The limit of 190 bpm was not reached during any single EHST. Maximum recorded HRs in the subjects without cooling and with cooling systems were 179 and 166 bpm, respectively. In despite of increased cardiovascular strain, the subjects maintained the given level of physical activity during the EHST. These results are in agreement with the suggestion of Ftaiti et al. [19] who reported that, in trained subjects, exercise-induced hyperthermia had only minor effects on the neuromuscular performance. In their study, six trained males ran on a treadmill at 65% of their VO_{2max} while wearing impermeable suit. After 40 minutes, their physiological status was close to exhaustion, with average HR of 196 ± 8 bpm and Tty 40 ± 0.3ºC, however, they managed to maintain the given intensity of physical work.

Evaporation of sweat as a mechanism for dissipation of excess heat has a special importance in heat stress caused by physical activity, when it occurs not only as a consequence of thermal factors (increasing of Tc and Tsk), but also non-thermal factors such as central activation, activation of muscle-mechanoreceptors metabolism and activation of baroreflex due to physical activity. According to our test results, the rate of sweating is lower when using body cooling systems average for 0.13 L/m^2/h (25%). This represents a significant percentage considering the impermeable material that behaves as heat transfer barrier. Our results indicate that the usage of cooling vests can spare a quarter of total sweat loss, which can contribute to prevention of dehydration during military missions while wearing NBC clothing.

Our results have confirmed that the cooling system based on PCM in the form of vest covering the torso show effectiveness in combination with protective clothing isolating type, while cooling underwear practically does not give significant results. According to our experience, cooling underwear tends to become soaked with sweat during testing. On one hand, wet underwear impairs evaporation of sweat, and on the other hand, it adds some weight and compromises body movements. Both facts mentioned above influence the thermal comfort of our subjects, making this variant of cooling less effective in given conditions.

Our results are consistent with the study of Hadid et al. [4] who carried out investigation on effects of the cooling system based on air circulation on thermal stress caused by physical effort in soldiers. In their study, done by the similar methodology, the ballistic vests were used instead of protective clothing, while cooling was provided by using personal ambient ventilation system (blowing air from the environment using two small fans with batteries, with total supply of approximately 180 L/min of air). Twelve male volunteers were exposed to climatic conditions of 40ºC/ 40% relative humidity, and 35ºC/ 60% relative humidity, during two cycles of exercise/rest periods (total exercise time 100 min, total exposure with rest 180 min), while wearing a battle dress uniform and a ballistic vest, with cooling system and without it. Compared to the condition without cooling, mean skin temperatures while cooling were significantly lower in both exercise periods (by 0.9 ± 0.4ºC in 40/40 condition, and by 0.6 ± 0.5ºC in 35/60 condition) and dropped faster in rest periods. The mean values of heart rates and core temperatures (measured rectally), were lower with cooling systems, but a statistical difference was not reported except for several time points. In this study, the most evident influence of the cooling system was on sweat rate, which was by 21% and 25% lower, ($p < 0.05$); for 40/40 and 35/60 climate conditions, respectively. Considering a larger body surface covered with impermeable suit in our investigation, we assume that our results confirm the effectiveness of the used cooling systems on fluid balance maintenance during uncompensated heat stress.

Conclusion

Evaluation of various cooling system effectiveness led as to the two important conclusions: in case of cooling garment wearing in a form of vest covering the torso area (A, S, and T variants) body core temperature (measured through tympanic temperature) grow slower, and the mean body skin temperature is significantly lower. Moreover, heart rate val-

ues and subjective comfort point to a much expressed soldiers' physiological stability, which is a very important result from the aspect of confidence and efficiency in fulfilling the given military missions.

Finally, the conducted laboratory tests based on a specific methodology, confirm that the use of a PCM personal body cooling vest under the NBC protective impermeable equipment significantly improves physiological suitability of the equipment in soldiers who conduct tasks and missions in extreme situations including high outside temperature and highly toxic contamination, and allow them to prolong mission duration.

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Gender differences in suicide in Serbia within the period 2006–2010

Razlike u polu kod samoubistava u Srbiji u periodu 2006–2010

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Abstract

Background/Aim. The complex multifactorial etiology of suicide suggests the need to consider gender differences when developing effective strategies for suicide prevention. The aim of this study was to examine the suicide rates and/or trends obtained for population as a whole, including gender differences in cases of committed suicide and to consider factors (age groups, education, employment, marital status, nationality and methods) associated with it in Serbia within the period 2006–2010. **Methods.** Data were obtained from the Statistical Office of the Republic of Serbia. Their classification related to the suicide method was carried out on the basis of ICD-X Code, WHO 1992 (International Statistical Classification of Diseases and Related Health Problems 10th revision, World Health Organization). Statistical analysis was done by using the crude specific suicide rate. **Results.** Within the period 2006–2010 the total number of suicides in Serbia was 6,673, of which 71.9% were males and 28.1% females (male to female suicide ratio 2.56 : 1). Their average rate was 18.15 *per* 100,000 persons, namely, 26.85 *per* 100,000 for males and 9.92 *per* 100,000 for females. Suicide was most often committed by married males and females with high school education, retired, by the Serbs. The suicide rate in Serbia increased paralelly with the age of suicide committers and it was the highest in subjects of both genders aged over 75 years. The most common suicide method in males (62.78%) and in females (58.38%) was hanging and strangling. The second most common method in males was by firearm (18.65%) and in females poisoning (19.26%). **Conclusions.** Suicide prevention Programme should be primarily oriented toward the male population because it is more exposed to stress in the period of social transition, but males are still less ready to ask for doctor's help when having some problems with mental health.

Key words:
suicide; serbia; gender identity; risk factors.

Apstrakt

Uvod/Cilj. Kompleksna multifaktorska etiologija suicida ukazuje na potrebu da se utvrde polne razlike u suicidu kako bi se primenila efikasna strategija za prevenciju suicida. Cilj istraživanja bio je utvrđivanje stope suicida, kako za populaciju u celini, tako i prema polnim razlikama, i utvrđivanje faktora povezanih sa suicidom (godine života, obrazovni nivo, zaposlenost, bračno stanje, nacionalnost, metode suicida) izvršenog u Srbiji u periodu od 2006. do 2010. godine. **Metode.** Podaci za istraživanje dobijeni su od Republičkog zavoda za statistiku Srbije. Klasifikacija podataka koji se odnose na metod suicida utvrđeni su na osnovu ICD-X code, WHO 1992 (*International Statistical Classification of Diseases and Related Health problems, 10th revision*, *World Health Organization*). Statistička analiza rađena je korišćenjem sirovih podataka stope suicida. **Rezultati.** U periodu od 2006. do 2010. godine u Srbiji je izvršeno ukupno 6 673 suicida, od toga su 71,9% bili muškarci i 28,1% žene. Prosečna stopa suicida iznosila je 18,15 na 100 000 osoba, odnosno 26,85 na 100 000 za muškarce i 9,92 na 100 000 za žene. Muškarci su češće izvršavali suicid od žena (odnos 2,56 : 1). Suicid su najčešće izvršavali oženjeni muškarci i udate žene, sa srednjim obrazovanjem, penzioneri, srpske nacionalnosti. Stopa suicida u Srbiji rasla je sa godinama života suicidanata i najveća je bila kod osoba oba pola starijih od 75 godina. Najčešći metod suicida kod muškaraca (62,78%) i žena (58,38%) bilo je vešanje i davljenje. Kod muškaraca na drugom mestu bilo je vatreno oružje (18,65%), a kod žena trovanje čvrstim i tečnim supstancama (19,26%). **Zaključak.** Program prevencije suicida trebalo bi da bude usmeren prvenstveno na mušku populaciju koja je u periodu tranzicije više izložena stresu, ali je manje spremna da se obrati lekaru kad ima probleme vezane za mentalno zdravlje.

Ključne reči:
samoubistvo; srbija; pol, faktor; faktori rizika.

Introduction

Regardless the undoubtedly important medical, social and psychological aspect of suicide, when considering the complexity and seriousness of this problem, it is also significant from the demographic point of view. According to data from the World Health Organization (WHO) [1] suicides are considerably more common among males in all European countries, while attempted suicides are considerably common in females. These differences can be explained by expressive impulsiveness in males who more often choose more effective (more lethal) suicide methods, as well as by the fact that important roles

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in the suicidal behavior have also various cultural expectations both from males and females [2–4]. Then suicide becomes an option they think about. All this is influenced by their behaviour related to asking for help when being in the suicidal crisis [5–7].

In Serbia, an average number of 1,200 persons annually committed suicide within the period 1953–2005. Their number within this period was doubled and there was a significant tendency toward its increase from 725 cases in 1953, to 1,442 suicides in 2005 [8].

If we divide this 50-year period into the three ones, the first one of the Socialist Yugoslavia (1953–1992), the second period of the combat operations on the territory of the former Yugoslavia including also the period of bombing Serbia (1993–1999) and the third period after 2000 and after introducing democratic changes in Serbia, it can be noted that within the first 40-year period there was the gradual increase of the suicide number reaching its maximum of 1,638 cases in 1992 [8].

Within the second period, after 1992, and in the course of several following years there was an obvious more intensive decrease of the suicide number in Serbia even up to 1997 when its number exceeded 1,600 again. This increased suicide number can be explained by economic crisis, inflation in Serbia in 1993/4. After that, the number of suicides was decreased despite the war and bombing in 1999, especially among the elderly. The male suicide number slightly decreased after the war of 1991–1994 just to 1997 when an increased number of suicide in male population was also registered. Thereafter, such a high level kept on in the course of the 90s. Male suicides outnumbered female ones by the ratio 2 : 1 [8].

Later on, in the third observed period after 2000, the tendency of the repeated decrease of the total number of suicides was noted. The male suicide number reached its peak again in 2002. nearly 29/100,000. In 2005 an increased number of suicides was registered from 1,346 (2004) to 1,442 (2005) [8].

The suicide rate in Serbia showed the tendency to the increase from 1953. The lowest suicide rates were registered at the beginning of 50s of the 20th century, about 12 *per* 100,000 persons, and the highest one in 1992 and 1997 with the rate of 20.9 *per* 100,000. The suicide rate in Serbia decreased after 2000 [9]. If regions of Serbia are observed within the last half of the century, Vojvodina had 2–3 times higher suicide rate on average than Central Serbia [10].

The aim of this study was to examine the suicide rates and/or trends for the population as a whole, gender differences in cases of committed suicide and to consider factors associated with the suicide in Serbia within the period 2006–2010.

Methods

Data for this study were obtained from the Statistical Office of the Republic of Serbia (Department for Demography).

The total population in Serbia was from 7,411,569 in 2006 to 7,291,436 inhabitants in 2010. All the committed suicides recorded in the foregoing population during the period from 2006 to 2010 were included in the study.

For the statistical analysis a crude specific rate based on the number of suicides within the specific population (female or male) *per* 100,000 persons was used. We calculated the standardized suicide rate according to the direct standardization method.

Gender differences were analyzed by descriptive statistical method. The male/female ratio of suicide is calculated for total number of suicide and for suicide within the total mortality, for annual and age-specific suicide rates, for socio-demographic characteristic (education, employment, marital status, nationality) and for methods of suicide. Classification of data related to the suicide methods were defined on the basis of the ICD-X Code (International Statistical Classification of Diseases and Related Health Problems, 10th revision, WHO) [11].

Data processing was carried out in the statistical package program IBM SPSS 20.

Results

A total of 6,673 suicides were committed in Serbia (Central Serbia and Vojvodina) within the period from 2006 to 2010. In that period 4,799 (71.9%) males and 1,874 (28.1%) females committed suicide, namely, males did it on average 2.56 times more often than females (Table 1).

Table 1

Number of suicides in Serbia (Central Serbia and Vojvodina)

Year of suicide	Region	Total (n)	Males (n)	Females (n)	M/F ratio
2006	Central Serbia	909	645	264	
	Vojvodina	535	377	158	
	Total	1444	1022	422	2.42
2007	Central Serbia	849	596	253	
	Vojvodina	505	373	132	
	Total	1354	969	385	2.51
2008	Central Serbia	826	574	252	
	Vojvodina	464	329	135	
	Total	1290	903	387	2.33
2009	Central Serbia	892	649	243	
	Vojvodina	484	351	133	
	Total	1376	1000	376	2.66
2010	Central Serbia	765	558	207	
	Vojvodina	444	347	97	
	Total	1209	905	304	2.98
Total	Central Serbia	4241	3022	1219	
	Vojvodina	2432	1777	655	
	Total	6673	4799	1874	2.56

M/F = male/female.

The suicide number in the total mortality in Serbia within the period 2006–2010 was 1.29%; 1.84% for males and 0.73% for females. This is 2.52 times higher in males in comparison with that in females (Table 2).

The average suicide rate within this period was 18.15 *per* 100,000 persons, namely, 26.85 *per* 100,00 males and 9.92 *per* 100,000 females (Table 3).

Table 5 shows that within the period 2006–2010 the suicide rate in Serbia was increasing together with the age of the suicide committers. Suicide rate is the highest in subjects of both genders aged over 75 years.

The most common method of suicide both in males (62.78%) and females (58.38%) was hanging and strangling. The second most common method in males was by firearm (18.65%) and poisoning with solid or liquid substances (19.26%) in females (Table 6).

Table 2

Suicides within the total mortality

Year of suicide	Total (%)	Males (%)	Females (%)	M/F ratio
2006	1.40	1.95	0.83	2.35
2007	1.31	1.85	0.76	2.43
2008	1.26	1.74	0.76	2.29
2009	1.32	1.90	0.73	2.60
2010	1.17	1.74	0.59	2.95
Mean	1.29	1.84	0.73	2.52

M/F = male/female.

Table 3

Annual suicide rates (*per* 100.000)

Year of suicide	Total	Males	Females	M/F ratio
2006	19.43	28.35	11.08	2.56
2007	18.34	26.99	10.25	2.63
2008	17.55	25.27	10.25	2.46
2009	18.79	28.08	9.99	2.81
2010	16.58	25.51	8.11	3.14
Mean	18.15	26.85	9.92	2.70

M/F = male/female.

Sociodemographic data show that both married males and females with high school education, retired and Serbs most often committed suicide within the mentioned period (Table 4).

Table 4

Socio-demographic characteristic of persons who committed suicide

Sociodemographic status	Males (%)	Females (%)	M/F ratio
Marital status			
single	22.19	13.34	1.66
married	48.34	38.26	1.26
widowed	18.64	37.73	0.49
divorced	9.27	9.49	0.97
unknown	1.56	1.18	1.32
Educational level			
no school	3.25	13.39	0.24
uncompleted primary school	15.53	24.18	0.64
primary school	29.29	25.93	1.13
secondary school	43.25	29.40	1.47
high school	3.54	2.62	1.35
university	3.69	2.99	1.23
no data	1.45	1.49	0.97
Employment status			
employed	24.63	9.49	2.59
not employed	21.59	11.85	1.82
retired	50.36	50.22	1.01
dependents	3.42	28.44	0.12
Nationality			
Serbs	80.47	79.99	1.01
Hungarians	8.00	8.97	0.89
Croats	1.44	1.44	1.00
Slovaks	1.42	0.80	1.77
Roma	0.92	1.12	0.82
others	7.75	7.68	1.01
Total	100.00	100.00	

M/F = male/female.

Table 5

Age-specific suicide rates (*per* 100,000)

Age range (years)	Total (n = 6,673)	Males (n = 4,799)	Females (n = 1,874)	M/F ratio
< 15	0.04	0.06	0	0.06
15–24	4.11	4.58	2.88	1.59
25–34	8.32	9.12	6.24	1.46
35–44	10.16	11.02	7.95	1.38
45–54	18.70	19.39	16.91	1.15
55–64	18.08	18.36	17.39	1.06
65–74	18.85	17.31	22.78	0.76
> 75	21.61	19.98	25.77	0.77

M/F = male/female.

Table 6

Methods of suicide

Methods of suicide characteristics by groups		Males (%)	Females (%)	M/F ratio
X60-65, X 68-69	self-poisoning by drugs and by exposure to liqued substances	5.71	19.26	0.29
X66-67	exposure to gases	0.23	0.16	1.43
X70	hanging, strangulation and suffocation	62.78	58.38	1.07
X71	drowning and submersion	2.39	7.32	0.32
X72-X75	firearm and explosive material	18.65	3.31	5.60
X76-X77	smoke, fire, flames and hot vapors	0.22	0.16	1.37
X78-X79	sharp and blunt object	2.57	1.39	1.85
X80	jumping from a high place	3.10	5.55	0.56
X81	jumping or lying before moving object	0.33	0.37	0.89
X82	motor vehicle crashing	0.35	0.37	0.94
X83-X84	other specified and unspecified means	3.67	3.73	0.98
Total		100.00	100.00	

M/F = male/female.

Discussion

On the basis of data obtained from the Statistical Office of the Republic of Serbia in the course of the analyzed 5-year period the average suicide rate in Serbia of 18.15 *per* 100,000 within the period 2006–2010 was higher than the average rate in the world, estimated at 11.6 *per* 100,000 [12].

Males in Serbia committed suicide 2.56 times more often in comparison with females, which was unchanged in comparison with the previous 5-year period, 2001–2005 [8, 9]. The suicide male/female ratio in Serbia is lower in comparison with the average male/female ratio in the Western Europe (4 : 1) [12].

Gender differences in the suicide number are maintained in the same ratio in the Central Serbia and Vojvodina, which is also characteristic for the neighbouring countries regions [13, 14] and Mediterranean part of Croatia (2.36 : 1) [15]. But on the territory of Kosovo the ratio of gender differences for the period 2007–2008 was somewhat higher (3 : 1) [16]. In Montenegro it was lower (1.7 : 1) in comparison with that in Serbia [17].

The suicide number in the total mortality in Serbia within the observed period was lower than the total mortality in the whole world which, according to the data from WHO, was 1.4% [1]. In the male population of Serbia the suicide number in the total mortality from 2006 to 2010 was 2.5 times higher than in females. Taking into consideration that the suicide rate in females was dropping from 2006 to 2010 and in males was dropping up to 2009 and afterwards showing an increase, it can be stated that the increase in the total suicide number in 2009 was the consequence of the increased suicide number in males in that very year.

The average suicide rate within the analyzed 5-year period was for males 2.46 in 2008, and 3.14 in 2010, namely, it was 2.70 times higher than that in females.

The suicide rate in females from 2006 to 2010 dropped from 11.08 *per* 100,000 inhabitants (2006) to 8.11 *per* 100,000 (2010). So, the highest registered annual level of the suicide rate within the observed 5-year period in females never exceeded its lowest rate in male population.

Sociodemographic data showed that within the period 2006–2010 the suicide was most often committed by married men and women with high school education, retired, Serbs.

With regard to the marital status suicide was most often committed by married men, then unmarried men and widowers. Among females, it was most often committed by married women and widows. Concerning the gender differences, suicide was more often committed by both unmarried and married men then by unmarried women, and widows twice often committed suicide in comparison with widowers. This difference was not noticed in divorced either men or women. Such structure of the died due to suicide in accordance with the marital status is influenced upon composition of population in dependence of the marital status (most of them are married), then upon differences present in the marital structure of both male and female population (there was much more celibates among men and considerably less among widowers) and upon clearly differentiated population structure by age with regard to the marital status (widowers/widows are also the oldest) [8].

Concerning educational level, the suicide incidence drops together with its higher level. The suicide is more often committed by more educated males (completed primary and high school, faculty) and uneducated females (incomplete primary school or without it), which is in accordance with other studies from the territory of the former Yugoslavia [13–17].

Suicide was most often committed by retired of both sexes, followed by employed and unemployed males and finally dependents females. Employed males 2.5 times more often committed suicide and twice more often those unemployed in comparison with females of the same professional status, while differences did not exist for retired of both sexes. These differences could be explained by the fact that the males accept changes of socioeconomic conditions with more difficulties, particularly those related to (un)employment, amount of earnings and property. All this has a more important influence upon male than female suicide [18].

When explaining gender differences in suicide rates in the aged, changes that ageing and retirement bring themselves are primarily associated with the change in social and financial status which more affects males because their capabilities to satisfy own existential needs are drastically reduced. For females, changes in the social environment they are to the greater degree sensitive to, are less emphasized so that the risk of suicide in them is less present [19, 20].

As expected, males and females of the Serbian nationality are those who most often commit suicide, then follow Hungarians, Croats and Slovaks, less frequently those of the Roma (Gypsies) minority. As for the gender, the Serbs, both males and females as well as Croats, also both males and females equally committed suicide, but in other nations some differences with regard to gender were noticed. Namely, the Slovak males considerably more often committed suicide than the Slovak females, but Hungarian and Roma (Gypsy) females more often committed suicide than males of their national minority.

The suicide rate in females increased together with the age. In males, it increased even to the age of 65 and then evidently declined. In males, the highest suicide rate was within the period 55–64 years of age (19.39 *per* 100,000 persons), which was the highest suicide rate with regard to the age for both gender groups. This means that in Serbia age has the higher position when the highest suicide rate is concerned in comparison with European population where its highest rate is registered for males aged 45–59 years [11].

Concerning gender, suicide was more often committed by younger males, up to 55 years of age and by elderly females over 65 years of age, while for the age 55–65 there was no difference between genders.

Regarding the suicide method within the period 2006–2010 both males and females most often committed suicide by hanging, strangling, drowning, then by firearm in males and poisoning either with solid or liquid substances in females. With regard to gender, males 5.6 times more often than females committed suicide by firearm and almost twice more often by sharp and blunt objects and by gas poisoning. Suicide by firearm was a method usually characteristic for the military population [21, 22], and possession of firearm often illegal in the civil population is a consequence of keeping firearm as a "trophy" after taking part in wars. On the other hand, females unlike males, almost four times more often committed suicide by poisoning either with solid or liquid substances, three times more often by strangling or drowning, and twice more often by jump from height. This result coincides with the existing studies [2–4].

Although in our study we primarily focused on psychosocial and demographic risk factors that could help us to explain gender differences in suicide rates, an important question that follows is whether or not the differences found in this study between male and female suicides are the consequence of gender differences in the prevalence of the possible role of psychiatric and/or behavioural characteristics, which may also mediate gender differences in suicide risk [23, 24].

Our results showing gender differences provide initial data for researchers in the field of suicidology and should be further investigated.

Conclusion

Our results suggest that the suicide prevention programme should be oriented toward the male population that is, in comparison with the female one in Serbia, exposed to stress in the period of social transition, but less ready to refer to the doctor for help because of problems related to their mental health. This would certainly make easier detection and treatment of psychiatric disorders and would also the reduce risk of suicide. For this reason, health education should have the aim to improve motivation in male population particularly to be ready to ask for expert's help and this would reduce suicide risk.

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Morphometric parameters as risk factors for anterior cruciate ligament injuries – A MRI case-control study

Morfometrijski parametri kao faktori rizika od nastanka povrede prednjeg ukrštenog ligamenta

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Abstract

Background/Aim. The anterior cruciate ligament (ACL) is the most frequently injured ligament of the knee, representing 50% of all knee injuries. The aim of this study was to determine the differences in the morphometry of knee injury patients with an intact and a ruptured anterior cruciate ligament. **Methods.** The study included 33 matched pairs of patients divided into two groups: the study group with the diagnosis of anterior cruciate ligament rupture, and the control group with the diagnosis of patellofemoral pain but no anterior cruciate ligament lesion. The patients were matched on the basis of 4 attributes: age, sex, type of lesion (whether it was profession-related), and whether the lesion was left- or right-sided. Measurements were carried out using magnetic resonance imaging (MRI). **Results.** The anterior and posterior edges of the anterior cruciate ligament in the control group were highly significantly smaller ($p < 0.01$; in both cases). The control group showed a statistically significantly larger width of the anterior cruciate ligament ($p < 0.05$). A significant correlation between the width of the anterior cruciate ligament and the width ($p < 0.01$) and height ($p < 0.05$) of the intercondylar notch was found to exist in the control group, but not in the study group ($p > 0.05$). The patients in the control group showed a shorter but wider anterior cruciate ligament in comparison to their matched pairs. The control group of patients was also characterized by the correlation between the width of the intercondylar notch and the width of the anterior cruciate ligament, which was not the case in the study group. **Conclusions.** According to the results of our study we can say that a narrow intercondylar notch contains a proportionally thin anterior cruciate ligament, but we cannot say that this factor necessarily leads to rupture of the anterior cruciate ligament.

Key words:
anterior cruciate ligament; injuries; risk factors; anthropometry.

Apstrakt

Uvod/Cilj. Prednja ukrštena veza je veza kolena koje se najčešće povređuje, što čini 50% od ukupnih povreda kolena. Cilj ove studije bio je da se utvrde razlike u morfometriji zgloba kolena kod bolesnika sa intaktnom i rupturisanom prednjom ukrštenom vezom. **Metode.** Ispitanike ove studije činili su 33 para sa povredom zgloba kolena, podeljena u dve grupe: ispitivanu grupu činili su bolesnici sa dijagnostikovanom rupturom prednje ukrštene veze, a kontrolnu bolesnici sa dijagnostikovanim patelofemoralnim sindromom bez povrede prednje ukrštene veze. Bolesnici su bili upareni na osnovu četiri karakteristike: godine, pol, vrsta povrede (koja je uslovljena vrstom sporta kojim se bave) i na osnovu strane tela. Sva merenja su vršena na snimcima magnetne rezonance. **Rezultati.** Ispitanici bez rupture prednje ukrštene veze posedovali su statistički visokoznačajno kraću prednju i zadnju ivicu prednje ukrštene veze od svojih parova ($p < 0,01$; u oba slučaja). Takođe, kontrolna grupa za razliku od ispitivane, imala je statistički značajno veći sagitalni prečnik prednje ukrštene veze ($p < 0,05$). Postojala je statistički značajna povezanost sagitalnog prečnika prednje ukrštene veze sa širinom ($p < 0,01$) i visinom ($p < 0,05$) međukondilarne jame unutar kotrolne, ali ne i unutar ispitivane grupe ($p > 0,05$; u oba slučaja). Bolesnici kontrolne grupe posedovali su kraću ali širu prednju ukrštenu vezu od svojih parova. **Zaključak.** Na osnovu podataka naše studije možemo reći da uska međukondilarna jama sadrži proporcionalno tanju prednju ukrštenu vezu, ali ne možemo tvrditi da ovaj faktor nužno vodi rupturi prednje ukrštene veze.

Ključne reči:
ligament, prednji ukršten; povrede; faktori rizika; antropometrija.

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Introduction

The anterior cruciate ligament (ACL) is the most frequently injured ligament of the knee, representing 50% of all knee injuries [1]. ACL injury is almost always associated with physical activity which is why the incidence of this type of injury is the highest amongst the population of athletes. It is often necessary to reestablish the continuity of the ruptured ACL in order to avoid giving way episodes.

In addition to the morphometric characteristics of the intercondylar notch and the tibial slope, the morphometric characteristics of the ligament also have effect on the frequency of ACL injury [2]. These characteristics are primarily its length and thickness. An increased length can increase laxity of the joint while a ligament that is too thin may rupture more easily. On the other hand, a short ligament may restrict movement of the knee joint, primarily extension. As early as 1938 Palmer [3] reported that the ACL may sustain injury from the medial edge of the lateral condyle. Norwood and Cross reported that, in extension, the ACL can come in contact with the lateral wall of the intercondylar notch which can result in injury [4]. Many studies have shown the correlation between a narrow intercondylar notch and ACL ruptures [5–7]. It is a generally accepted fact that a small intercondylar notch contains a small and weak ACL [8, 9].

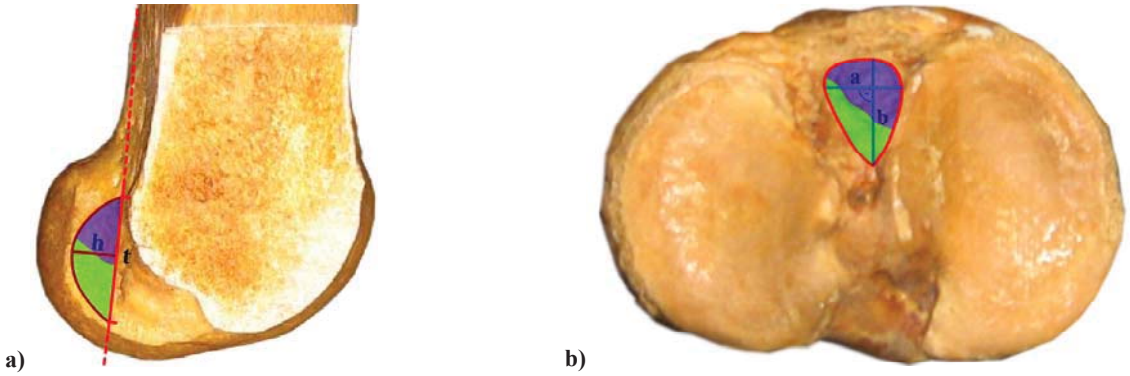
In addition to the length and thickness of the ACL, the morphometric characteristics of the femoral and tibial attachments of the ligament were also observed in this study. Edwards et al. [10, 11] described the anatomic localization of the tibial insertion and the femoral origin of the ACL and of its parts. They emphasized the significance of the choice of attachment location on the femur and tibia for the preservation and normal functioning of the implanted graft. The anterior part of the ACL origin on the femur has the form of a straight line [1] extending from the posterior femoral cortex line. The posterior edge of the insertion has the form of an arc of 4 mm in width [9] (Figure 1a). The ACL insertion on the tibia is somewhat larger and stronger than the insertion on the femur [12]. It has an elliptic form with a greater anteroposterior diameter (Figure 1b). It is situated between the anterior horn of the medial meniscus in the front and the anterior horn of the lateral meniscus at the back. The edges of the insertion are limited by the joint surface of the tibial condyles.

The aim of this study was to determine the differences between ACL morphometry in patients with and intact and those with a ruptured ACL.

Methods

The study group consisted of 205 patients with isolated noncontact ruptures of the ACL and with no reported lesions of collateral ligaments, posterior cruciate ligaments or other bone elements. The control group consisted of 258 patients whose major complaint was patellofemoral pain, but did not have any dysplastic change of the knee. After matching 33 pairs from the two groups, a total of 66 patients were taken into consideration for the study. The patients were matched according to their age at the time of accident (a difference of up to 5 years was tolerated), sex, type of lesion (whether it was profession-related), and whether the lesion affected the left or right side of the knee. There were 21 male and 12 female pairs: 9 pairs with soccer related, 4 pairs with ski related, 3 pairs with gymnastics related, and 16 pairs of patients with other sports-related lesions as well as one case of a motorbike accident. Twenty pairs had the lesion on their right knee and thirteen pairs on the left knee. The average age of the patients was 30 ± 10 years (range, 15–48 years) in the study group, and 30 ± 11 years (range, 15–48 years) in the control group. All measurements were performed by radiography and magnetic resonance imaging (MRI). All MRIs were made using 1.5 T magnets in Schweizer Paraplegicer-Zenturin (SPZ) Nottwil (Schweiz) within 7 days of knee injury.

The following anatomical parameters were measured: the length of the anterior and posterior edge of the ACL on the sagittal MR section; the mean length and the sagittal diameter (width) of the ligament; the length of the femoral origin; the length and width of the tibial insertion; the width and the height of the intercondylar notch.



a) b)

Fig. 1 – A schematic presentation of the femoral origin (a) and tibial insertion (b) of the anterior cruciate ligament (ACL) and its parts.

a) blue – the anteromedial part; green – the posterolateral part (t – length of origin; h – width of origin);
b) blue – the anteromedial part; green – the posterolateral part (a – insertion width; b – insertion length).

The frontal MR section was used for the selection of the sagittal section that best covered the ACL (Figure 2). The borders of the tibial and femoral attachments were drawn on

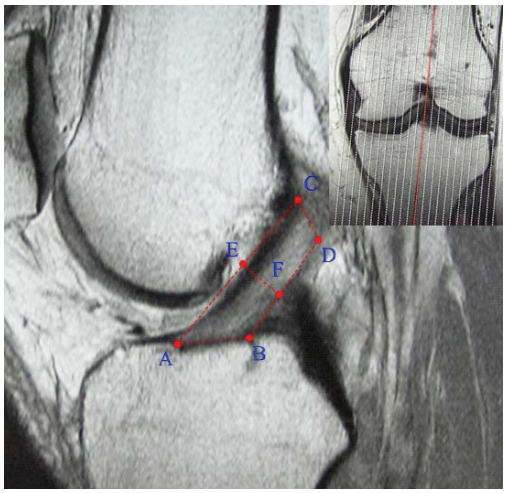


Fig. 2 – Selected sagittal section. Method of measuring anterior cruciate ligament (ACL) dimensions and the dimensions of its attachments on the sagittal magnetic resonance (MR) section
(AC – anteromedial edge; BD – posterolateral edge; AB – length of tibial insertion; CD – length of femoral origin; EF – sagittal diameter or width). Picture in the upper right corner shows selected sagittal section (red section) in coronal plane.

the selected section and the distance from the most anterior point on the tibia to the proximal point on the femur (the length of the anterior edge) and the distance from the most posterior point on the tibia to the distal point on the femur (length of the posterior edge) of the ACL were measured. The same image was used to measure the sagittal diameter (width) of the ACL represented as the length perpendicular to the direction of the ligament, at an equal distance from the tibial to the femoral attachment. The length of the tibial insertion was measured as the distance between the anterior and the posterior point of the insertion. The length of the femoral origin was measured as the distance between the most proximal to the most distal point of the origin. The width of the tibial insertion was measured on the frontal image running through the widest segment of the insertion (Figure 3).

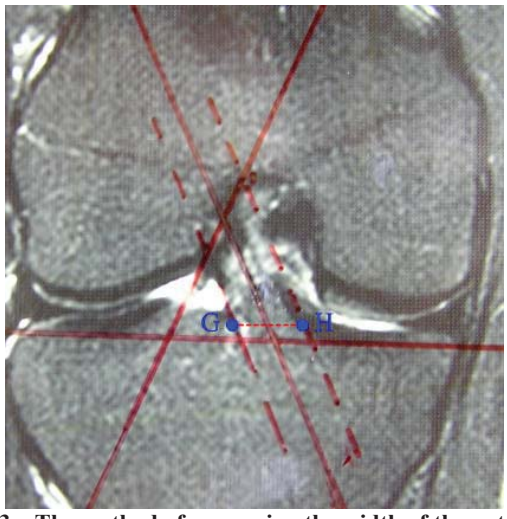


Fig. 3 – The method of measuring the width of the anterior cruciate ligament (ACL) tibal insertion (GH distance).

The intercondylar notch dimensions were measured on the horizontal MR section passing through the most posterior points of the medial and lateral condyle of the femur (Figure 4). The following were measured on the selected MR image: the width of the intercondylar notch at the level of the popliteal groove (ICW), the maximum intercondylar width (ICW_{max}) and the intercondylar height (ICH) measured as the shortest distance between the highest point of the intercondylar notch and the line passing through the most posterior point of the medial and lateral condyles.

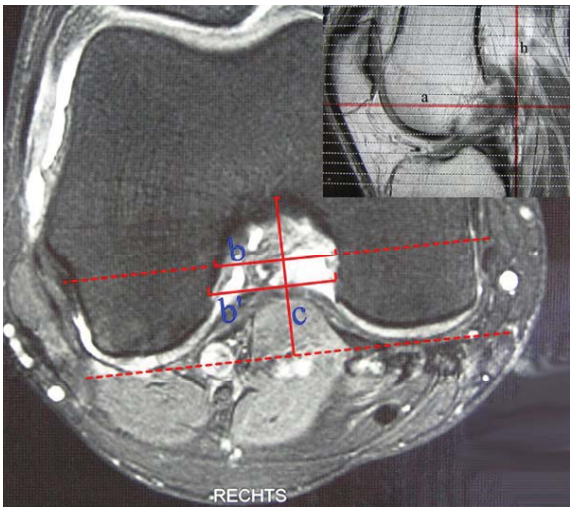


Fig. 4 – The section (a) used for measurements was determined on the basis of the vertical line (h) passing through the most posterior point of the lateral condyle (picture in the upper right corner). The width of the intercondylar notch at the level of the popliteal groove (b), the maximum width of the intercondylar notch (b') and the height of the notch (c) were measured.

In order to estimate intraobserver variation, all morphometric parameters were measured twice by one observer, with a coefficient of variance of less than 3%. The differences between the groups in relation to the above mentioned anatomical parameters were tested with the use of the Student's *t*-test for matched pairs. The relation between the ACL sagittal diameter (width) and the morphometric parameters of the intercondylar notch was tested via the Pearson's coefficient of correlation within the SPSS 11.0 programme. The level of statistical significance was $p < 0.05$.

Results

The lengths of the anterior and posterior ACL edges in the study group, as well as their mean value were greater by approximately 4 mm than in the control group (Table 1). This difference is of high statistical significance ($p < 0.01$). The study group displayed a narrower ACL width by some 1.1 mm in comparison to the control group. This difference is statistically significant ($p < 0.05$). No statistically significant difference was determined between the study and control groups as regards to the length and width of the ACL tibial and femoral attachments nor the width of the intercondylar notch at the level of the popliteal groove and at the widest point ($p > 0.05$).

Table 1

Morphometric parameters of the anterior cruciate ligament (ACL) and the intercondylar notch. (mean values and standard deviations)

Variables	Examined group (mm)	Control group (mm)	*p* value
Length of the ACL anterior edge	46.6 ± 4.7	42.6 ± 3.0	< 0.01
Length of the ACL posterior edge	27.8 ± 3.6	23.6 ± 2.6	< 0.01
Median ACL length	37.2 ± 3.9	33.2 ± 2.2	< 0.01
ACL width	11.0 ± 1.8	12.1 ± 1.7	< 0.05
Tibial insertion width	11.3 ± 1.5	11.9 ± 1.9	= 0.092
Tibial insertion length	19.4 ± 2.7	18.4 ± 2.8	= 0.102
Femoral origin length	13.0 ± 2.6	13.5 ± 2.4	= 0.446
ICW	21.2 ± 2.5	22.3 ± 3.0	= 0.083
ICW_{max}	22.9 ± 2.7	23.1 ± 2.9	= 0.771
ICH	31.9 ± 3.2	30.6 ± 2.4	< 0.05

ICW – the widh of the intercondylar notch at the level of the popliteal groove; ICW_{max} – maximum intercondylar width; ICH – intercondylar height.

The ACL width correlates with the width of the intercondyar notch at the level of the popliteal notch (r = 0.580) and at the widest point (r = 0.506), in patients whose ACL remained intact after knee joint injury ($p < 0.01$), but not in the patients with a ruptured ACL ($p > 0.05$; Table 2). Also, the ACL width correlates with the height of the intercondylar notch (r = 0.347) in the patients with an intact ACL ($p < 0.05$), but not in the patients with a ruptured ligament ($p > 0.05$).

Table 2

Correlation between the anterior cruciate ligament (ACL) width and the morphometric parameters of the intercondylar notch

Group	Coefficient of correlation		
	ICW	ICW_{max}	ICH
Examined	0.100	0.204	0.243
Control	0.580**	0.506**	0.347*

ICW – the widh of the intercondylar notch at the level of the popliteal groove; ICW_{max} – maximum intercondylar width; ICH – intercondylar height.
***$p < 0.05$; ****$p < 0.01$.**

Discussion

Measuring the width of the ruptured ACL using sagittal MR image posed a problem due to the broken continuity of the ruptured ligament. This is why, on MR images of both groups of patients, we measured the length of the ACL anterior edge as the distance from the most anterior point of the tibial insertion to the most proximal point of the femoral origin, and the length of the posterior edge, as the distance between the most posterior point of the tibial insertion to the most distal point of the femoral origin. Also, the width was measured at an equal distance from the tibial and femoral attachments, perpendicular to the direction of the ACL, as the distance between the approximate anterior and posterior edges.

The study group showed greater values for the anterior ACL edge length than the control group, and a similar difference was also noted regarding the posterior ACL edge ($p < 0.01$; in both cases). In their study, performed on 9 volunteers using 3D MR images, Iwahashi et al. [13] reported that the length of the anteromedial ACL bundle was 34 mm and the length of the posterolateral bundle was 27 mm. The length of the anteromedial bundle was shorter, and the length of the posterolateral bundle was greater than the lengths obtained in our study. The reason for greater values in our study can be explained by different places of measurement. The above mentioned author measured the length of the anteromedial and posterolateral parts of the ACL while we measured its anterior and posterior edges.

In our study, the mean length of the ACL showed greater values ($p < 0.01$) in the study group than in the control group. Bradley et al. [14] measured an average ACL length of 32 mm on four cadaverous knees with no pathological changes of the joint, obtaining a result rather similar to our results in the control group. In the study of 33 cadaverous knees Odensten and Gillquist [15] reported an average ACL length of 31 mm.

In our study the acquired values of ACL width are statistically significantly greater in the control than in the study group ($p < 0.05$). Anderson et al. [16] measured the width of the ACL on oblique sagittal MR images and obtained significantly lower values in female (7.6 mm) than in male basketball players (8.7 mm) aged 16 years, on average. Also, the reason for lower values of the ACL width could be the result of the fact that the examinees' body growth was not yet complete.

The width of the intercondylar notch of the control group at both points of measurement (at the level of the popliteal groove and at the level of maximum width) showed somewhat greater values than in the case of the study group. However, this difference is not statistically significant ($p > 0.05$). Other authors report generally lower values in the width of the intercondylar notch, which is probably the reason for measuring the width at different depths of the notch, in patients of different sex and in different age groups. Both of our groups covered adult subjects, mostly male, who displayed no osteoarthritic changes, i.e. a population whose

growth process was complete and the process of ageing had not yet started. Lund-Hanssen et al. [17] reported that an intercondylar width below 17 mm was critical for the increase of risk of ACL injury. Only one examinee (a woman) in our study had the value of the intercondylar width below this critical amount. Lombardo et al. [18] measured the width of the intercondylar notch on X ray images and also found no difference between professional basketball players with a ruptured ACL (23.4 mm) and those whose ACL was intact (23.5 mm). These values are only slightly greater than the values obtained in our study, which is probably the result of measuring being performed in different population groups and the use of MR during measurement. In their study on 213 track-and-field athletes Laprade and Burnet [6] concluded that the narrowing of the intercondylar notch was associated to ACL injury. Good et al. [19] measured a somewhat smaller ICW in three groups of patients: patients with chronic ACL insufficiency (16.1 mm), patients with acute ACL injury (18.1 mm) and cadaveric material (20.4 mm). The intercondylar notch width was measured at the widest part of the anterior outlet of the intercondylar notch, just above the meniscal plane. In this case the presence of osteophytes in patients with chronic ACL insufficiency led to the narrowing of the intercondylar notch. Odensten and Gillquist [15] did not find a statistically significant difference in ICW between the control group and the group with a ruptured ACL.

In the control group, but not in the study group, our study determined the existence of a highly statistically significant correlation between the value of the ACL's width and the width of the intercondylar notch at the level of the popliteal groove and at the widest point ($p < 0.01$), as well as between the values for the ACL's width and the height of the intercondylar notch ($p < 0.05$). We can assume that this correlation between the ACL's width and the size of the intercondylar notch has a positive effect on the preservation of the ACL. Based on the data from our study we can conclude that there is a disproportion between the ACL's width and the intercondylar notch in patients with a ruptured ACL. As the intercondylar notch is filled by the ACL and PCL, further studies should determine whether in the case of a thin ACL the remaining space is filled by the PCL thus increasing the misbalance between the stronger PCL and the weaker ACL, i.e. whether a wide ACL damages itself by pressing against the lateral femoral condyle or against the PCL.

On the other hand the data about the existence of a correlation between ACL width and the width of the intercondylar notch were explained by Dienst et al. [20] in their study on MR images of 20 volunteers whose knees showed no pathological changes. They established that there was a highly statistically significant correlation ($p < 0.01$) between ACL transverse sections and transverse sections of the inlet i.e. the outlet of the intercondylar notch. In the above mentioned study the ACL transverse section, at the point where it is closest to the PCL, was compared, as well as the mean value of the cross-sectional notch area on the notch inlet (the distal part of the notch) and the notch outlet (the proximal part of the notch). Davis et al. [8] also analyzed "normal" knees using MR images. They found that there was a significant correlation between the ACL and the intercondylar width. They measured the width of the notch and the width of the ACL at the point where the two ligaments (ACL and PCL) cross one another. The section chosen in each knee was the section where the ACL and the PCL cross one another as close as possible to the mid-substance of the ACL). Similar results were obtained by Stäubli et al. [21] on oblique frontal MR images (showing a significantly positive correlation between the width of the ACL and the intercondylar width). This study was also performed on knees with an intact ACL. On the other hand, in their study performed on cadavers, using a caliper and mould technique (a positive mold of the entire anterior cruciate ligament was created with silicone rubber and plaster commonly used for dental molding), Muneta et al. [9] did not find a significant correlation between the intercondylar width and the different measurements of the ACL (the width, sagittal length, and the cross-sectional area of the mid-substance and the femoral and tibial insertions of the ACL), with the exception of the length of the tibial insertion. A possible explanation for these results might lie in the fact that the donors were 40 years older, on average, than our donors, which could have influenced the dimensions of the intercondylar notch, as well as the dimensions of the ACL. In the study of 50 cadaverous knees Stijak et al. [22] found a significant correlation between the ACL width and the male intercondylar width but not with the female intercondylar width.

The data obtained in our study do not describe the length and width of the ACL tibial insertion nor the length of the ACL femoral origin as significant for ACL injury ($p > 0.05$; in all three cases). Papachristou et al. [23] obtained very similar values of the tibial insertion for men (19.5 mm) and women (17.4 mm), by direct measurements on the tibiae of 55 cadavers (30 male and 25 female). In their study performed on 55 cadaverous knees of an older mixed population, Edwards et al. [10] also obtained the result of 18 mm for the length of the tibial insertion. Stäubli and Rauschning [24] compared 3 different methods of measuring the length of the tibial insertion: method one – direct measurement performed on 10 cadaverous knees; method two – the cryoplaning technique (on 5 knees); and method three – use of MR imaging on 25 knees (23 male and 12 female). The published values for the length of the tibial insertion were: 15 mm for cadaverous knees; 17.4 mm for the cryoplaning technique and 16.9 mm and 16 mm for the MR imaging of men and women, respectively.

Upon measuring 22 cadaveric knees Edwards et al. [11] obtained the result of 14 mm for the length of the femoral origin, while Bradley et al. [14] obtained the result of 14.5 mm for the length of the femoral origin, also on cadavers. These values are only slightly greater than the values obtained in our study and are probably the result of the indirect measuring method and the different population groups.

Conclusion

Upon studying the ACL morphometric characteristics in 33 matched pairs we can say that the patients whose ACL remains intact after knee joint injury have a shorter

but wider ACL in comparison to their matched pairs. Also, the control group of patients is characterized by a correlation between the width of the intercondylar notch and the width of the ACL, which is not the case with the study group. In this case we can conclude that a narrow intercondylar notch contains a narrow ACL, but this fact is not significant to ACL rupture. What is significant to rupture is the fact that a narrow intercondylar notch can contain a wide ACL and *vice versa*, a wide intercondylar notch can contain a narrow ACL.

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Do women in rural areas of Serbia rarely apply preventive measures against cervical cancer?

Da li žene iz seoskog područja Srbije ređe sprovode preventivne mere protiv karcinoma grlića materice?

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Abstract

Background/Aim. The incidence of cervical cancer in Central Serbia has the higher rate as compared with that in other European countries. Considering mortality rate for cervical cancer, the standardized rate in Serbia is 10.1 per 10,000 females, which is the second highest one after that in Romania with 13.0. The aim of this study was to examine application of preventive measures for cervical cancer in women both from rural and urban areas in Serbia and if they are associated with sociodemographic characteristics and sexual behaviour. **Methods.** We analyzed secondary data of the 2006 National Health Survey of the population of Serbia focused on characteristics of adult females aged 25 to 65 years (5.314 in total) taking into consideration that programme of the organized screening will include female population aged over 25 years. **Results.** Respondents from rural areas have gynecological examination less than once a year in comparison with those from urban areas (OR = 0.60, 95% Cl 0.54–0.68). Less women from rural areas did Pap test during the last 12 months in comparison with respondents from urban areas (OR = 0.55, 95% Cl 0.48–0.64). Respondents from urban areas less often do the Pap test on doctor's advice in comparison with those from rural one (OR = 0.55, 95% Cl 0.42–0.62). **Conclusion.** This study shows that women in rural areas rarely implement preventive gynecological measures againt cervical cancer in comparison with those in urban areas. Implementation of preventive measures among rural women is conditioned by lower levels of education and lower socioeconomic status.

Key words:
uterine cervical neoplasms; rural health; urban health; vaginal smears; socioeconomic factors; women; serbia.

Apstrakt

Uvod/Cilj. U poređenju sa drugim evropskim zemljama, učestalost raka grlića materice u centraloj Srbiji je najviša. Sa standardizovanom stopom mortaliteta od 10,1 na 1000 000 žena, Srbija je na drugom mestu u Evropi. Cilj istraživanja bio je da se ispitaju razlike u primeni mera prevencije raka grlića materice kod žena seoskih i gradskih područja u Srbiji i ustanovi da li su one povezane sa sociodemografskim karakteristikama ispitanica i njihovim seksualnim ponašanjem. **Metode.** Izvršili smo sekundarnu analizu Nacionalnog istraživanja zdravlja stanovništva Srbije iz 2006. godine sprovedeno na reprezentativnom uzorku populacije, po metodi slučajnog uzorka. U ovom radu analizirane su karakteristike ukupno 5 314 žena starosti od 25 do 64 godine. **Rezultati.** Ispitanice iz seoske sredine idu ređe nego jednom godišnje na konrolne ginekološke preglede (OR = 0,60 95% CI 0,54–0,68). Manje je ispitanica iz seoskih sredina koje su u poslednjih 12 meseci uradile PAPA test, nego ispitanica iz gradskih sredina (OR = 0,55; 95% CI 0,48–0,64). Ispitanice iz grada ređe idu na PAPA test po savetu lekara, u odnosu na ispitanice sa sela (OR = 0,51 95% CI 0,42–0,62). **Zaključak.** Žene iz seoskih područja Srbije u povećanom su riziku od raka grlića materice nego žene iz gradskih područja. Nesprovođenje preventivnih mera kod seoskih žena nije posledica njihovog mesta boravka, već nižeg obrazovnog i socioekonomskog statusa.

Ključne reči:
grlić materice, neoplazme; zdravlje, ruralna populacija; zdravlje, urbana populacija; vaginalni brisevi; socioekonomski faktori; žene; srbija.

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Introduction

Incidence of cervical cancer in central Serbia has the highest rate among the other European countries. Significant regional differences range from the lowest rate (16.6 per 100,000 females) registered in the Machvan region to the highest one in eastern Serbia and the Belgrade region (32.5–38.1 per 100.00 females) [1]. Considering mortality rate for cervical cancer, the standardized rate in Serbia is 10.1 per 100.00 females, which is the second highest one after that in Romania with 13.0 [2]. According to the current knowledge, human papillomavirus (HPV) infection has an important role in the development of the cervical cancer [3, 4]. Other important risks are poor socioeconomic conditions, [5] chemical agents (smoking), [6] sexual habits (early sexual activities), promiscuity [7, 8] factors associated with male partners [9], abortions and deliveries in adolescent as [8]. There is an increased risk for women taking oral contraceptives [3]. Women from rural areas are at higher risk of cervical cancer associated with factors such a: lower educational level, [10] poorer socioeconomic conditions [11] and insufficient awarness of necessary regular preventive control examinations [12]. Women at high risk of cervical cancer are those unreliable for follow-up, those who have no regular Pap test, those with high parity [13].

Cervical cancer is preventable and can be effectively treated if early diagnosed. The problem of both high incidence and mortality rate in Serbia can be partly attributed to the lack of awarness about health, but also to the problem in the system of health care approach and lack of the prevention programme. A key reason for higher incidence of cervical cancer in developing countries is the lack of effective screening programs [14].

So far, in Serbia except for pilot projects in some regions, there was no organized screening for cervical cancer, but only the oportune one [15]. Alarming is the fact that 7.9% of women from rural areas in Serbia have never visited the gynecologist and that only 25.6% of them did the Pap test within a 3-year period [16]. Sociodemographic factors (educational level, occupation, socioeconomic status) are the dominant factors influencing upon application of preventive gynecologic examinations of women [17]. The study by Matejić et al. [18] have shown that the lack of women's knowledge on reproductive health in Serbia, inappropriate gynecologists' attitude and personal problems are associated with negative experience in the primary health care and influence upon low priority of preventive measures both for women and gynecologists [18]. All these factors result each year in about 500 fatal outcomes in Serbia due to cervical cancer.

According to the available literature no study has so far systematically examined differences in behaviour related to reproductive health in our country referring to either regular visits to gynecologist, colposcopic examinations and Pap test, or differences in usage of preventive health services among women living both in rural and urban environment of Serbia and being relevant for the cervical cancer prevention. This study has been designed to complement previous studies and point out women from rural areas as a target group with less probability to respond to organized screening programme for cervical cancer.

The aim of this study was to examine application of preventive measures against cervical cancer in women both from rural and urban areas in Serbia and to determine their association with sociodemographic characteristics and sexual behaviour.

Methods

This study was a secondary data analysis of the 2006 National Health Survey of the population of Serbia (without data concerning Kosovo and Metohia), carried out by the Ministry of Health of the Republic of Serbia with financial and professional support from the World Bank, the WHO regional Office for Europe (Country Office of Serbia) and the Institute of Public Health of Serbia "Dr Milan Jovanovich Batut". This was a cross-sectional study on a randomly selected representative population sample including 14,522 subjects aged 20 years and more [16]. In order to provide statistically reliable estimates of the health indicators on the national level, firstly was formed a stratified two-stage randomized sample of all registered housholds in the 2002 Serbia population census. Out of 7,673 randomly selected housholds, 6,156 were interviewed within the period September to October 2006. The houshold response rate was 80.2%. In these housholds there were 7,664 women aged 20 years and older. Individual response rate was 93.2%. We focused on characteristics of adult females aged 25 to 65 years (5,314 in total) taking into consideration that the programme of organized screening will include female population aged over 25 years [19]. Information about sociodemographic and socioeconomic characteristics as well as about preventive measures were obtained through interviews (face-to-face questionnaire and self-administered questionnaire) administered by the trained interviewers.

The three groups of data relevant to cervical cancer were analyzed: sociodemographic characteristics, sexual behaviour and application of preventive gynecological measures.

Of the analyzed sociodemographic variables there were: age of responders (shown in the ten-year intervals from 25 to 65 years); education (primary, high school and university); socioeconomic status measured by the houshold wealth index); region (Vojvodina, Central Serbia, Belgrade) and the number of children (0, 1, 2, 3 or more). According to the calculated wealth index values respondents were classified into five socioeconomic categories or quintiles: poorest, poor, medium, rich and wealthy [16].

Of the variables related to sexual behaviour we analyzed: early sexual activity (< 16 years, 17–19, 20–22, 23–25 and > 26 years), the number of sexual partners in the last 12 months but not regular partners (1–3, or more) and the number of abortions (0–3, or more).

Of the variables related to the use of preventive measures we analyzed: frequency of regular gynecological examinations (once a year once every two years less than once in two years never) and time when the last Pap test was done

(during the last year 1–3 years ago more than 3 years ago more than 5 years ago I do not remember never). Pap testing reasons (own decision on doctor's advice in the screening) were also analyzed.

All the above mentioned data are presented and compared with each other in relation to place of residence (urban/rural, urban = 0, rural = 1).

To find out whether the place of respondents' residence was a key factor influencing upon women's decision to practice prevention for cervical cancer, the variables (regular gynaecological examination, during the last Pap test and reasons for it) were analyzed as dependent ones and place of the residence as an independent one. Dependent variables were regular gynecological examinations (once a year, less than once a year), time of the last Pap test (in the last year, infrequently) and the reason for the Pap test (on their own initiative, on doctor's advice).

All the data were analyzed in accordance with the methods of descriptive and inferential statistics. The difference in distribution of the mentioned variables among women living in rural and urban areas was tested by the χ^2 test. For the minimum level of statistical significance $p < 0.05$ was used, where $p < 0.01$ was taken as highly statistically significant. Variables shown as highly significant after univariate analysis, were further tested by using multivariate analysis.

The association between gynecological measures preventive application [dependent variables: regular gynecological examinations (once a year, less than once a year), time of the last Pap test (in the last year, infrequently), and reasons for the Pap test (on their own initiative, on doctor's advice)] and sociodemographic factors (independent variables) was tested by both univariate and multivariate logistic regression analysis. Multivariate logistic regression model was created by adding place of living. Associations were expressed by the odds ratio (OR) and 95% of the confidence interval (95% CI).

Analyses were performed by using the SPSS software (version 19).

Results

The study included women aged 25 to 65 years (mean age 44.9 ± 11.3 years). Table 1 shows the frequency and the results of the univariate logistic regression for sociodemographic characteristics of respondents by the place of living.

Table 1

The frequency of demographic and socioeconomic characteristics of the studied women population

Variables	Place of living			
	Total, n (%)	Urban, n (%)	Rural, n (%)	*p*
Age (years) mean ± SD	44.9 ± 11.3	4.47 ± 11.0	45.0 ± 10.8	
Age (years)	5314 (100.0)	2951 (55.5)	2363 (44.5)	0.593
25–34	1216 (22.9)	673 (22.8)	543 (23.0)	
35–44	1293 (24.3)	731 (24.8)	562 (23.8)	
45–54	1482 (27.2)	803 (27.2)	679 (28.7)	
55–64	1323 (24.9)	744 (25.2)	579 (24.5)	
Education	5058(100.0)	2809 (55.5)	2249 (44.5)	< 0.000
elementary	1768 (35.0)	640 (22.8)	1128 (50.2)	
secondary	2526 (49.9)	1556 (55.4)	970 (43.1)	
university	764 (15.1)	613 (21.8)	151(6.7)	
Wealth Index	5314 (100.0)	2951 (55.5)	2363 (44.5)	< 0.000
the poorest	904 (17.0)	200 (6.8)	704 (29.8)	
poor	1107 (20.8)	395 (13.4)	712 (30.1)	
average	1137(21.4)	557 (18.9)	580 (24.5)	
moderately	1105 (20.8)	823 (27.9)	282 (11.9)	
the wealthiest	1061(20.0)	976 (33.1)	85 (3.6)	
Region	531 (100.0)	2951 (55.5)	2363 (44.5)	< 0.000
Vojvodina	1345 (25.3)	805 (27.3)	540 (22.9)	
Belgrade	968 (18.2)	729 (24.7)	239 (10.1)	
Central Serbia	3001 (56.5)	1417 (48.0)	1584 (67.0)	
Children	5058 (100.0)	2809 (55.5)	2249 (44.5)	< 0.000
0	542 (10.7)	360 (12.8)	182 (8.1)	
1	958 (18.9)	595 (21.2)	363 (16.1)	
2	2837(56.1)	1498 (53.3)	1339 (59.5)	
> = 3	611 (12.1)	285 (10.1)	326 (14.5)	

There were no differences in the age of women living either in urban or in rural areas of Serbia ($p = 0.593$). The number of examinees of all the age groups was equal both for those living in urban and rural regions (22–28%). With regard to the number of children, the difference is significant: in rural areas there are more women with two, three or more children. As for education, women with secondary or high educational level considerably more often live in urban areas. According to the socioeconomic status more women belonging to the category of the wealthiest live in urban areas in comparison with those living in rural ones.

Table 2 shows the number of variables related to women's sexual behaviour in relation to the place of residence. Concerning the number of partners (not regular), there is no difference between respondents from rural and urban areas ($p = 0.931$). Also, there is no difference in the number of abortions ($p = 0.452$) among women living either in rutral or urban areas. In our sample, respondents from rural areas are more often younger when start with sexual relationships than those from urban environment ($p < 0.000$).

Table 3 shows the variables related to applications of preventive measures against cervical cancer in Serbia by the women's place of residence. Respondents from urban areas apply them considerably more often (gynecologycal examination and Pap test), in comparison with those from the rural areas ($p < 0.000$). Respondents from urban areas considerably more often do Pap test on their own, unlike those from the villages who more often do it owing to the doctor's advice.

Table 4 shows the results of the univariate regression analysis. Whether the respondents' place of residence is the key factor influencing upon women's decision to apply preventive measures for cervical cancer, then variables (regular gynecological examination during the last Pap test and the reasons for

Table 2

The frequency of sexual and other behavior in the studied women by the place of living

Variables	Place of living			
	Total, n (%)	Urban, n (%)	Rural, n (%)	*p*
Age of first sexual intersourse (years)	4642 (100.0)	2610 (56.2)	2032 (43.8)	< 0.000
>16	843 (18.2)	401 (15.4)	442 (21.8)	
17–19	1992 (42.9)	1116 (42.8)	876 (43.1)	
20–22	1331 (28.7)	794 (30.4)	537 (26.4)	
23–25	367 (7.9)	225 (8.6)	142 (7.0)	
> = 26	109 (2.3)	74 (2.8)	35 (1.7)	
Partner in the last 12 months	128 (100.0)	90 (70.3)	38 (29.7)	0.931
1	90 (70.3)	64 (71.1)	26 (68.4)	
2	20 (15.6)	14 (15.6)	6 (15.8)	
> = 3	18 (14.1)	12 (13.3)	6 (15.8)	
Abortus	2129 (100.0)	1175 (55.4)	984 (44.6)	0.452
0	988 (45.8)	531 (45.2)	457 (46.4)	
1	328 (15.2)	175 (14.9)	153 (15.5)	
2	375 (17.4)	199 (16.9)	176 (17.9)	
> =3	468 (21.7)	270 (23.0)	198 (20.1)	

Table 3

The frequency of preventive practice relevant to women for cervical cancer by the place of living

Variables	Place of living			*p*
	Total, n (%)	Urban, n (%)	Rural, n (%)	
Regular check-ups	4927 (100.0)	2755 (55.9)	2172 (44.1)	< 0.000
once a year	1642 (33.3)	1051 (38.1)	591 (27.2)	
once a two year	501 (10.2)	296 (10.7)	205 (9.4)	
rarely	1543 (31.3)	814 (29.5)	729 (33.6)	
not at all	1208 (24.5)	576 (20.9)	632 (29.1)	
PAP test in the last 12 months	5058 (100.0)	2809 (55.5)	2249 (44.5)	< 0.000
within the last 12 months	1006 (19.9)	672 (23.9)	334 (14.9)	
1–3 years ago	821 (16.2)	535 (19.0)	286 (12.7)	
more than 3 years ago	292 (5.8)	192 (6.8)	100 (4.4)	
more than 5 years ago	491 (9.7)	316 (11.2)	175 (7.8)	
rarely	254 (5.0)	131 (4.7)	123 (5.5)	
never	1862 (36.8)	838 (29.8)	1024 (45.5)	
I do not know what that is	310 (6.1)	109 (3.9)	210 (8.9)	
Reason for PAP test	2632 (100.0)	1731(65.8)	901(34.2)	< 0.000
self initiated	769 (29.2)	583 (33.7)	186 (20.6)	
following doctor’s advice	1695 (64.4)	1035 (59.8)	660 (73.3)	
following call for screening	130 (4.9)	88 (5.1)	42 (4.7)	

Table 4

Use of preventive practices: univariate logistic regression analysis

Place of living	Regular check-ups Yes / No		Last Pap smear Yes / No		Reasons for Pap smear self-initiated / screening	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Urban	1.00	<0.001	1.00	<0.001	1.00	<0.001
Rural	0.60 (0.54–0.68)		0.55 (0.48–0.64)		0.51 (0.42–0.62)	

it), were all analyzed as dependent, but the place of residence as an independent one. Respondents from the rural areas had gynecological examination less than once a year in comparison with those from the urban areas (OR = 0.60, 95% Cl 0.54–0.68). Less women from rural areas did Pap test during the last 12 months in comparison with respondents from urban areas (OR = 0.55, 95% Cl 0.48–0.64). Respondents from the urban areas less often did the Pap test on doctor's advice in comparison with those from the rural one (OR = 0.55, 95% Cl 0.42–0.62).

Table 5 shows results of multivariate regression analysis for cervical cancer preventive measures (regular gynecological examinations and during the last Pap test). Multivariate logistic regression showed that the difference in implementation of cervical cancer preventive measures present between respondents from urban and rural areas were not caused by the place of living, but by their educational level and financial status being lower in women from the rural areas. The middle aged and older respondents went to preventive examination for cervical cancer less often than the youger ones (aged 25–34 years). College-educated women often go to preventive gynecological examinations in comparison with those with only primary school education (OR = 1.32, 95% Cl 1.10–1.58). The richest women in comparison with the poorest ones went often to control gynecological examinations (OR = 1.29, 95% Cl 1.05–1.52). In the last 12 months the Pap test was more often performed in college-educated women in comparison with those with primary education (OR = 1.42, 95% Cl 1.17–1.72). When compared with the poorest women, the richest ones went to the Pap tests more frequently in the last 12 months (OR = 1.27, 95% Cl 1.04–1.56). Age was also a factor influencing upon women's decision to do preventive controls. The oldest category subjects rarely went to preventive gynecologic examinations in comparison with the youngest ones (25-34 years), (OR = 0.41, 95% Cl 0.4–0.50) and to the Pap test (OR = 0.44, 95% Cl 0.35–0.55).

Table 6 shows the results of the multivariate regression analysis of the reasons to go to the Pap test. This analysis shows that the difference existing between the respondents from urban and rural areas is not only caused by the place of respondents' living, but also by their educational and financial status being lower in women from rural areas. Urban areas respondents did the Pap test less often on doctor's advice than on their own initiative (OR = 0.79, 95% Cl 0.63–1.00). Age was not a factor influencing upon reason for the Pap test. Only those aged 35–44 years did the Pap test less often on the doctor's advice in comparison with younger than 35 years (OR = 0.75, 95% Cl 0.58–1.00).

Table 5

Regular check-ups and last Pap smear: controlled (multivariate) logistic regression analysis

Variables	Regular check-ups yes / no		Last Pap smear yes / no	
	AOR* (95% CI)	*p*	AOR* (95% CI)	*p*
Place of living				
urban	1.00		1.00	
rural	0.93 (0.80–1.08)	0.334	0.95 (0.80–1.13)	0.590
Education				
elementary	1.00		1.00	
secondary	2.24 (1.79–2.80)	< 0.000	1.91 (1.48–2.45)	< 0.000
university	1.32 (1.10–1.58)	0.003	1.42 (1.17–1.72)	< 0.000
Walth index				
the poorest	1.00		1.00	
poor	2.51 (1.73–2.88)	< 0.000	3.53 (2.57–4.85)	< 0.000
average	1.94 (1.45–2.23)	< 0.000	3.11(2.38–4.05)	< 0.000
moderately wealthy	1.74 (1.40–2.08)	< 0.000	1.63 (1.30–2.04)	< 0.000
the wealthiest	1.29 (1.05–1.52)	0.008	1.27 (1.04–1.56)	0.018
Age (years)				
25–34	1.00		1.00	
35–44	0.21 (0.17–0.26)	< 0.000	0.39 (0.31–0.50)	< 0.000
45–54	0.36 (0.30–0.49)	< 0.000	0.43 (0.37–0.54)	< 0.000
55–64	0.41 (0.34–0.50)	< 0.000	0.44 (0.35–0.55)	< 0.000

***ajusted for education, wealth index and age; **$p < 0.01$.**

Table 6

The reasons for PAP smear: controlled (multivariate) logistic regression analysis

Variables	Reasons for Pap smear self-initiated / screening	
	AOR* (95% CI)	*p*
Place of living		
rural	1.00	
urban	0.79(0.63–1.00)	0.041
Education		
elementary	1.00	
secondary	2.35 (1.69–3.26)	< 0.000
university	1.26 (1.02–1.55)	0.034
Wealth idex		
the poorest	1.00	
poor	2.43 (1.55–3.81)	< 0.000
average	1.91 (1.40–2.61)	< 0.000
moderately wealthy	2.00 (1.52–2.62)	< 0.000
the wealthiest	1.42 (1.14–1.78)	0.002
Age (years)		
25–34	1.00	
35–44	0.75 (0.58–1.00)	0.042
45–54	0.88 (0.68–1.15)	0.359
55–64	1.01 (0.78–1.30)	0.934

*** adjusted for education, wealth index and age; **$p < 0.01$.**

Discussion

The aim of this study was to examine applications of preventive measures among women in rural and urban areas of Serbia and to identify whether they have any association with women′s sociodemographic characteristics and sexual behaviour.

It was found out that women in rural areas rarely apply preventive measures against cervical cancer (gynecological controls and Pap tests) in comparison with those living in urban areas. However, after considering effects of educational level, socioeconomic status and age, this difference was no longer significant. Women from rural areas, less educated, and with lower socioeconomic status, middle-aged and elderly, rarely apply preventive measures against cervical cancer.

Numerous studies have identified demographic and behavioural factors associated with cervical cancer prevention [12, 20]. Higher socioeconomic status is associated with more frequent application of preventive measures against cervical cancer in female population on the Belgrade territory [21].

Our study confirms that girls from the rural areas often have sexual activities before the age of 16 years in comparison with those from urban areas. The majority of our respondents had the first sex at the age of 19. Early sexual activity is a risk factor for reproductive organs health and for sexually transmitted diseases (STDs) including HPV infections [3]. In the study performed by Stanković et al. [22], most of girls have sexual activities at the age of 17.9. Asked about the number of not regular partners within the last 12 months, only 2.4% of respondents answered. According to the obtained answers there was no difference between respondents' place of residence. Having more sexual partners is a risk factor for reproductive organs health and numerous studies emphasize the importance of reducing irregular partners number for cervical cancer prevention [7]. As for the number of abortions, 40.3% of respondents gave this information with no significant differences with regard to the place of respondents' residence. These data are inconsistent with the study written by Rasevich and Sedlecki [23] in which the projected number of abortions in Serbia was over 200,000 a year. However, registered data on induced abortions since 1999 are not reliable (the number of registered abortions in 2000 was 42,322 and in 2007 was 24,273).

According to our results, women from urban areas considerably more often go to gynecological examinations in comparison with those from rural areas. Also, the Pap test once a year did significantly more respondents from urban than from rural areas. The fact that every other woman from rural area as well as one-third of those from urban environment have never done a Pap test. Since the same number of women (4,894) in our study gave information about gynecological examination and the Pap test, but because their medical reports were not used for verification of their statements, we could not confirm that any of them did both gynecological examination and the Pap test. The fact that 8.9% of women from rural areas do not know what kind of a test it is, our results may appear to be doubtful. In a study on Serbian population health in 2006, in a sample of women older than 20 years, 6.3% of respondents had never visited a gynecologist. Organized prevention activities and screening cover only a small part of female population and there are also considerable geographic differences and variations by the type of a settlement (5.2%) in Eastern Serbia where the incidence of cervical cancer is highest). Many women do not go to gynecological examination because they are symptomless and have finished the reproductive function, postmenopausal and elderly women from rural areas [16].

In our study as a part of the organized screening, the Pap test was done only by 4.7% of women in rural areas and by 5.1% of them in urban ones. Women from rural areas were screened more frequently upon gynecologist's advice, as a type of opportune screening. Women from urban areas did more frequent Pap screening independently. The study by Spaczinski et al. [20] as well as our study confirm that women from villages less often than those from urban areas comply to the Pap screening. Some studies indicate that Pap screening is associated with the socioeconomic women's status [11, 24]. This study as well as those by Franceschi et al. [5], Sabates and Feinstein [11], and Spaczynsky et al. [20] confirm that higher level of education is an important factor for women's decision to initiate the Pap screening test.

Screening was conducted in some other countries such as Hungary until 2003, but it did not offer satisfying results aiming to reduce morbidity and mortality rate from cervical cancer [25]. Efforts to prevent cervical cancer in women are worldwide focused on organized screening and treatment of precancerous lesions. When screening of high quality and coverage were realized, the incidence of invasive forms of cervical cancer in Serbia was reduced even by 90% [26]. Since 2012 in Serbia a classical cytodiagnostics has been applied as a part of the programme of organized cervical cancer screening [19]. American Association of Obstetrics and Gynecology and the European Association for Infectious Diseases in Gynecology and Obstetrics have given different recommendations for screening such as: to initiate screening at the age of 21 with a 2-year intervals up to 30 years of age and afterwards, combination of ligniol based cytology (LBC) and HPV testing at a 3-year intervals. This instruction was aimed to prevent many unnecessary tests for women who are not at risk of cervical cancer [27, 28]. Only 16 European Union countries have organized the National Screening Programme for cervical cancer and they applied it for women aged 20–30 and 60–65 years after 3- or 5-year intervals [29].

In Poland, highly educated women from urban areas more frequently do screening in private health institutions [20]. Numerous studies both from developed countries, Greece, Sweden as well as from China and South Africa confirmed the association between the place of residence and preventive measures against cervical cancer, with more frequent application of preventive measures in urban female population [30–32, 14].

Conclusion

Our study shows that women in rural areas rarely implement preventive gynecological measures against cervical

cancer in comparison with those in urban areas. Women from rural areas have more risk factors (early sexual relationships, higher parity, lower educational and socioeconomic status). Implementation of preventive measures among rural women is conditioned by lower levels of education and lower socioeconomic status. A particular attention should be paid to reducing identified differences. Education and preventive gynecological practices should be provided and available to rural women.

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Competing interests

None declared.

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A novel framework for fluid/structure interaction in rapid subject-specific simulations of blood flow in coronary artery bifurcations

Nova platforma za brzo simuliranje interakcije fluida i strukture pri strujanju krvi kroz realne geometrije bifurkacija koronarne arterije

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Abstract

Background/Aim. Practical difficulties, particularly long model development time, have limited the types and applicability of computational fluid dynamics simulations in numerical modeling of blood flow in serial manner. In these simulations, the most revealing flow parameters are the endothelial shear stress distribution and oscillatory shear index. The aim of this study was analyze their role in the diagnosis of the occurrence and prognosis of plaque development in coronary artery bifurcations. **Methods.** We developed a novel modeling technique for rapid cardiovascular hemodynamic simulations taking into account interactions between fluid domain (blood) and solid domain (artery wall). Two numerical models that represent the observed subdomains of an arbitrary patient-specific coronary artery bifurcation were created using multi-slice computed tomography (MSCT) coronagraphy and ultrasound measurements of blood velocity. Coronary flow using an in-house finite element solver PAK-FS was solved. **Results.** Overall behavior of coronary artery bifurcation during one cardiac cycle is described by: velocity, pressure, endothelial shear stress, oscillatory shear index, stress in arterial wall and nodal displacements. The places where (a) endothelial shear stress is less than 1.5, and (b) oscillatory shear index is very small (close or equal to 0) are prone to plaque genesis. **Conclusion.** Finite element simulation of fluid–structure interaction was used to investigate patient-specific flow dynamics and wall mechanics at coronary artery bifurcations. Simulation model revealed that lateral walls of the main branch and lateral walls distal to the carina are exposed to low endothelial shear stress which is a predilection site for development of atherosclerosis. This conclusion is confirmed by the low values of oscillatory shear index in those places.

Key words:
models, theoretical; computer simulation; coronary vessels; blood flow velocity; atherosclerosis; risk factors.

Apstrakt

Uvod/Cilj. Praktične poteškoće, posebno dugo vreme razvoja modela, ograničavaju tipove i primenljivost računske dinamike fluida u numeričkom modeliranju strujanja krvi za veći broj bolesnika. U ovim simulacijama, parametri strujanja koji najviše pokazuju su endotelijski smicajni napon i oscilujući smicajni indeks. Cilj rada bio je da se analizira njihova uloga u dijagnozi i prognoziranju razvoja plaka na račvama (bifurkacijama) koronarnih arterija. **Metode.** Razvili smo novu tehniku kompjuterskog modeliranja za potrebe brzih kardiovaskularnih hemodinamičkih simulacija uzimajući u obzir interakcije između domena fluida (krv) i domena strukture (arterijskog zida). Generisana su dva numerička modela koja predstavljaju posmatrane poddomene bifurkacije koronarne arterije slučajno izabranog bolesnika, korišćenjem multi-slajsne kompjuterizovane tomografije (MSCT) koronarografije i ultrazvučnog merenja brzine strujanja krvi. Simulacija koronarnog strujanja je izvršena korišćenjem sopstvenog softvera PAK-FS. **Rezultati.** Sveukupno ponašanje strujanja krvi u bifurkacijama koronarnih arterija je opisano preko sledećih parametara: brzina, pritisak, endotelijski smicajni napon, oscilujući smicajni indeks, napon na zidu arterije i čvorna pomeranja. Mesta gde je (a) endotelijski smicajni napon manji od 1,5 i (b) oscilujući smicajni indeks veoma mali (blizak ili jednak 0) su sklona razvoju plaka. **Zaključak.** Simulacija interakcije fluida-strukture metodom konačnih elemenata je korišćena da se ispitaju dinamika strujanja krvi i mehaničke karakteristike zida bifurkacije koronarne arterije slučajno izabranog bolesnika. U numeričkom modelu je otkriveno da lateralni zidovi glavne grane i lateralni zidovi distalno od karine imaju nizak endotelijski smicajni napon što je preduslov za razvoj ateroskleroze na tim mestima. Ovaj zaključak je potvrđen i niskim vrednostima oscilatornog smicajnog indeksa na istim mestima.

Ključne reči:
modeli, teorijski; simulacije, kompjuterske; koronarni krvni sudovi; krv, brzina protoka; ateroskleroza; faktori rizika.

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Introduction

Bifurcation sites of human arteries are among the most frequent locations affected by atherosclerosis, being involved in up to 20% of percutaneous interventions. Several studies on the distribution of atherosclerotic plaques in human arterial systems have shown that atherosclerosis occurs predominantly at branching locations of the vascular tree where the arteries have relatively complex geometry that result in disturbed blood flow behavior [1–2]. In these regions, complex hemodynamic conditions prevail and local flow disturbances dictate the localization and progression of atheroma. Endothelial shear stress (ESS), as the main local flow-related factor, was investigated for the first time on computational fluid dynamics models of carotid and coronary bifurcation [3] and distal abdominal aortas [4] based on autopsy material. Those studies demonstrated that areas with low ESS correlate with atherosclerotic plaque development confirmed at autopsy [5]. In addition, several *in vivo* experiments on animal models confirmed proatherogenic effects of low ESS [6]. Recently human *in vivo* studies of arterial models derived from multislice computed tomography (MSCT) or intravascular ultrasound demonstrated the role of low ESS in the initiation and progression of atherosclerosis and arterial remodeling [7]. According to ESS spatial distribution plaques are more prevalent in low ESS areas, lateral walls of the main vessel and side branches, while they are less common in the flow divider or carina, which is characterized by high ESS [8]. Recent basic research studies have shed light on the precise pathways by which low ESS leads to atherosclerosis [5].

Over the years, mathematical modeling has become complementary to experimental testing in predicting the biomechanical behavior and investigating clinical problems [9, 10]. Finite element analysis allows us to repeat numerical experiments changing some parameters, thus analyzing the effect and influence of a single component within the observed phenomenon [11, 12]. While multiphysics problems, particularly fluid–structure interaction (FSI) problems, are too complex to solve analytically, computational simulations have become a useful tool in studying blood flow in the cardiovascular system. Coupled problems require software to analyze the fluid domain (blood) and the solid domains (artery wall).

There are many reports in which the arterial wall is observed as rigid. Some papers report that wall deformation caused by interaction between the blood flow and artery wall changes the hemodynamic forces acting on the arterial wall compared to the rigid wall simulation [13, 14]. Rigid wall simulations overvalue the magnitude and the distribution of ESS on the arterial wall [14, 15].

The aim of this study was to present a new computational framework for rapid modeling, considering a fluid structure interaction, and calculation of ESS and oscillatory shear index (OSI) of atherosclerotic plaque free coronary artery bifurcation obtained from MSCT, as well as to prove if specific bifurcation segments (lateral walls of main vessel, side branch lateral walls) correlate with low ESS and discuss the influence of this local hemodynamics conditions for potential plaque formation.

Methods

Definition of ESS and flow characteristics

ESS is the component of stress coplanar with an endothelial surface caused by the friction of the flowing blood and the arterial wall. ESS is expressed in units of force *per* unit area (1 N/m2 = 1 Pascal [Pa] =10 dyne/cm2) [16, 17].

In relatively straight segments of the artery, ESS is pulsatile and unidirectional and varies within a range of 1.5 to 3 Pa (physiological ESS) throughout the cardiac cycle and yields a positive time-average [18, 19]. In contrast, in arteries with geometrically irregular regions, and disturbed laminar flow, pulsatile flow causes low and/or oscillatory ESS. Low ESS may be unidirectional at any point, but has a periodically fluctuating magnitude in a considerably low time-average (less than 1–1.5 Pa) [18–20]. Low ESS usually appears at the inner segments of curvatures and upstream of stenosis [16]. Oscillatory ESS is described by changes in both directions (bidirectional) and magnitude between systole and diastole, with a result of very low time-average, commonly close to 0 [18, 19]. Oscillatory ESS qualifies predominantly downstream of stenosis, at the bifurcation lateral walls, and in the area of branch points [3, 19, 21–22].

The OSI is a dimensionless index that describes the variation of ESS at the arterial wall during the cardiac cycle taking into account only the changes of ESS direction [23]. At the places where ESS have extreme changes the value of this index is 0.5. As opposed, at the places where ESS have no changes the value of this index is 0.

Numerical simulation was performed on one model of plaque-free coronary artery bifurcation based on MSCT coronary angiography.

Fluid-structure interaction governing equations

Fluid and structure occupy different subdomains, thus their system of equations can be set-up individually within their subdomains. The governing equations for the fluid domain are based on the Navier-Stokes equations and the equation of continuity [24]. These equations can be expressed in the matrix form as:

$$\mathbf{M}_f \dot{\mathbf{V}} + \mathbf{K}_{vv}\mathbf{V} + \mathbf{K}_{vp}\mathbf{P} = \mathbf{F}_v \quad (1)$$

$$\mathbf{K}_{vp}^T \mathbf{V} = 0 \quad (2)$$

where $\mathbf{M}_f$ is the mass matrix, $\mathbf{K}_{vv}$ is the convective matrix, $\mathbf{K}_{vp}$ is the matrix of pressure gradient, $\mathbf{F}_v$ is the vector of external forces. The vectors $\dot{\mathbf{V}}$ and $\mathbf{V}$ represent the acceleration and velocity of fluid. A discrete system of equations for the dynamics of solids is:

$$\mathbf{M}\ddot{\mathbf{U}} + \mathbf{C}\dot{\mathbf{U}} + \mathbf{K}\mathbf{U} = \mathbf{F}_s \quad (3)$$

where $\mathbf{M}$ is the constant mass matrix, $\mathbf{C}$ is the constant damping matrix, $\mathbf{K}$ is the stiffness matrix which may depend on displacement, $\mathbf{F}_s$ is the vector of external forces

and $\ddot{\mathbf{U}}, \dot{\mathbf{U}}, \mathbf{U}$ are the vectors of acceleration, velocity and displacement, respectively. A detailed explanation of variables in the equations 1–3 is available in [24–26].

Among others, we calculate the distribution of OSI and ESS in the desired number of discrete time instants within the cardiac cycle. ESS was calculated based on the equation:

$$ {}^{t}\tau_{ij} = \mu \frac{\partial^{t} v_t}{\partial n}\bigg|_{wall} \tag{4} $$

where τ_{ij} are the components of endothelial shear stress, μ is the dynamic viscosity, v_t is the tangential velocity and n is the direction of a unit vector normal to the wall at the moment t.

The OSI was calculated based on equation:

$$ OSI = \frac{1}{2}\left(1 - \frac{\left|\frac{1}{T}\int_0^T \mathbf{t}_s dt\right|}{\frac{1}{T}\int_0^T |\mathbf{t}_s| dt}\right) \tag{5} $$

where $\mathbf{t}_s$ is the surface shear vector, defined as:

$$ \mathbf{t}_s = \mathbf{t} - (\mathbf{t}\cdot\mathbf{n})\mathbf{n} \tag{6} $$

and $\mathbf{t}$ is the shear vector, defined as:

$$ \mathbf{t} = \boldsymbol{\sigma}\cdot\mathbf{n} \tag{7} $$

In the equation (7) $\boldsymbol{\sigma}$ is the stress tensor.

Simulation code

The two main approaches for the numerical simulation of fluid–structure interaction problems are: (a) monolithic approach (strong coupling), and (b) partitioned approach (weak coupling). The monolithic approach involves the development of new software, while the partitioned approach uses the existing software to solve new classes of problems. The software PAK-FS is developed by coupling existing computational solid dynamics (CSD) software PAK-S and computational fluid dynamics (CFD) software PAK-F the using partitioned approach [27]. The algorithm of developed code is shown in Figure 1. This algorithm partially separates the used solvers in space. As boundary conditions the CFD program uses the current geometry of the interface and the velocity of the interface nodes. This information is obtained from the CSD program for solving the solids. On the other hand, loads from the fluid domain obtained using the CFD program is transmitted to CSD program.

Model generation

The finite element method requires the physical domain in which the problem is discretized. To date, the methodologies to characterize local shear stress distribution and other hemodynamic parameters in circulation have been used for research purposes only, because no tools are available to provide this information in a routine manner. Artery bifurcations may have a very complicated configuration [28]. Lately, the trend and need is patient-specific modeling [29, 30]. It is very challenging to generate quality hexahedral meshes for complicated structures [31]. The hexahedral mesh quality has a significant role in the simulation by the finite element method [32]. This is very important in CFD, where numerical errors become visible in the flow field. During generating procedures and developing software for the creation of the finite element model the authors have sought to satisfy all the listed constraints.

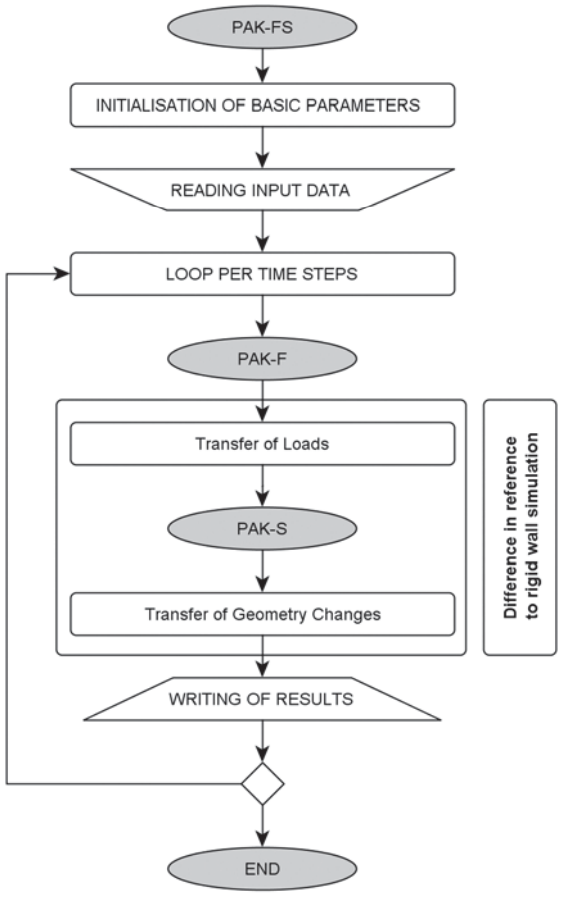

Fig. 1 – Global algorithm of software PAK-FS. The labeled part of the algorithm takes into account the interaction between blood and arterial wall. Omitting this part of the algorithm, the calculation of hemodynamics parameters inside the lumen is reduced to the case when the arterial wall is approximated as a rigid.

The original images, comprising MSCT image data of the human coronary artery bifurcation, were acquired from patients of Clinical Center of Serbia using a CT750HD scanner (Discovery, General Electric) [33]. Image segmentation and geometry identification of the blood vessels were made in the software Mimics (Figure 2).

Structured mesh generation is the most appropriate method for discretizing domains. It produces a body fitted mesh, exactly describing domain's boundaries and hence boundary conditions can be accurately modeled. Application of structured mesh for complex arterial geometries is very difficult or infeasible. Hence, the entire computational model

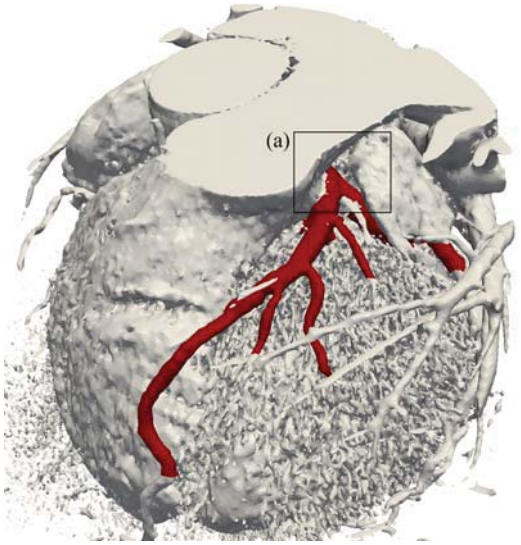

Fig. 2 – Volumetric model obtained from the original multislice computed tomography (MSCT) data. The left coronary artery is marked in red. The modeled segment of plaque free coronary artery bifurcation is marked with (a).

is subdivided into the number of small blocks [34]. Blocks are generated around a volumetric model (Figure 3a). This topology of building blocks is used to generate the finite element mesh of real patient-specific bifurcation of coronary artery using structured mesh techniques (Figures 3b and 3c). Blocks are then linked together to produce finite element mesh describing arterial lumen. The described method is implemented in in-house rapid mesh generator STL2FEM. The two obtained computational models are generated in less than an hour.

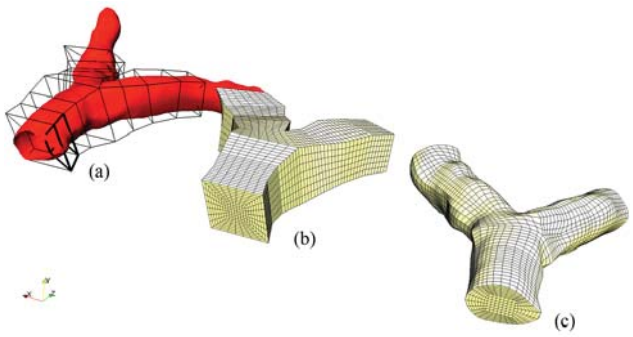

Fig. 3 – Multiblock approach implemented in a rapid mesh generator stl2fem: (a) topology of building blocks, (b) computational model before mapping to the real model, and (c) computational model. Blocks [bold lines in (a)] are represented by 8-node hexahedrons, described by vertices and edges.

Quadratic 8-node isoparametric elements are generated using transfinite interpolation without smoothing [35]. The solid domain is modeled by linear 4-node quadrilateral (shell) elements. The solutions were obtained using 20,237 elements and 21,848 nodes for lumen while arterial wall contains 2,303 elements and 2,344 nodes (Figure 4).

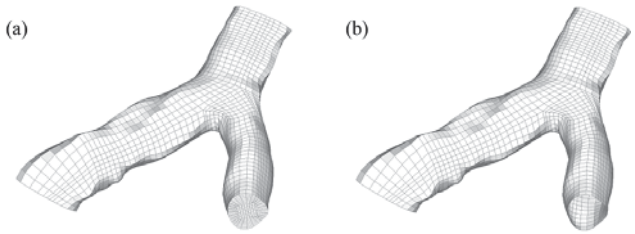

Fig. 4 – Finite element models of (a) arterial lumen and (b) arterial wall of the studied patient's coronary bifurcation. The numerical models exactly fit in the real coronary artery bifurcation.

Initial and boundary conditions

According to Perktold et al. [36, 37], blood is approximated as an incompressible Newtonian fluid with the density of 1,050 kg/m^3 and a dynamic viscosity of 0.003675 Pas. Blood vessel walls are modeled with a linearly elastic material with the Poisson's ratio of 0.49, the wall density of 1100 kg/m^3, and the uniform wall thickness of 0.8 mm. One cardiac cycle (0.89 s) is simulated in 20 steps with the time step size of 44.49 ms. The maximal diastolic flow velocity in the inlet is 23 cm/s. The velocity profile used for simulating pulsatile flow is shown in Figure 5. For fluid–structure interface, small displacements of the vessel wall are assumed, while the lumen mesh is fixed [12].

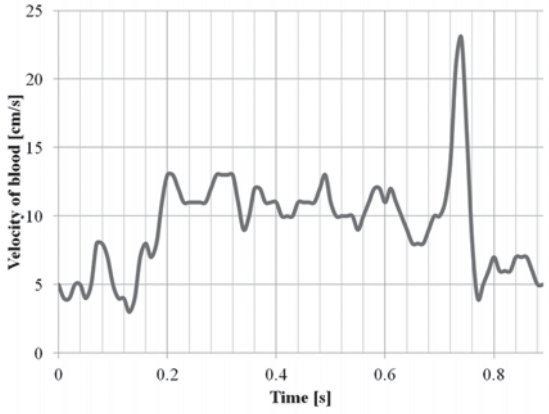

Fig. 5 – Maximal velocity profile in one human's cardiac cycle. When viewed in cross-section plane, velocity is increased gradually. Velocity profile is parabolic: the value of velocity near to the arterial wall is equal to 0, and value at the center of the vessel's cross section has a maximum value. The obtained ultrasound measurement of the flow rate gives the amount of blood that elapses through the vessel's cross section in the time unit. The maximal velocity value is determined on the basis of equality of volumetric flows through vessel's cross section calculated based on the maximal and mean velocities.

The mesh discretization of the fluid and the structure on the interface are compatible. The nodes of the solid model in the inlet section of the artery are constrained to have no displacement in the direction of fluid moving. Velocities of nodes on the contact surfaces are equal. We calculate ESS, OSI index, velocity, pressure and equivalent stress in coronary artery wall throughout the cardiac cycle.

Results

Endothelial shear stress in some steps is shown in Figure 6. The calculated values of ESS through the cardiac cycle were from the lowest 0.03 Pa to 3.3 Pa. Low ESS was present in specific bifurcation segments: main branch lateral wall, lateral wall distal to carina, and lateral carina wall. In this segments ESS values were in the range from 0.03 Pa (in lateral wall distal to carina at the beginning of the cycle) to 0.8 (at the main branch lateral wall). Consequently, for specific segments: ESS of main branch lateral wall 0.07–0.8 Pa, carina lateral wall was 0.04–0.37 Pa and lateral wall distal to carina 0.03–0.3) (Figure 7). In contrast, the highest ESS was at the main branch anterior wall. A more complete picture of hemodynamic conditions inside the lumen gives the OSI index (Figure 8). In specific low ESS bifurcation segments OSI index is 0 or close to 0. Areas with high values (up to 0.5) of this index are characterized by changes in the ESS direction. On the other hand, the places where this index is very small (close or equal to 0) are disposed to plaque genesis.

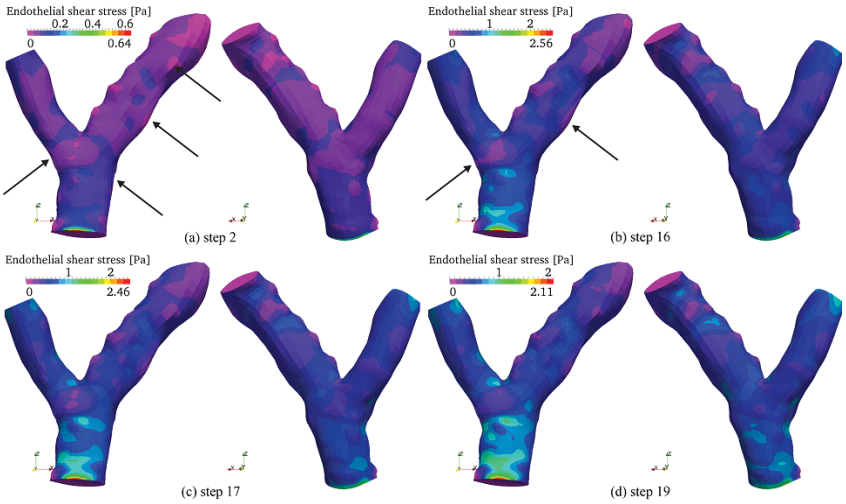

Fig. 6 – Endothelial shear stress in some steps of the cardiac cycle: lateral walls of the main branch, carina lateral walls and lateral walls distal to the carina are exposed to low endothelial share stress (ESS). The arrows indicate low ESS areas.

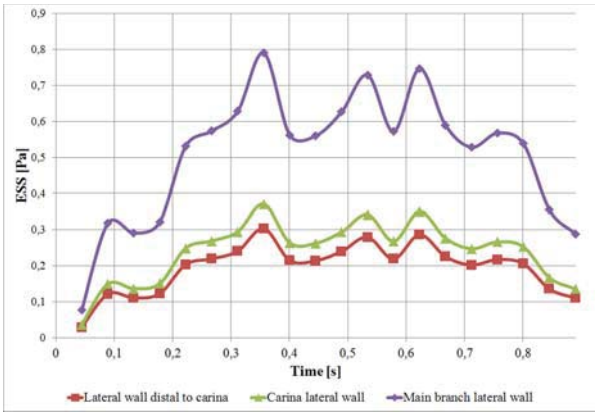

Fig. 7 – Magnitude of endothelial share stress (ESS) throughout the cardiac cycle at specific bifurcation segments characterized with low ESS.

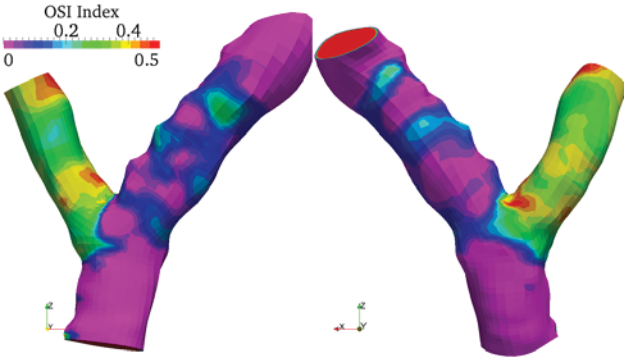

Fig. 8 – Oscillatory shear index: segments with low endothelial share stress (ESS) correlate with oscillatory share index (OSI) index O or close to O. In the areas with the OSI index value of 0 or close to 0 ESS is unchanged in the direction within the cardiac cycle.

The overall picture of hemodynamic conditions prevailing coronary artery complements streamlines and pressure field in the blood (Figure 9), and the equivalent stress in the arterial wall (Figure 10).

Discussion

The main findings of our study are as follows: simulations of fluid–structure interaction can be used in serial manner to investigate patient-specific hemodynamics conditions at the coronary artery bifurcation; CFD coronary artery model reveals that the lateral walls of the main branch and lateral walls distal to the carina are exposed to low ESS which is a predilection site for development of atherosclerosis; thanks to a novel algorithm that we implement, hardware- and time-consuming procedures for the surface reconstruction and computed aided design (CAD) modeling are now completely skipped.

The benefits of applying this procedure in clinical practice are presented on the basis of the numerical results.

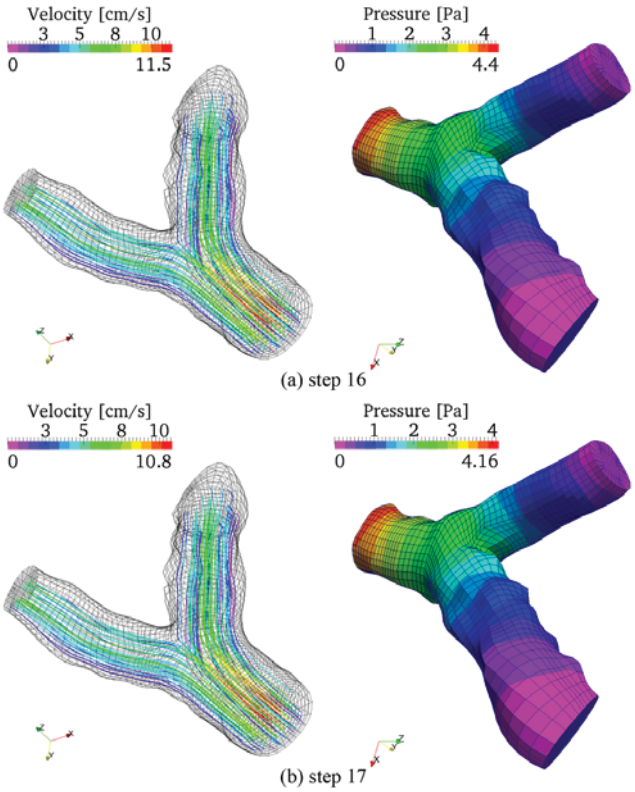

Fig. 9 – Streamlines and pressure in (a) step 16 and (b) step 17 of the cardiac cycle.

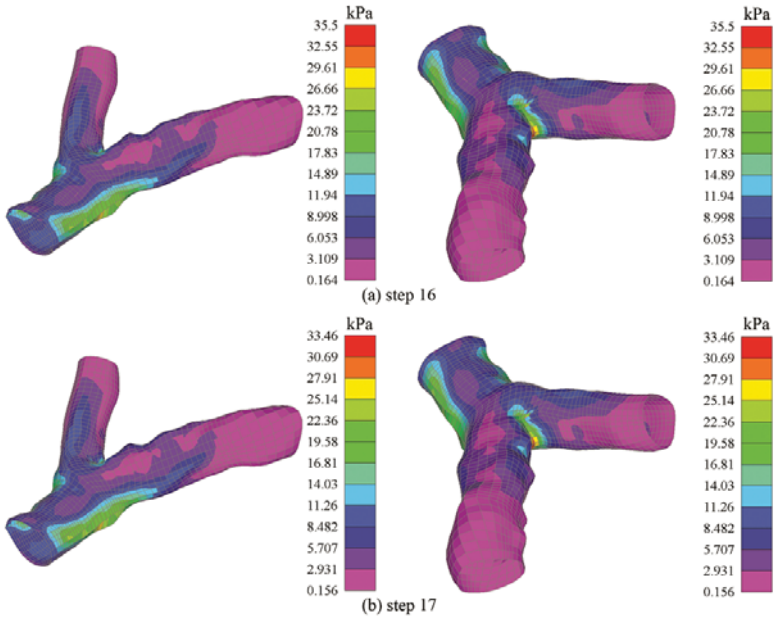

Fig. 10 – Equivalent (Plate top Von Misses) stress in the coronary artery wall: (a) step 16 and (b) step 17. This stress is the response of the arterial wall material to local hemodynamic conditions. Higher values of effective stress indicate higher strain in the arterial wall and *vice versa*. It depends on the material characteristics of the arterial wall. Calcified lesions and other diseases can be taken into account by the experimentally determined mechanical characteristics during arterial wall modeling.

CFD is currently being used as a means of enhancing our understanding fluid flow in arteries, while CSD is used to calculate associated vessel wall forces. In this paper we presented a computational framework for FSI simulation. Making new solvers to simultaneously solve FSI is very difficult and time-consuming task. To successfully solve such interdisciplinary problems, CFD and CSD software that already exists are coupled. The multiblock approach embedded in in-house software STL2FEM is used for mesh generation. It is a very effective tool for generating computational meshes for complex geometries such as artery bifurcations in biomechanics and engineering. This approach dramatically speeds up the process of generating patient-specific finite element bifurcation models with minimum errors in the nu-

merical solution. The methodology was applied to a vascular patient-specific model of coronary artery bifurcation including elastic wall modeling in simulations. Previous considerations indicate that developed computational frame gives useful inputs to cardiologists. Thanks to the obtained results, cardiologists are set in the role of decision makers. They have a clear view of blood flow through a coronary artery bifurcation, so they can suggest optimal treatment strategies.

ESS is one of the most essential factors influencing endothelial structure and function, and it is the main local flow related factor responsible for coronary atherosclerotic plaque formation and progression [2, 5]. A CFD model of plaque free coronary bifurcation reveals that the lateral walls of the main branch, and the lateral walls distal to the carina are exposed to low ESS. Thanks to the clear picture of this parameter behavior during the cardiac cycle, it is possible to predict the positions that are suspectible to plaque with a high probability. Using this facts, formation and progression of atherosclerotic, a plaque can be predicted. This low ESS specific bifurcation segment has higher probability for plaque development. In contrast ESS in the carina region is higher and this area is less likely to develop plaque.

According to several recent studies, low ESS promote atherosclerosis with several mechanisms: through nitric oxide (NO)-dependent athero-protection, increased low-density lipoprotein cholesterol uptake, sustain increase in oxidative stress, inflammation and smooth muscle cell proliferation and migration [5, 20].

Better understanding a complex dynamic interplay between local flow conditions and the plaque formation and progression in bifurcations may express areas of angiographic interest [8]. Plaque distribution may provide a useful information for appropriate technique selection in treatment of complex bifurcation lesions. It gives the operator a chance consider to protection of the side branch with additional wire or to decide in advance between one and two stent techniques. It is also valuable knowledge for future stent designs.

We presented a model of plaque-free coronary artery, but this methodology may be applicable in different clinical and angiographic circumstances. This analysis takes into account only kinematic and dynamic effects. Calcifications on the wall and other disorders are not included in the model because based on current knowledge it was not possible to predict the extent of calcification deposition in relationship with fluid behavior. However, the presence of calcification is possible to simulate in future studies by changing characteristics of the arterial wall at calcification place.

Examining ESS in a diseased coronary artery may enable identification of the initial stages of plaques that potentially evolve a high-risk lesion.

Thanks to rapid modeling, this methodology not only allows characterization of arterial plaque at a single point in time but, also allows prognostic insight into how plaques evolve over time [38]. If it were possible to recognize *in vivo* plaques that were expected to develop features of rupture prone lesions, specific interventions could be performed to avoid adverse cardiac event.

Conclusion

Rapid modeling of patient-specific artery bifurcation opens new avenues in the investigation of the role of ESS in the natural history of atherosclerosis and in future we hope it will be a powerful tool in everyday medical practice in the decision making process for every single patient.

Acknowledgements

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ORIGINAL ARTICLE

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A 60-year expirience in the treatment of pancreatic insulinoma in the Military Medical Academy, Belgrade, Serbia

Lečenje insulinoma pankreasa u Vojnomedicinskoj akademiji, Beograd: 60-godišnje iskustvo

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Abstract

Background/Aim. Insulinomas are rare benign tumors in the most cases and the most frequent endocrine tumors of the pancreas. A wide spectrum of clinical manifestations in patients with insulinoma is the reason for difficult recognition of the disease with a long period of time between the onset of symptoms and the diagnosis. Diagnostic procedures include Whipple's triad, 72-hour fast test and topographic assessment. The only currative therapy for patients with insulinoma is operative treatment. **Methods.** This retrospective study included 42 patients with diagnosis of insulinoma treated in our institution in a 60-year period. In all the patients a demographic and clinical data, types of biochemical methods for diagnosis, and diagnostic procedures for insulinoma localization were analyzed. Tumor size and localization, surgical procedures, postoperative complications and outcome were assessed. **Results.** A study included 42 patients, 29 women and 13 men. The median age at diagnosis was 43 years. Median time between the onset of symptoms and diagnosis was 3 years. The most common clinical symptoms and signs were disturbance of consciousness and abnormal behavior in 73%, confusion and convulsions in 61% of patients. The diagnosis of insulinoma was estimated by Whipple's triad and 72-hour fast test in 14 patients. Determination of insulinoma localization was assessed by angiography in 16 (36%) of the patients, by ultrasound (US) in 3 of 16 (18.8%) patients, by abdominal computed tomography (CT) in 8 of 18 (44.5%) patients, and magnetic resonance imaging (MRI) in 2 of 8 (25%) patients. Insulinoma was found in 13 of 13 (100%) patients by arterial stimulation with venous sampling (ASVS) and in 13 of 14 (93%) patients by endoscopic ultrasound (EUS). Of the 42 patients, 38 (90.5%) underwent operative procedure. Minimal resection was performed in 28 (73.6%) of the patients [tumor enucleation in 27 (71%) and central pancreatectomy in one (2.6%) of the patients], and the major resection was performed in 9 (23.6%) of the operated patients [distal splenopancreatectomy in 8 (21%) and pancreaticoduodenectomy in one (2.6%) patient]. The overall mortality rate in postoperative period was 2.6% (one patient). **Conclusion.** A combination of ASVS and EUS as diagnostic procedures ensures high accuracy for preoperative determination of insulinoma localization. Minimal resection such as enucleation shoud be performed whenever it is possible.

Key words:
insulinoma; diagnosis; digestive system surgical procedures; treatment outcome.

Apstrakt

Uvod/Cilj. Insulinomi su retki, najčešće benigni tumori i najčešći endokrini tumori pankreasa. Širok spektar kliničkih manisfestacija kod bolesnika sa insulinomom razlog je za otežano otkrivanje bolesti sa dugim periodom od početka simptoma do postavljanja dijagnoze. Dijagnoza se postavlja na osnovu Whipple-ove trijade, 72-časovnog testa gladi i morfoloških ispitivanja. Terapija koja može dovesti do potpunog izlečenja je hirurško uklanjanje tumora. **Metode.** Retrospektivnom studijom obuhvaćeno je 42 bolesnika sa dijagnozom insulinoma, lečenih u našoj ustanovi u 60-godišnjem periodu. Kod svih bolesnika analizirane su demografske i kliničke karakteristike, načini postavljanja dijagnoze i dijagnostičke procedure za određivanje lokalizacije insulinoma. Procenjivana je veličina tumora i lokalizacija, vrsta hirurške intervencije, postoperativne komplikacije i ishod lečenja. **Rezultati.** Studijom je obuhvaćeno 42 bolesnika, 29 žena i 13 muškaraca. Medijana starosti u vreme postavljanja dijagnoze bila je 43 godine. Medijana vremena

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proteklog od početka simptoma do dijagnoze bila je tri godine. Najčešći klinički simptomi i znaci bili su poremećaji stanja svesti i ponašanja kod 73%, konfuzija i konvulzije kod 61% bolesnika. Dijagnoza insulinoma potvrđena je pomoću Whipple-ove trijade i 72-časovnog testa gladi kod 14 bolesnika. Lokalizacija insulinoma određena je angiografijom kod 16 (36%) bolesnika, ultrasonografijom (US) kod tri od 16 (18,8%) bolesnika, kompjuterizovanom tomografijom (KT) abdomena kod osam od 18 (44,5%) bolesnika i magnetnom rezonancijom (MR) kod dva od osam (25%) bolesnika. Insulinom je pronađen kod 13 od 13 (100%) bolesnika uz pomoć arterijske stimulacije sa venskim semplovanjem (ASVS) i kod 13 od 14 (93%) bolesnika pomoću endoskopske ultrasonografije (EUS). Od ukupno 42 bolesnika, 38 (90,5%) je operisano. Minimalna resekcija izvedena je kod 28 (73.6%) bolesnika [enukleacija tumora kod 27 (71%) i centralna pankreatektomija kod jednog (2.6%) bolesnika] i velika resekcija samo kod devet (23,6%) operisanih bolesnika [distalna splenopankreatektomija kod osam (21%) bolesnika i duodenopankreatektomija kod jednog (2,6%) bolesnika]. Ukupna stopa smrtnosti u postoperativnom periodu bila je 2,6% (jedan bolesnik). **Zaključak.** Kombinovanje ASVS i EUS kao dijagnostičke procedure omogućava veliku tačnost u preoperativnom određivanju lokalizacije insulinoma. Minimalna hirurška resekcija, kao što je enukleacija, trebalo bi da se sprovodi kada je god moguće.

Ključne reči:
insulinom; dijagnoza; hirurgija digestivnog sistema, procedure; lečenje, ishod.

Introduction

Insulinoma is a tumor of the pancreas that is derived from beta cells of Langerhans islands. It is small, ussualy solitary tumor, which can be localized throughout the pancreas. Insulinoma is a benign tumor in 90% cases with the incidence of 1 to 4 per one milion humans per year [1, 2]. It can appear as solitary sporadic tumor in patients without other diseases, but can be a part of multiple endocrine neoplasia type 1 (MEN 1), usually in a form of multiple tumor. The average age of its occurrence is 45 years for sporadic cases and 25 years for MEN 1 [1, 3, 4]. Typical manisfestations of insulinoma are the symptoms of hypoglicemia usually provoked by fasting or exercising [5]. A wide spectrum of clinical manifestations in patients with insulinoma is the reason for difficult recognition of disease with a long time interval between the onset of symptoms and the diagnosis. Insulinoma is confirmed by the presence of endogenous hyperinsulinemic hypoglycaemia. A diagnostic "gold standard" for insulinoma is the 72-hour fast test [6]. One third of patients develops corresponding symptoms within 12 hours, 80% within 24 hours, 90% within 48 hours and almost 100% of patients within 72 hours after test initiation [7]. Because of the size of insulinomas (< 2 cm in diameter usually), it is usually difficult do determine their localization. In a number of cases it is impossible to determine insulinoma localization before the operation [1, 3]. All diagnostic procedures for insulinoma localization could be preoperative and intraoperative. They include: transabdominal ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), somatostatin receptor scintigraphy, endoscopic ultrasound (EUS), angiography, arterial stimulation with venous sampling (ASVS), fluorine-18-L-dihydroxyphenylalanine (^{18}F-DOPA) positron emission tomography and glucagon-like peptide (GLP) 1–receptor scintigraphy, bidigital palpation and intraoperative ultrasound [3, 8–11]. The only currative therapy for those with insulinoma is operative treatment. As approximately 90% of insulinomas are benign, enucleation of the tumor is the method of choice whenever it is possible to be performed [12, 13]. Conservative, medical treatment may control hypoglycaemia in 50–60% of patients with insulinoma, but this therapy is reserved only for patients not reluctant for surgery on or for those with unresectabile metastatic disease [3, 4].

The aim of this study was to evaluate all the patients with insulinoma treated in the Military Medical Academy (MMA), Belgrade, in a 60-year duration period.

Methods

This retrospective study included 42 patients with the diagnosis of insulinoma treated in the MMA (Belgrade, Serbia) from 1951 to 2012. In all patients demographic characteristics, including gender and age, clinical characteristics (symptoms and signs of the disease, as well as the duration of symptoms before the diagnosis), types of biochemical methods for diagnosis, and diagnostic procedures for insulinoma localization in regard to the number of diagnosed insulinomas were analyzed. Also, the types of surgical procedures, tumor size and localization, postoperative complications and outcome were assessed.

Results

The first patient with insulinoma was treated in the MMA in 1951 [14]. The diagnosis was established on the basis of the clinical picture, Whipple's triade and the 72-hour fast test. Before 1970 in the MMA the diagnostic procedures for insulinoma localization were not performed. Until then, 15 patients with insulinoma and one with malignant insulinoma were treated in the MMA [15]. Thirteen of those patients were operated successfully. After introducing angiography as diagnostic procedure for insulinoma in the MMA in 1970, 16 patients were assessed and in all of them insulinoma localization was confirmed intraoperatively. In the 80s of the last century in the MMA began the usage of the non-invasive methods for insulinoma diagnosis. Since 1983, US has been applied and a small number of insulinomas were localized using this technique. In the same year CT started to be used for insulinoma diagnosis, while MRI was introduced in 1985. In 1992 ASVS was introduced, and EUS 10 years later.

Out of the 42 patients, 29 were women and 13 men (ratio 1.2:1). At the time of diagnosis their median age was 43 (8–77) years. The median time between the onset of symptoms to diagnosis of insulinoma was 3 years (one day – 25 years). The clinical characteristics of the patients are listed in Table 1.

pancreatic head 12/41 (29.2%), pancreatic neck 4/41 (9.7%), processus uncinatus 4/41 (9.7%), pancreas body 6/41 (14.6%), pancreas tail 14/41 (34.1%), and outside of the pancreas 1/41 (2.4%). The size of insulinomas was < 1.0 cm in 7/41 (17%), 1–1.9 cm in 20/41 (49%), 2–2.9 cm in 11/41 (27%), and > 3 cm in 3/41 (7%) of patients.

Table 1

The clinical characteristics of 42 patients with insulinoma

Neuroglycopenic symptoms	Number of the patients [n (%)]	Adrenergic symptoms	Number of the patients [n (%)]
Disturbance of consciousness	32 (73)	Palpitations	22 (5)
Abnormal behavior	32 (73)	Sweating	23 (53)
Confusion	27 (61)	Tremor	17 (38)
Convulsions	27 (61)	Hunger	23 (53)
Blurred vision	18 (41)		
Amnesia	10 (23)		
Hallucinations	5 (11)		
Weakness	25 (56)		
Nocturia	3 (6)		

The diagnosis of insulinoma was estimated by provocing Whipple's triads with 72-hour fast test in 14 patients, and/or by low blood glucose level and hiperinsulinemia. Determination of insulinoma localization was assessed by angiography in 16 (36%) of the patients, by US in 3 of 16 (18.8%) patients, by abdominal CT in 8 of 18 (44.5%) patients, and by MRI in 2 of 8 (25%) patients. Since the introduction of EUS and ASVS as diagnostic procedures in the MMA, insulinoma has been found in 13 of 13 (100%) patients by ASVS, and in 13 of 14 (93%) patients by EUS. The difference between EUS and ASVS and other diagnostic procedures for determination of insulinoma localization was significant ($p < 0.001$). There were 6 patients with ocult insulinomas. Of 42 patients, a total of 38 (90.5%) patients underwnet operative procedure (Table 2). In all the operated patients the open surgical procedure was performed.

Table 2

Operative procedures on 38 patients with insulinoma

Surgical procedure	n (%)
Tumor enucleation	27 (71)
Distal splenopancreatectomy	8 (21)
Pancreaticoduodenectomy	1 (2.6)
Central pancreatectomy	1 (2.6)
Only laparotomy	1 (2.6)

In 4 of the patients „blind“ distal pancreatectomy was performed due to the cases of ocult insulinoma. The second operation was required in 4 (10.5%) patients because of histopathological finding of resected specimens without insulinoma in 3 patients, and early postoperative recurrent hyperinsulinemic hypoglycaemia (unrecognised multicentric insulinoma) in one patient. The overall mortality rate in the postoperative period was 2.6% (one patient). One insulinoma was found in 35 (92%) and two in 3(8%) of the patients ($p < 0.001$). The distribution of insulinomas was in the

Discussion

Insulinomas are rare endocrine tumors developed from pancreatic beta cells with the incidence about 1 in 250,000 patient-years [16]. As in our series, insulinomas are more common in female patients with the median age at the diagnosis of 47 years approximately [17]. About 90% of insulinomas are single, benign and sporadic tumors that are located in the pancreas, but about 10% of patients with insulinomas have MEN-1. Those patients are often presented with multiple insulinomas and other secreting or non-secreting endocrine tumors. Finally, a particular condition is malignant insulinoma, also found in about 10% of insulinoma patients [18]. Insulinomas are the most common pancreatic endocrine neoplasms present with a typical clinical syndrome known as Whipple’s triad. Patients will often present with a profound syncopal episode and will admit to similar less severe episodes in the recent past. They also may admit to palpitations, trembling, diaphoresis, confusion, seizure, and family members may report that the patient has undergone a personality change [5]. The most common clinical symptoms and signs in our patients were disturbance of consciousness and abnormal behavior in 73% of patients, confusion and convulsions in 61% of patients. A wide spectrum of clinical manifestations in patients with insulinoma as well as a large number of diseases that have similar symptoms and signs, may be the reasons for difficult recognition of disease and explain a long period between the onset of symptoms and the diagnosis. In the literature, the time from the onset of symptoms to insulinoma diagnosis varies widely, from 10 days to more than 20 years [19, 20], as in our patients. Since surgery is the only curative treatment of insulinomas, topographic assessment of insulinoma must be performed after the conformation of biological diagnosis of hypoglycemia related to inappropriate insulin secretion. Although intraoperative bidigital palpation and US of the pancreas have been presented as the best methods for detecting insulinomas [18], radiological examina-

tion must be performed before surgery in order to avoid failure of surgery and reoperations. Insulinomas are usually localized with CT scan and EUS. With the meticulous technique, the sensitivity of multi-slice CT for insulinomas detection could reach 94% [21]. MRI is complementary to CT, in order to confirm the suspected lesion on CT or to search for an insulinoma that CT has not been able to localize. Combining both methods (CT and MRI) the accuracy of insulinomas detection improves. According to our practice CT scan showed to be better than MRI for insulinomas localization, with sensitivity of 44.5% versus 25% on MRI. Technical advances in EUS have led to preoperative identification of > 90% of insulinomas [22]. Even though ASVS is rarely required to localize insulinomas, this methods is a valuable tool when conventional imaging is negative. In contrast to the others where the sensitivity of ASVS rarely reached 70% [19, 23], we had very good results using ASVS for insulinomas localization. Insulinomas were found in all patients who were assessed with ASVS, and in 93% of the patients who were assessed with EUS. We consider that combining EUS and ASVS the sensitivity of insulinomas detection could reaches 100%, although those invasive methods were described as a last-line investigation in patients with hypoglycaemia related to endogenous hyperinsulinism.

Improvement in the preoperative diagnostic procedures for insulinomas localization determination enables the surgeon to have an accurate topographic assessment before surgery and to decide about surgical approach preoperatively. However, intraoperative bidigital palpation and US remain the valuable diagnostic methods, as well to confirm previously determined insulinoma localization. There are two types of surgery which can be performed. They include minimal resection (tumor enucleation or central pancreatectomy) and more extended resection (left-sided pancreatectomy with or without spleen-preserving or pancreaticoduodenectomy) [24]. The type of surgery depends on the size and the location of insulinoma and on its relationship with pancreatic duct, vessels and adjacent organs. Tumors located close to the main pancreatic duct and large (> 2 cm) tumors may require a distal pancreatectomy or pancreaticoduodenectomy. In all other cases and whenever it is possible, simple tumor enucleation is the surgical method of choice [12, 13, 25]. We performed minimal resections in 73.6% of the patients (tumor enucleation in 71% and central pancreatectomy in 2.6% of the patients). Although there were 14 (34%) patients with insulinoma > 2 cm in diameter, the major resections were performed only in 9 (23.6%) of the operated patients (distal splenopancreatectomy in 8 and pancreaticoduodenectomy in one patient). When insulinoma is localized preoperatively with accuracy, enucleation or left-sided pancreatectomy by laparoscopy is performed in many expert medical institutions. It reduces hospital stay duration and improves postoperative quality of life [13, 24, 26]. A "blind" distal pancreatectomy was proposed several years ago in cases with insulinoma not found intra-operatively. However, in such cases where no insulinoma wos found intraoperatively, it is recommended today to finish the operation and plan the additional procedures in order to localize insulinoma, including invasive techniques [27]. Before the introduction of EUS and ASVS in the MMA, a "blind" distal pancreatectomy was performed in one patient. Morbidity and mortality depend on the type of surgery. Mortality is almost 0% for enucleation, but may reach 1–2% for left-sided pancreatectomy and up to 4–5% for pancreaticoduodenectomy[18]. In our series, the mortality rate in a postoperative period was 2.6% (one patient) due to postoperative complications. After enucleation our patients had no complications and reoperations were not needed, so this type of surgical procedure should be performed whenever it is technically possible.

Conclusion

A spectrum of clinical manifestations in patients with insulinoma could be the reason for difficult recognition of the disease with a long period of time between the onset of symptoms and diagnosis. Although invasive, EUS and ASVS are the best methods for insulinoma localization assessment. Combining these two methods ensures high accuracy in preoperative determination of insulinoma localization. "Blind" distal splenopancreatectomy should be avoided due to the possibility of failure in curing the disease and postoperative complications, while minimal resection such is enucleation shoud be performed whenever it is possible.

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Metabolic syndrome and restenosis of carotid artery

Metabolički sindrom i restenoza karotidne arterije

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Key words:
carotid artery diseases; risk factors; metabolic syndrome x; cardiovascular diseases.

Ključne reči:
karotidna bolest; faktori rizika; metabolički sindrom x; kardiovaskularne bolesti.

Introduction

Clustering of risk factors for cardiovascular disease has been investigated from the third decade of the 20th century [1–3]. It was named metabolic syndrome (MSy) by World Health Organization in the year 1999 [4]. In 2001, the National Cholesterol Education Program – Adult Treatment Panel III (ATP III) (NCEP-ATP III) proposed both diagnostic criteria for MSy and cut-off points for its components [waist circumference, blood pressure, high-dentsity lipoprotein cholesterol (HDL-C), triglycerides and fasting blood glucose], which are considered acceptable for everyday clinical work [5]. NCEP-ATP III criteria were revised in 2005 by the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) – modified NCEP-ATP III criteria, called also NHLBI-AHA criteria [6]. In 2006 International Diabetes Federation (IDF) recommended a new definition of the MSy – IDF definition [7]. There is no general agreement as to which definition is more suitable for diagnosis of MSy, but it seems that the modified NCEP-ATP III criteria are the most appropriate [8].

According to literature data, the frequency of MSy varies from 9% to 34% depending on studied population and MSy definition which was used in investigation [9–12]. The frequency of MSy is related to age. For example, in the USA population, in subjects more than 60 years old the frequency of MSy was 51.5%, and in subjects 40–60 years old it was 40.8% [10]. MSy is also more frequent in obese [13].

The MSy prevalence is higher in patients with atherosclerotic disease. In a study of Gorter et al [14], which included 1,117 patients aged 18–80 years (mean age 60 ± 10 years) with verified atherosclerotic disease, MSy prevalence, defined according to ATP III criteria, was 46%. There are differences in MSy prevalence depending on the type of atherosclerotic disease. In the above mentioned study of Gorter et al. [14] and in an Olijhoek et al. [15] study the prevalence of MSy was about 58% in patients with peripheral vascular disease, about 41% in patients with coronary disease, 43% in patients with carotid disease and 47% in subjects with abdominal aortic aneurysm.

According to recently published data from a study conducted in Belgrade, the MSy prevalence, defined according to ATP III criteria, was 55.6% in patients with carotid disease [16] and 59.8% in patients with peripheral vascular disease [17].

Carotid artery restenosis

Carotid endarterectomy (CEA) has been proved as successful in prevention of disabling and fatal strokes in patients with asymptomatic and symptomatic carotid diseases [18–20].

CEA is one of the most frequent vascular operations in the USA, with more than 117,000 of this intervention per year [21]. Several large, multicentric controlled trials showed that among carefully selected patients CEA had better effect as stroke prevention than medical therapy [22]. In a study conducted in Belgrade which included a total of 309 symptomatic patients with near total internal carotid artery occlusion, those who underwent CEA had lower incidence of transient ischemic attack, ipsilateral stroke, and neurologic death during follow-up than medically treated patients [23].

After CEA in some patients reccurent carotid stenosis occur. Reviewing over 200 references Lattimer and Burnand [24] found that the overall incidence of symptomatic recurrent stenosis ranged from 0% to 8.2%, and the one of asymtomatic restenosis was between 1.3% and 37%. In a Liapis et

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al. [25] study the incidence of restenosis was 4.0%, all restenosis were asymtomatic, and average time from CEA and occurence of restenosis was 47.4 months.

In a Fluri et al. [26] study, 5 years after CEA, the probability for the ipsilateral progressive carotid disease was 5.2%, and after 15 years, the likelihood was 37%.

Recurrent carotid stenosis higher than 60% the most frequently occurs two years after CEA [27]. Postoperative oclusion develops in about 1% of operated [24, 28].

Risk factors for carotid artery restenosis

Risk factors for restenosis have been investigated in many studies [25, 26, 29–31]. According to Lattimer and Burnand [24], for early restenosis, within 2 years after CEA, risk factors are smoking, lower diameter of carotid artery, some anomalies found during operation and some genetic factors. Cerebrovascular risk factors such are hypertension, hyperlipidemia, diabetes, obesity and smoking are important for progressive restenosis, which occurs at least 2 years after operation. In a study of Reina-Gutierrez et al. [28], the highest risk for serious restenosis had women and subjects with diabetes. In a Volteas et al. [32] investigation, diabetes, ishaemic heart disease, hyperlipidemia and family history of cardiovascular diseases were significantly more frequent in patients with restenosis in comparison with those without restenosis. Rapp et al. [33] found that hypercholesterolemia was related to early restenosis, and that hypertension was related to both early and late restenosis. Association of cerebrovascular risk factors with restenosis has not been proved in any investigations [29–31]. For example, Strineka et al. [34] did not find this association and concluded that restenosis was not caused by cerebrovascular risk factors, but by perioperative complications. One of the reasons for these inconsistencies could be a different number of patients studied and different duration of their follow-up.

In a study of Fluri et al. [35], published in the year 2010, a group of 361 patients with CEA was followed 7 years after operation, out of cerebrovascular risk factors present before operation, smoking, diabetes and hypercholesterolemia were significantly related to progressive restenosis. However, more important were newly acquired cerebrovascular risk factor, that is the factors not present before CEA. Acquisition of at least one new cerebrovascular risk factors (with exception of hypercholesterolemia) significantly increased the risk for progressive restenosis [35].

Metabolic syndrome as a predictor of adverse outcomes after carotid revascularization

It is well known that MSy is associated with cardiovascular diseases. This association has been found in a large number of studies [10, 36, 37]. Compared with persons without MSy, persons with MSy had both increased mortality from cardiovascular diseases (12.0% *vs* 2.2%) and increased total mortality (18.0% *vs* 4.6%) [10]. Whether MSy is associated with restenosis is not known yet.

Since the majority of MSy components have been found to be related to restenosis it could be expected that restenosis is more frequent in patients with MSy. So far, only a study of Protack et al. [38] described the outcomes for patients with MSy after carotid revascularization (carotid endarterectomy and carotid stenting). In a total of 921 patients of which 750 underwent CEA and 171 carotid stenting, 31% were identified as having MSy. During follow-up (on an average of 4.5 years) there were no differences between MSy and No-MSy patients with respect to patency, restenosis, reintervention, or survival. Differences, however, existed for freedom from stroke, myocardial infarction (MI) and major adverse event defined as the occurrence of ipsilateral stroke, MI or death during follow-up MI. In comparison with No-MSy, those with MSy had more frequently perioperative morbidity, stroke, MI and major adverse event. These differences were significant for patients with diabetes, but not in those without diabetes. The authors concluded that a long-term stroke prevention is poor in the presence of MSy and that MSy should be considered as significant risk factor for patients undergoing carotid revascularization.

Conclusion

Although there is no evidence that MSy is a risk factor for carotid restenosis, the fact that a majority of its components are related to restenosis, and finding that stroke prevention is poor in the presence of MSy, suggest that MSy is an important risk factor for adverse outcomes after carotid revascularization.

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GENERAL REVIEW

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Smallpox and globalization or the first achieved plannetary goal

Variola i globalizacija ili prvi ostvareni planetarni cilj

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Introduction

The subject of the review is the relation between the socio-historical process of globalization and spreading of smallpox in the world, including its epidemic in Yugoslavia in 1972, as well as the eradication of this disease by the Assembly of the World Health Organization in 1980.

The idea of globalization conventionally comprises the phenomenon of social contemporaneity for which Giddens consider that it started as "the fall of Soviet communism" in 1989 [1], which might be considered as its narrower comprehension in the sense that Pečujlić terminologically marked as "turboglobalization" [2]. Other authors put the start of this process in the 19th [3] or even in the 15th century [4], making the connection with the discovery of America by Christopher Columbus, while those with greater understanding for sociological comprehension of history, like the Dutchman Jan-Aart Scholte, consider that "globalization has no historical beginning" [5]. It is difficult to agree with the assumption about the "absence of the beginning", since every social phenomenon has it, but we point out that it is a long-lasting social process, which appears with establishing of the first social groups and then the traditional states-empires, developing during the history with discontinuity, but progressively, changing occasionally the form of manifestation. Therefore, those who claim that the globalization is a completely new phenomenon do not recall the warning of Marcel Mauss that "every social phenomenon, even when it looks like new and revolutionary, like for example an invention, always is fraught with the past in spite of it. It is the harvest of circumstances the most distant in time and multiple connections in history and geography" [6]. We consider that globalization is the legitimate social process of "interconnecting people (meaning: individuals, groups, organizations, companies, societies) at planetary level" [7] that is enabled and stimulated by the scientific, especially the technical-technological progress, overcoming political barriers and tendencies for creation of the world market. Our academician Lukić in 1957 was writing about such the process of "humanity unification", pointing out that it was very slow and contradictory, but also that it led towards numerous important changes that "for the first time in the history of mankind have led to something that looks like unified mankind" [8]. Keeping all this in mind, it is absolutely unacceptable to evaluate socially this process: it is the legitimate process that is going on during the human history, it carries along both positive (e.g. getting to know the whole world by the people, making the unique world market, exchanging products between distant continents, e.g. teas and spices that have reached Europe and America from India due to this) and negative (e.g. spreading of variola to all continents, possibility to assimilate cultures and loose identities of small nations by the process of culturalization from big and powerful countries, and similar) characteristics. That is why confronting globalization is meaningless, but it is not meaningless to confront some of the consequences nor to the ideology of globalism, which is the product of the end of the 20th century.

Giddens proclaimed almost a decade ago that we live in the "global period" [9], although it seems to us that it is more correct to say that the "globalizing society" [10] is in question. Whatever we call it, it is certain that the world society as entity has not been constituted, primarily due to differences in the development level of individual states and regions and interests based on it, but also due to the consciousness on certain needs that is not equally developed with individuals in different parts of the world; in some parts people are conscious that they need to provide food for children to survive, in other parts the same food is being wasted. It is hard to dis-

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cuss about the global – in the sense of planetary – social goals on the contemporary level of social development, since the goal implies also a realistic perception of the accomplishment, knowledge of the path and manner to accomplish it, awareness of its importance, determination for the activity on its accomplishment. Planetary ideas might rather be the themes – e.g. freedom, universal justice – since the values are in question that are generally accepted, but which suffer also from the possibility of different interpretation, and especially from the lack of elements for their operationalization. However, in certain areas it is possible also to discuss about constituted (healthcare, ecology) [7], even about accomplished global (planetary) social goals.

Our hypothesis is that the epidemic spreading of smallpox in the world scale, including its last epidemic in Europe that happened in Yugoslavia in 1972, which represented the greatest epidemic in our continent after World War II, is the consequence of the social process of globalization development, but simultaneously its eradication is the consequence of the same process, which resulted in accomplishment of the first specific global social goal on planetary scale.

Regarding the methods for collecting data, content analysis is used of the literature that refers to this disease and its epidemiological, clinical, historical-medical and sociological-medical aspects, literature that refers to the process of globalization and its different comprehension, as well as observing with participation (type complete participant) [11], since one of the authors of the paper was direct participant in suppressing the epidemic, in the focus, at Kosovo and Metohija in 1972. By combining these methods (so-called mix-method procedure) of collecting data and using analytic-synthetic methods, the authors will try to prove the correctness of their hypothesis.

Smallpox and globalisation

According to the literature, smallpox was known about one thousand years before Christ. Kosta Todorović [12] mentions that the first data about this disease originate from India and China, referring to the assumptions of historians that the origin of the disease was in the Central Africa, from where it was transferred to the Far East. It was transferred to the Arabian Peninsula in the 6th century, and soon into Europe. It was endemic in some regions of Africa and Asia, from where it was transferred to Europe, and then to other parts of the world [13]. The Crusades helped the spreading in the European continent and outburst of great epidemics [14]. Bishop Marius from Avenches (Switzerland) mentioned smallpox for the first time in Europe, naming it variola (in the year 570). He also described the epidemics during his period that raged throughout the continent. There were also crowned heads that became the victims of smallpox: Bourgogne queen Aufregalde died from this disease in 580, and much later, in the 18th century, even five European rulers died: Joseph I of Habsburg (in 1711), Spanish King Luis (in 1724), Russian King Peter II (in 1730), Swedish Queen Urlike (in 1741) and French King Louis XV (in 1774) [15], who shared the faith of 30,000 Frenchmen of that period. Filip Višnjić, our famous gusle-player and poet, outlived the disease, but he lost sight in his youth because of it. However, although raging throughout Europe for almost thousand years, smallpox was not treated as a specific disease, "but was considered as the 'plague' with all other hard diseases" [12]. Yet, Thomas Sydenham (1624–1689) in his book *Dissertatio epistolaris* clearly distinguished smallpox as the specific infective disease. With Spanish conquest of the Latin America in the 15th and the 16th century, smallpox reached the territory of this continent, firstly in the Caribbeans, and then in Mexico and Brazil. This assisted the Spanish conquest, since native inhabitants knew nothing about this disease, so that the number of victims was enormous [16]. With colonization of the North America by Dutchmen, Britons and Frenchmen, variola was transferred to this continent also, where the first epidemic outburst was in Massachusetts in 1617–1619. "The disease was usually coming by ship to the east coast, or with settlers from the Great Britain, or, later, with slaves from Africa. Boston suffered great losses from epidemics in 1636, 1659, 1666, 1677–1678, 1689–1690 and 1697–1698, and there were victims in New York City, Jamestown (Virginia), Charleston (South Carolina) and elsewhere… One of the consequences of the obvious connection of smallpox epidemic with cases on ships was imposing the quarantine for the infected in ships". Europeans imported variola to Australia also, through the sea also, and the first case there was recorded near Sydney in 1789 [16].

Such a treatment of ship passengers, actually creation of ship-quarantine, was familiar in the Europe also, as a preventive measure against smallpox epidemic, which confirms the thesis that "legends about cursed vessels are not the fruit of people's imagination, since there were examples that certain ships by which pilgrims traveled slowly and long, if they had only one person infected on the pilgrimage, or brought with him only one infected thing, were condemned on inhospitality of all ports. During the journey that lasted for two or three months, several persons would get sick in the ship and the ship would be forced to stay anchored offshore until everyone in it died, or until it was confirmed that survivors were not dangerous for the environment" [17]. Ships that circled around the Near East and the Mediterranean Sea, both trading and war vessels, represented a special danger. Development of maritime trade, transport of goods, their entering into various ports, resulted that they "by conjunction were playing the role of the carrier" of the disease. "On the other hand, the regions which ships and traders were not visiting, or where goods were not delivered, suffered less from infections… Therefore, among other things, these regions were lagging behind in the economic development regarding the regions in which the people were dying due to illnesses and diseases, but where new groups of people were coming to replace the dead because of the turnover and prospects for profit" [18]. The Dubrovnik Republic created the quarantine for all passengers that wanted to enter into this city even at the end of the 14th century. They had to spend a month in Cavtat or in Mrkan, Bobara and Supetar, without any contacts with local inhabitants, and both sides were punished most severely for this. For Serbia and other Yugoslav countries that

were under the Ottoman occupation, especially in the period of the 14th to 19th century, the problem was that Turks had no strict regulations for curing quarantine diseases, unlike the Western Europe that created them even then. Therefore, "the majority of wars waged by the Turks were accompanied by epidemics" [17].

As Kosanović-Ćetković [14] indicated four decades ago, in contemporary period "smallpox is often carried by airplane passengers from endemic regions, since they can fly to Europe within 1–2 days. They usually arrive at the very end of incubation or at the beginning of variola… they have many meetings with relatives and business friends just within these first days". Therefore, "due to the vivid airplane and other traffic", smallpox was reaching Europe even 52 times from the end of World War II till the end of the epidemic in Yugoslavia in 1972.

It is important to point out that the virus responsible for the spreading of this disease is ultrafiltrable; smallpox can be transferred not only by direct contact with a diseased or by air, but also indirectly – by contact with his things and again e.g. by aspiration of the dust from his things. "Germs penetrate in the human body mostly through the nose mucous membrane and eye conjunctiva, probably even through the apparently uninjured skin. The diseased himself is contagious even before the appearance of clinical symptoms, during the incubation stadium, as well as all the time during the sickness and during recovery, while desiccated crusts from pustules are on his body, and undestroyed virus in his environment, before finished desinfection" [12]. Easy transfer of the virus enables great epidemics, which was confirmed by the experience of our physicians in 1972 (Figure 1). Infected baby, in Čačak, had no contact whatsoever with diseased from smallpox and "that infection might be explained only by the air flow from the upper floor to the ground floor" [19]. Just the easiness of transfer was the reason for quarantine being the main measure in the history for preventing epidemics, while the diseased were usually left to their own destiny. The idea was to protect the healthy citizens, i.e. to prevent spreading of the infection. On the other hand, incubation lasts "in average 10–11 days, sometimes longer, about 2 weeks, sometimes shorter, about 6–8 days", in certain cases even shorter: 3–4 days [12].

Edward Jenner (1749–1823) made the revolutionary improvement in protection of citizens and the crucial step towards elimination of this disease with his discovery and proving the efficiency of the antivariolic vaccine, Jenner's vaccine, in 1797. Janner's vaccine soon found the application, first in England, and then in Spain and their colonies in the South America, and later in the whole world. The inventor himself believed that his vaccine was giving a permanent protection, while later the finding was established that the protection was absolutely efficient for the first five years, then its efficiency was not the hundred percent and revaccination was introduced later. This was confirmed by the experience of our clinical physicians during the epidemic in 1972 in Yugoslavia (Figure 2). Death rate of persons without vaccinal scars was "three times greater than of persons with old scars" [20].

Epidemic in Yugoslavia in 1972

Historically, the first regulations on vaccination against this disease in Serbia "Rules for Inoculation of Smallpox", were brought in 1839 by Prince Miloš. Obligatory vaccination for the Kingdom of Serbia was established only in 1881, and that law was valid both for territories liberated in the Balkans Wars 1912/13, and for territories incorporated after World War I. According to the data given by academician

a) b) c) d)

Fig. 1 – Smallpox, pustule stage: a) at infant; b) at child age; c) and d) at adults

Fig. 2 – Smallpox at adults – pustule stage

Todorović, in the period 1895–1911 there were 13,603 persons diseased from variola in Serbia, and almost every fifth died – 2,292 of them [12]. This number was significantly reduced in Yugoslav state, and after the epidemic in 1972, which lasted from 16 February to 11 April, there were no more cases of variola (Table 1). The importance of the applied vaccine is inevitable.

Table 1

Smallpox in Yugoslavia in the 20th century [12, 21]

Year	Infected	Died
1919	5278	1100
1920	4150	941
1921	2119	483
1922	728	165
1923	1042	198
1924	330	330
1925	14	3
1926	4	2
1927	3	0
1928	0	0
1929	0	0
1930	1	0
1972	175	35
After 1972	0	0

However, it should be pointed out that, although antivariolic vaccine and revaccination were obligatory, these were not performed systematically and in time, which resulted in lost lives. The reason for inobservance of the lawful regulations should be found in the fact that the previous case of variola in our country was 42 years earlier, but it was surely no excuse. The datum that the percentage in that period of obligatory vaccinated persons in Yugoslavia was at the level of 80% is poor, as well as that "the control of successful vaccination in some regions was not adequate or even was not performed at all" [21]. Although the majority of children 1–6 years of age should be well-protected with the first vaccine against variola, only 1 out of 15 diseased of this age was vaccinated. In the age 7–14 years, when both revaccinations should be performed, even 13 out 19 diseased children were not vaccinated, etc. With the growth of age, the number of previously vaccinated was also growing, which helped them to survive. Out of 175 cases (there are no data for 4 cases) of diseased from smallpox in Yugoslavia in 1972, even 66 were not vaccinated before, which makes 38.6%, while out of 35 dead (there are no data for 4 cases), even 23 were not vaccinated, (74.2)%. These data also show the fatality of non-applied vaccination: the death rate with previously vaccinated diseased was 8%, and with those who were not vaccinated even 35% [21]. "There were even babies and all other age groups among the diseased in Kosovo, since the citizens were not vaccinated systematically" [4]. On the other hand, there were also political influences not to publish immediately the outburst of epidemic, and when it was finally published – to end it as soon as possible, in order not to jeopardize the tourism. All this show that, from the aspect of management, serious defaults were made that promoted the development of the epidemic. The problem was also that active Yugoslav physicians of that period had no opportunity to see smallpox in their practice. That was the reason that only one diseased from Novi Pazar, infected even 38 persons, which was the record described in the world literature [22], and the greatest number of them were infected in hospitals, since nobody suspected in smallpox. The exception regarding the physician's expertise in confrontation with this disease were the two physicians from the Infective Clinic in Belgrade who had got familiar with it during their study visits of India (V. Šuvaković, M. Kecmanović, and the first had been trained in this variolic country for diagnostic and treatment of the disease as the scholar of the WHO within the program "Smallpox contro"). Immediately after suspecting the existence of smallpox in Kosovo and Metohija, the two of them were sent to Đakovica and stayed there during the whole period of the epidemic. Then, among the first, several eminent physicians were also sent to Kosovo and Metohija, military officers of the Yugoslav Peoples Army medical corps, professors of the Military Medical Academy, who very actively participated in suppression of smallpox epidemic – General Vračarić and Colonels Arsić and Birtašević among them. Military physicians participated also in curing diseased from smallpox in other parts of the country, e.g. Colonel Mijušković in Čačak.

It is considered that a man who returned from pilgrimage in Mecca brought variola to Yugoslavia. With 24 another pilgrims, he visited also dervish sanctuaries near Basra and Baghdad, where variola was registered just in that period. He returned by bus to his place Danjani in Kosovo and Metohija on 15 February and already the next day he was sick due to clinically unknown condition. According to the records, he was vaccinated, but there were no traces to confirm that. However, even seven of those who visited him were infected by variola, while his serological results confirmed the diagnosis.

The epidemic was revealed only a month later when Dr. Durmiš Celina and Dr. Džemail Džibo recognized the clinical picture of variola discovered in a 14-year-old girl located in the Infectious Department of the hospital in Prizren and informed authorized institutions about it. Kosovo and Metohija was the seat of this Yugoslav epidemic, since out of the total number of diseased even 124 were from this region – 70.9%, and out of the total number of dead 26 or 74.3% were from Kosovo and Metohija (Figures 3 and 4). The social conditions of living there also contributed to the development of the epidemic. "Families in which variola was present were usually very poor and lived in hard residential conditions. There was the custom that everyone ate and drank from the same dish and slept together in a bed littered at the floor without boarding… an advantage was that Albanians, making the majority of these two settlements [Danjane and Ratkovac from where the first diseased originated, note of the authors], were not practicing kissing when meeting" [23]. A diseased sickened on 20 March in Hanover (Germany) [24] was among those that were infected when visiting the village Danjane, which illustrates that the fast spreading of the disease to other countries was the consequence of the development in transportation. "However, the case that was introduced from our country to Germany has not led to spreading of the infection due to the applied prophylactic measures" [25].

Fig. 3 – Smallpox – hemorrhagic form

Fig. 4 – Smallpox – scab stage

Quarantine measures were applied for suppression of the epidemic, but the Federal Epidemiological Committee made a decision to perform vaccination of the complete population of Yugoslavia – 18 million people. These measures gave results and the epidemic ended already in April.

Yugoslav experts received commendations for the successful suppressing of the epidemic from the Director of the World Program for Eradication of Variola, and the highest Yugoslav medals decorated majority of those who directly participated in the action of curing and suppressing the epidemic. Just due to the Program for Eradication of Variola of the World Health Organization, adopted in 1959 (Resolution WHA 11.54) on the basis of a year before express initiative of the Soviet Ministry of Health deputy Victor Mikhailovich Zhdanov (*Викто̄р Михайлович Жданов*), in cooperation of states, physicians, medical personnel and people in the whole world, the disease was eradicated in the whole planet, which was ceremoniously declared on the 8 May 1980 at the WHO convention. The first global (planetary) goal in the history of humankind was achieved by that, in the area of human health protection. The second one was achieved 31 years later, in the area of veterinary medicine, when the United Nations declared on 25 May 2011 that the cattle plague (rinderpest or steppe murrain) was eradicated. That is the first animal disease that used to kill millions of cattle throughout Africa, Asia and the Europe, including Serbia during the 19th century, eradicated by man at the planetary level.

Conclusion

Causes of spreading smallpox throughout the world, in addition to medical and hygienic-epidemiological, were actually a tracker of wider social nature process: the need for new conquests, either for spreading religion or for capturing new colonies with the aim of their exploitation, profit growth through the trading with distant countries, the need for tourism (including the religious) and fast growth of income connected with it and similar. On the basis of the applied research methods, it may be concluded that globalization of smallpox through history was enabled by the progress of transportation means, either they served in war, trading or traveling purposes. It used to be a slow-sailing vessels cruising in the Mediterranean Sea connecting the three continents, later these were improved, which enabled them to reach also another, distant continents, which resulted in spreading smallpox to the South and the North America and Australia, which literally globalized this disease on planetary level. In the 20th century, the improvement of transportation means (massive usage of traffic means with motor drive: buses, trains and airplanes), but also the mass tourism, including the religious, contributed to the spreading of the disease. The Yugoslav epidemic broke out in 1972 also in this way. It shows that the cause that enabled spreading of smallpox on planetary level is the same that has accelerated the process of globalization. Actually, spreading of smallpox represents one of the (negative) consequences of

globalization. Simultaneously, the eradication of smallpox, officially announced on 8 May 1980, is the consequence of the global action led by the United Nations, starting from 1959, with the goal to eliminate completely this disease from our planet. This confirms our hypothesis that smallpox was eradicated just due to the progress of globalization process, i.e. that the elimination of this disease in natural environment on earth represents also the consequence of the globalization process (positive), by which the first concrete global social goal was accomplished on the level of the planet in human history. The process of globalization, as a legitimate historical process, influenced the planetary spreading of the disease, but also its planetary eradication.

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CASE REPORTS

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Erosive pustular dermatosis of the scalp – Is it really a rare condition?

Erozivna pustularna dermatoza skalpa – da li je to zaista retko stanje?

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Abstract

Introduction. Erosive pustular dermatosis of the scalp (EPDS) is a rare disorder of unknown etiology that usually occurs in the elderly and is characterised by multiple pustules, erosions and crusts that appear on the scalp leading to scarring alopecia. The histopathology and laboratory tests are not specific which is the reason that EPDS is a frequently misdiagnosed condition. **Case report.** We presented two patients with EPDS. The first patient had the known history of local trauma, both patients had chronic recidivant process, classic clinical presentations, and nonspecific histological findings. Each patient had prompt therapeutical response to potent topical steroids. **Conclusion.** The diagnosis of EPDS can be made if a condition fulfills the following criteria: atrophic or actinic damaged skin, clinical association of erosions, pustules, scales and crusts, no specific histopathology, no infectious agent found responsible for the condition, and chronic course leading to scarring alopecia, and prompt respnse to the treatment with topical steroids. The history of chemical or physical trauma is often present.

Key words:
skin diseases; scalp dermatoses; diagnosis; therapeutics; adrenal cortex hormones; treatment outcome.

Apstrakt

Uvod. Erozivna pustularna dermatoza skalpa (EPDS) je retka dermatoza nepoznate etiologije. Javlja se kod bolesnika starijeg životnog doba, a karakteriše pojavom brojnih pustula sa erozijama i krustama koje rezultuju ožiljnom alopecijom. U EPDS patohistološki i laboratorijski nalazi nisu specifični, što rezultuje čestim neprepoznavanjem ovog poremećaja. **Prikaz bolesnika.** Prikazali smo dva bolesnika sa EPDS hroničnog recidivantnog toka. Kod jednog bolesnika pojavi EPDS predhodila je trauma, a oba su imala klasičnu kliničku prezentaciju i nespecifičan histološki nalaz. Kod oba bolesnika postignut je brz terapijski odgovor na potentne topikalne kortikosteroide. **Zaključak**. Dijagnoza EPDS postavlja se ako su prisutni atrofična ili aktinički izmenjena koža, pustule, erozije, kruste i ožiljci, bez specifičnog patohistološkog nalaza i uzročnika u vidu infektivnog agensa, kao i hroničan tok koji vodi u cikatricijalnu alopeciju, uz brz terapijski odgovor na topikalne kortikosteroide. Često je prisutna istorija hemijske ili fizičke traume.

Ključne reči:
koža, bolesti; poglavina, dermatoze; dijagnoza; lečenje; kortikosteroidni hormoni; lečenje, ishod.

Introduction

Erosive pustular dermatosis (EPD) of the scalp (EPDS) is a rare disorder that mainly occurs in elderly patients often with previous trauma to the scalp [1]. It was first described in 1979 by Pye et al. [2]. Less than 50 cases have been reported since then. The first described patients were all women with involvement of the scalp. Biopsy specimens revealed marked chronic inflammatory changes with prominent plasma cells, epidermal atrophy, and, in most patients, epidermal erosion. The number of hair follicles appeared to be diminished. Patients were successfully treated with potent topical steroids. In instances when EPD has not been correctly diagnosed, the course of the process is continuous, and treatment lasts for years [3].

Case 1

A 59-year-old man with the 5-year history of erosive, pustular and crusted lesions on his scalp (Figure 1) was presented to our Clinic. The patient had previously been treated with antibiotics and sun protective cream without showing signs of improvement. A histopathological examination revealed the presence of unilocular subcorneal pustule in epidermis with flattened rete ridges. Solar degeneration of collagen fibers was present in the dermis (Figure 2). Direct immunofluorescence did not reveal deposits containing IgG, IgA, IgM, or C3 antisera. Wound swabs did not result in the isolation of pathogenic agents. The changes were treated with a potent topical corticosteroid – fluocinoloneacetonide ointment, with removal of crusts prior softened by a physio

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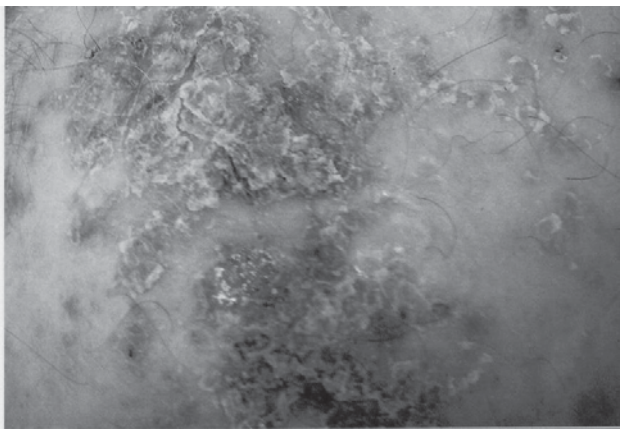

Fig. 1 – Erosive, pustular and crusted lesions on the scalp of the first patient before the treatment in our clinic.

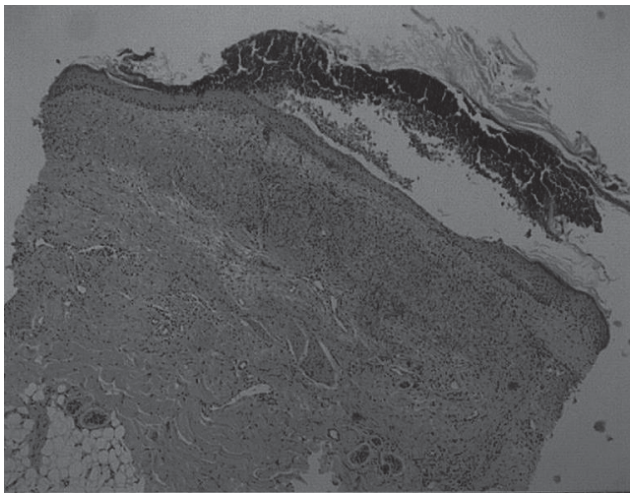

Fig. 2 – Unilocular subcorneal pustule in epidermis with flattened rete ridges; solar degeneration of collagen fibers (histopathological examination of the scalp lesions of the first patient) (HE, ×50).

logical solution and a rinse with 3% boric acid. Therapeutic response at the end of the second week of the treatment showed a 60% improvement, with the presence of rare changes: 2 pustules, 3 erosions, without crusts. At the end of the fifth week of the treatment the skin was completely epithelialized (Figure 3).

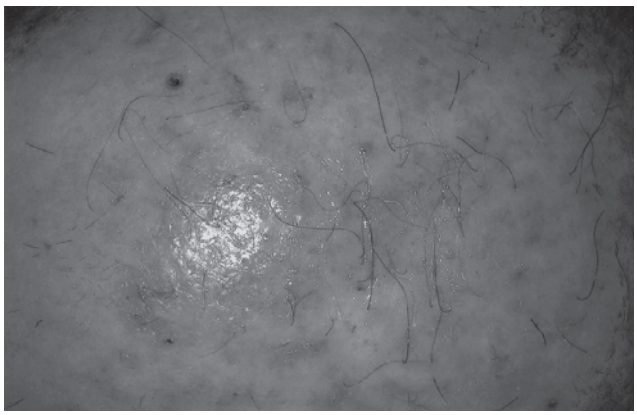

Fig. 3 – The completely epithelialized skin of the scalp of the first patient at the end of the fifth week of the treatment.

Case 2

A 87-year-old woman was presented to our Clinic because of the 5-year history of crusted lesions and inflamed erosions on her scalp (Figure 4).

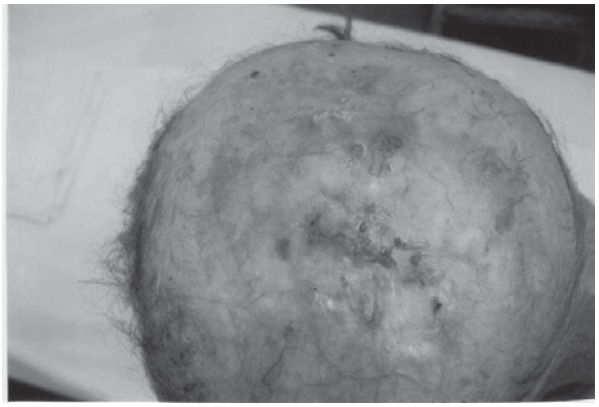

Fig. 4 – Crusted lesions and inflamed skin erosions on the scalp of the second patient (the first examination in our clinic).

Nine months after the onset of the condition, the patient underwent a radical excision procedure for a suspect tumour of the vertex of the scalp, and a split-thickness skin graft 70 mm in diametar was placed. Histopathological finding was as follows: pemphigoid dermatitis, with no tumour cells present. The acceptance of graft was pour with pustules, erosions and crusts occurring at the site of graft and the rest of the scalp. There was no necrosis of the graft. Excisional biopsy was taken by plastic surgeon with histology reporting chronic cutaneous ulcus. The patient was treated with an hydrocolloid wound compress with ionic silver after rinsing with a H_20_2 3% solution, after which occurred a temporary improvement, then a relapse without any provoking factors.

A subsequent skin biopsy from a temporal scalp region revealed hyperkeratosis, a flattened rete ridges, atrophy of the epidermis, and ulceration in the reticular dermis, and reduced appendages. Dense inflammatory infiltrate, numerous plasma cells, and histiocytes were found on the edges of ulceration (Figure 5). Direct immunofluorescence did not re-

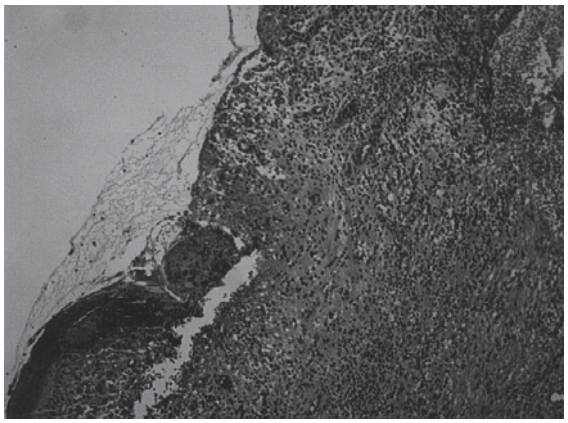

Fig. 5 – The dense inflammatory infiltrate, numerous plasma cells, and histocytes are found on the edges of ulceration (HE, ×100).

veal deposits containing IgG, IgA, IgM, or C3 antisera. Treatment with a potent topical corticosteroid ointment (betamethasone began), with removal of crusts prior softened by a physiological solution and a rinse with 3% boric acid. Three weeks of the therapy led to a significant improvement, approximately 70%. After five weeks of the therapy, there were three erosions of the skin, which was clearly atrophic, with cicatricial alopecia (Figure 6). Therapy with a corticosteroid lotion (mometasone furoate) continued, only to the areas where new pustules were forming.

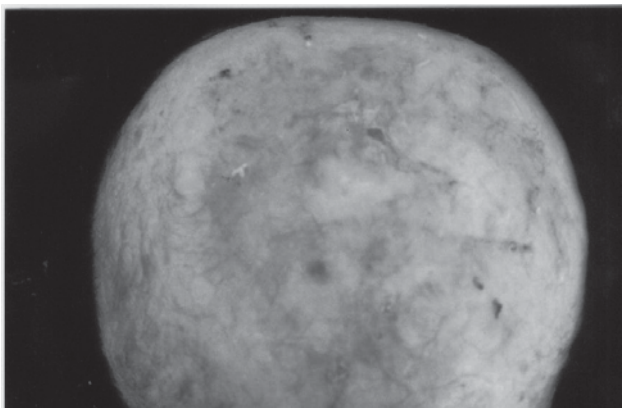

Fig. 6 – Three erosions of the skin, clearly atrophic, with cicatrial alopecia are shown after five weeks of the therapy.

Discussion

This is the first case report of EPDS in Serbia. Both patients presented to our clinic within one calendar year, with the history of unrecognised EPDS for longer than five years. Both were previously seen and treated by dermatologists for longer than 3 years under different diagnoses and with mild or no therapeutical response.

The exact cause of EPDS is unknown. Previous reports suggest that the development of EPDS is often associated with antecedent trauma to the skin and the areas of long-standing solar damage and that usually occurs in the elderly patients [4].

Actinic keratoses can sometimes be present clinically and/or histologically. Because this is the sun-damaged skin, it is not surprising that malignancy can either precede or follow EPD. For this reason, it may appear that epidermal dysplasia is causing the erosive disease. Arguments against this supposition are as follows: the treatment with cryotherapy, electrosurgery, laser or topical chemotherapy do not improve the condition and occasional development EPD in non sun-damaged skin of the legs. Conclusion is that atrophy caused by actinic damage, rather than actinic damage itself, is responsible for the development of EPD [3].

It is belived that trauma is one of the precipitating factors. A history of preceding tissue damage such as that caused by herpes zooster or iatrogenic insult: cryoteraphy, topical chemotherapy, laser therapy, electrosurgery, excisional surgery, grafting, is often found [5].

Hormones might have some influence in the pathophysiology of EPDS. It has been documented that it develops with a female predominance of about 2:1. There is evidence that in postmenopausal women estrogen loss is accompanied by many skin changes including atrophy and delayed wound healing, which might lead to the development of EPDS [3].

Chronic nonspecific inflammation (presence of plasma cells and lymphocites) is present in biopsy specimens. This observation suggests that inflammation plays an important role in the pathophysiology of the disease. Neutrophils are almost always present. It suggests that EPD should be classified as part of neutrophilic dermatoses. However, neutrophils do not predominate in the same way they do for other conditions classified as the neutrophilic dermatoses [3].

Cultures most often reveal only normal flora. Microorganisms found in EPDS represent a secondary colonization rather than primary infection. Even when *Staphylococcus aureus* is indentified, treatment with appropriate antibiotics leads to little or no improvement [6]. Crusted plaques on the scalp with accompanying hair loss suggest fungal infection of the kerion type. However, cultures and special stains on biopsy specimen rarely reveal the expected dermatophytes and empirical antifungal treatment fails to resolve the lesion [7].

The histopathology is not specific [8], with a spectrum of inflammatory changes involving epidermis and dermis, ulceration, atrophy or hyperkeratosis and reduced number or absence of hair follicles [9]. Occasionally, when neutrophils are numerous, small subcorneal, or mid-epidermal, spongiform pustules may be present [3]. In the biopsy specimens taken from the edge of erosions, epidermis is generally present, usually atrophic, and epidermal dysplasia or even frank actinic keratoses may be present. The dermis is often thinned but it is usually intact as would be expected for a condition that is more erosive than it is ulcerative [3]. Squamous cell carcinoma arising on the scars has also been reported [8].

Clinical hallmark of EPD is the presence of inflamed erosion. Most patients present with thick, yellow, or yellow-brown crusts covering one or more shallow inflamed erosions. Pustules have been reported to be present in many patients, they are usually flattened and contain little fluid. The skin around erosions is almost always atrophic. There is no swelling, warmth and regional lymphadenopathy. Pain or pruritus may be present [3].

EPDS treatment approaches include potent topical corticosteroids and oral isotretinoin; oral zinc sulfate or aspartate have been used, also. The best results have been achieved with topical corticosteroids [8]. The calcineurin inhibitors such as tacrolimus might have theoretic advantage over topical steroids, however, this advantage should be balanced by the possibility that these have oncogenic potential when used on chronically sun-exposed skin [3]. Topical tacrolimus is a potent anti-inflammatory and immunosuppressive molecule, which has been shown to be effective in the management of chronic inflammatory skin disease [9].

Two types of EPD have been discussed in the literature: EPD of the scalp and EPD of the lower legs. The clinical appearance, the histology, and the response to the therapy of lesions in these two sites are essentially identical but the settings in which they occur differ. Scalp lesions develop in the presence of atrophy secondary to actinic damage whereas the leg lesions occur only on non sun-damaged skin of patients with venous stasis disease. Controversy is whether the EPD at these two sites represent a single process or whether they are similar but separate, distinct conditions. It is belived that the unifying factor is predilection for atrophic skin of any cause to develop nonhealing, or slowly healing, shallow inflamed erosions [3].

The differential diagnoses of EPDS include pyoderma gangrenosum, pemphigus, cicatricial pemphigoid, bacterial and fungal infections, discoid lupus erythematosus, pustular psoriasis, subcorneal pustular dermatosis, infected eczema, epidermoid carcinoma, folliculitis decalvans, and lichen planus [10].

Conclusion

EPDS is not as rare condition in dermatology settings as speculated, but often goes unrecognized or misdiagnosed worldwide. These case reports are the first reports of EPDS in Serbia. EPDS is the diagnosis of exclusion, however it is the most likely diagnosis in cases of chronic shallow erosions that do not heal easily, in the background of actinic damaged skin or atrophic skin of the scalp in the elderly, with a prompt therapeutic response to the application of potent topical corticosteroids. These criteria, despite non-specific laboratory and pathological findings, are sufficient for diagnosis.

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CASE REPORT

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Spontaneous coronary artery dissection – rare but challenging

Spontana disekcija koronarne arterije – neuobičajeni izazov

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Abstract

Introduction. Spontaneous coronary artery dissection (SCAD) is a rare cause of the acute coronary syndrome. It occurs mostly in patients without atherosclerotic coronary artery disease, carrying fairly high early mortality rate. The treatment of choice (interventional, surgical, or medical) for this serious condition is not well-defined. **Case report.** A 41-year old woman was admitted to our hospital after the initial, unsuccessful thrombolytic treatment for anterior myocardial infarction administered in a local hospital without cardiac catheterization laboratory. Immediate coronary angiography showed spontaneous coronary dissection of the left main and left anterior descending coronary artery. Follow-up coronary angiography performed 5 days after, showed extension of the dissection into the circumflex artery. Because of preserved coronary blood flow (thrombolysis in myocardial infarction – TIMI II-III), and the absence of angina and heart failure symptoms, the patient was treated medicaly with dual antiplatelet therapy, a low molecular weight heparin, a beta-blocker, an angiotensin-converting enzyme (ACE) inhibitor and a statin. The patient was discharged after 12 days. On follow-up visits after 6 months and 2 years, the patient was asymptomatic, and coronary angiography showed the persistence of dissection with preserved coronary blood flow. **Conclusion.** Immediate coronary angiography is necessary to assess the coronary anatomy and extent of SCAD. In patients free of angina or heart failure symptoms, with preserved coronary artery blood flow, medical therapy is a viable option. Further evidence is needed to clarify optimal treatment strategy for this rare cause of acute coronary syndrome.

Key words:
acute coronary syndrome; dissection; coronary angiography; diagnosis; treatment outcome.

Apstrakt

Uvod. Spontana koronarna disekcija predstavlja neuobičajen uzrok akutnog koronarnog sindroma. Uglavnom nastaje kod bolesnika koji nemaju aterosklerotsku koronarnu bolest i nosi značajan rani mortalitet. Metoda izbora za lečenje ovog ozbiljnog stanja (interventno, hirurško ili medikamentno) još uvek nije jasno definisana. **Prikaz bolesnika.** U radu je prikazana bolesnica stara 41 godinu, primljena u našu bolnicu nakon neuspešne trombolitičke terapije akutnog anteriornog infarkta, iz lokalne bolnice bez sale za kateterizaciju srca. Hitan koronarni angiogram prikazao je spontanu koronarnu disekciju glavnog stabla i prednje silazne grane leve koronarne arterije. Kontrolna koronarografija nakon pet dana pokazala je proširenje disekcije u cirkumfleksnu arteriju. Zahvaljujući očuvanom koronarnom protoku (*thrombolysis in myocardial infarction* – TIMI II-III), odsustvu angine i simptoma srčane insuficijencije, bolesnica je medikamentno lečena dvojnom antiagregacionom terapijom, niskomolekularnim heparinom, beta blokatorom, ACE inhibitorom i statinom. Bolesnica je otpuštena nakon 12 dana lečenja. Na kontrolnim pregledima nakon šest meseci i dve godine, bolesnica je bila bez tegoba i koronarni angiogram je pokazao prisustvo disekcije uz očuvan koronarni protok krvi. **Zaključak.** Kod bolesnika sa spontanom koronarnom disekcijom, hitna koronarna angiografija je potrebna radi procene koronarne anatomije i zahvaćenosti disekcijom. Kod bolesnika koji nemaju anginozne smetnje ili simptome srčane insuficijencije, sa očuvanim koronarnim protokom, medikamentna terapija može biti prihvatljiv način lečenja. Dalja istraživanja su potrebna da bi se utvrdila optimalna strategija lečenja ovog retkog uzroka akutnog koronarnog sindroma.

Ključne reči:
akutni koronarni sindrom; disekcija; angiografija koronarnih arterija; dijagnoza; lečenje, ishod.

Introduction

Spontaneous coronary artery dissection (SCAD) is an infrequent cause of acute myocardial ischemia manifesting as acute myocardial infarction, unstable angina, cardiogenic shock or sudden cardiac death [1]. It has been reported to occur more often in women with or without risk factors for coronary artery disease (CAD). It can also occur in children, as

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well as in patients with risk factors or proven CAD [2]. The SCAD is commonly associated with atherosclerosis and peripartum vascular changes. It can be caused by connective tissue diseases (Ehlers Danlos type IV, Marphan's syndrome), systemic lupus erythematosus, cocaine abuse, use of oral contraceptives, vigorous exercise and prolonged sneezing. It can occur in patients without any of the conditions usually associated with SCAD – idiopathic SCAD [3–5]. Since this is a rare clinical entity, appropriate treatment strategy (interventional, surgical, or medical) is still unknown. Based on retrospective analysis of large data-bases of coronary angiograms, long-term survival of these patients, after initial event, is quite good, despite dramatic initial presentation and high early mortality rate. High early mortality rate is usually a consequence of myocardial infarction complications and unsuccessful revascularization procedures [6–8].

Case report

A 41-year-old female was admitted from a local hospital without cardiac catheterization facility less than 12 hours after the onset of chest pain at rest. There she was diagnosed with acute anterior myocardial infarction with ST elevation, and treated with thrombolysis. She had the history of smoking and childbirth 10 months earlier. She denied any previous hormonal disturbances.

On admission she complained of mild chest pain. Her body mass index (BMI) was 21.7 kg/m^2, blood pressure was 125/80 mmHg, pulse 80/min. ECG showed Q waves in leads V1-3, ST segment elevation of 2 mm in leads V1-4, and negative T waves in leads V1-6 (Figure 1). Laboratory analyses revealed creatine kinaze (CK) 1051 U/L, troponin T 3.4 ng/mL, alanine aminotransferase (ALT) 258 U/L, aspartate aminotransferase (AST) 256 U/L, total cholesterol 4.6 mmol/L, triglycerides 0.9 mmol/L. Other laboratory analyses were normal. Transthoracic echocardiography (TTE) showed decreased left ventricular systolic function due to akinesia of apex, distal two thirds of septum and anterior wall, and distal half of lateral wall, with ejection fraction of 35%. No valvular abnormality was noted.

Urgent coronary angiography (CAG) showed coronary dissection type B (National Heart, Lung and Blood Institute – NHLBI classification) of the distal left main (LM), and proximal, medial and initial segment of the distal left anterior descending (LAD) artery, with preserved blood flow (thrombolysis in myocardial infarction – TIMI III). Type C dissection was seen in the first diagonal (D1) coronary artery, with reduced blood flow (TIMI II). The left circumflex (Cx) and the right coronary artery (RCA) were normal (Figure 2).

The patient was presented to interventional cardiologists and cardiac surgeons who concluded that the lesions were not suitable for either percutaneous or surgical intervention. Medical therapy with oral aspirin, clopidogrel, metoprolol, captopril, high dose of simvastatin, and subcutaneous enoxaparin was initiated. On the day 5, CAG was repeated, and besides the persistence of coronary artery dissection in the LM and LAD, it revealed dissection type B in the proximal and distal part of circumflex artery (Cx); obtuse marginal (OM) branches were not involved (Figure 3).

These findings did not change already initiated medical therapy. During hospitalization, the patient was free of symptoms of angina or heart failure. The patient was discharged on the day 12, and was advised to continue with dual antiplatelet therapy, nitrates, beta-blocker, ACE inhibitor, and high dose of simvastatin.

After 6 months, the patient was still asymptomatic, without signs of ischemia on ECG. Transthoracic ultrasoho-

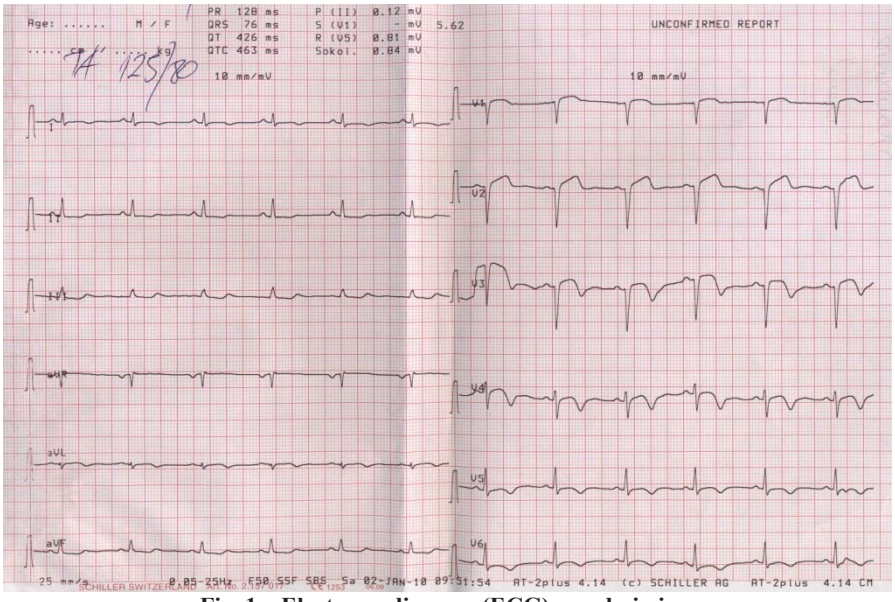

Fig. 1 – Electrocardiogram (ECG) on admission.

graphy showed a significant recovery of left ventricular systolic function, with hypokinesia restricted to distal half of the septum only. CAG revealed persistent dissection type B of LAD, and occlusive dissection type F of the second diagonal branch, with aneurysmatically changed proximal and medial

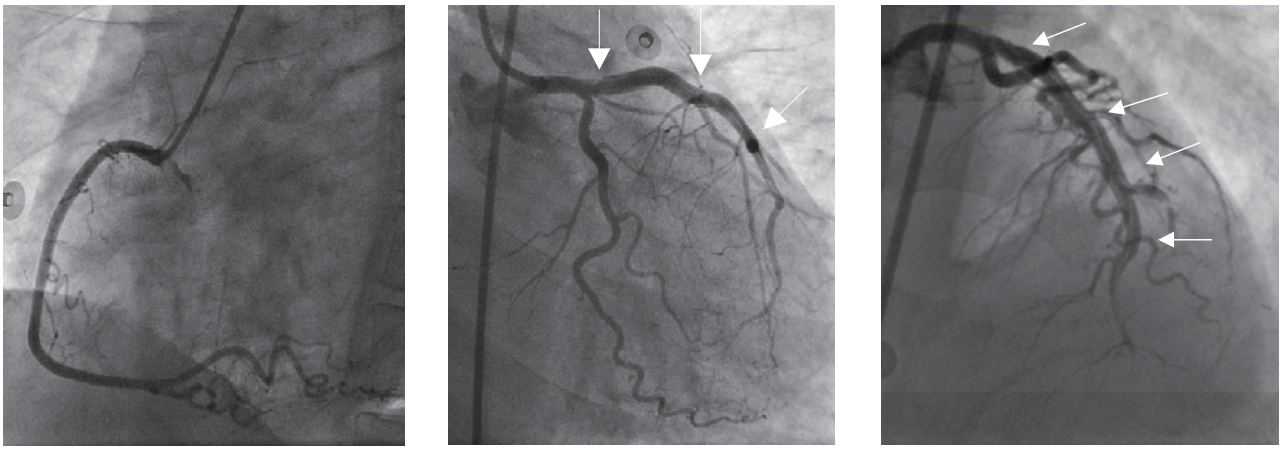

Fig. 2 – Coronary angiogram on the day 1 after admission (arrows indicating dissection line).

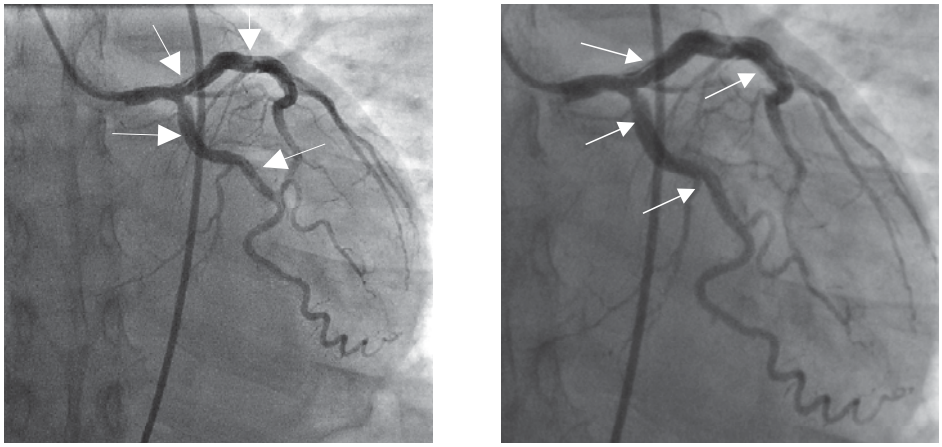

Fig. 3 – Coronary angiogram of the left coronary artery on the day 5 after admission (arrows indicating the dissection line).

segments of the LAD, and decreased coronary blood flow (TIMI II). There was no dissection in the LM and Cx. The right coronary artery was normal as on previous angiograms (Figure 4). Two years from the initial event, the patient was still asymptomatic, active, with good functional capacity, normal TTE findings, on the same medication except clopidogrel, which was stopped after one year.

Discussion

The first case of SCAD was described by Pretty [9] in 1931, the autopsy on a 42-year-old woman, who died suddenly after experiencing chest pain. The overall incidence of SCAD has reported to vary from 0.1% to 1.1% in angiographic studies [10–14]. The only study that reported on a lower

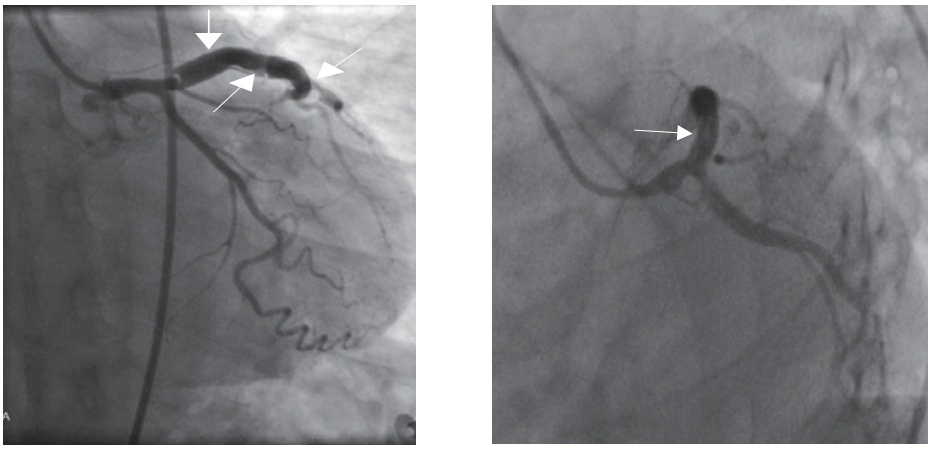

Fig. 4 – Coronary angiogram of the left coronary artery after 6 months (arrows indicating the dissection line).

incidence of SCAD is by Mortensen et al. [6], being only 0.07%. It affects predominantly women, with the reported ratio of 3:1 in large series of patients [1, 6, 7]. The mean age of SCAD patients is 44 years (range 17–69 years) in women, and 47 years (range 18–63 years) in men [6, 10–14]. There is also a case report of SCAD in a 14-year-old boy [2].

The cause of SCAD remains unknown. The most common conditions associated with SCAD are atherosclerosis and peripartum period. Rupture of atherosclerotic plaque can cause dissection of coronary artery. In autopsy studies, eosinophilic infiltrates have been described in *adventitia* of coronary arteries of SCAD patients, without coronary atherosclerosis [15]. During childbirth and peripartum period, eosinophils infiltrate the uterus, and serum collagenase levels increase. The presence of eosinophils in dissected coronary arteries may be local manifestation of systemic process. The occurrence of SCAD in peripartum women is explained by hormonal changes influencing collagen composition in arterial wall, which makes it weaker and ease to rupture [16]. A currently accepted theory considers the rupture of *vasa vasorum* causing haemathoma inside the media of the coronary artery, which spreads into intima. This may result in the rupture of the intima and lead to coronary artery dissection. Emotional or physical stresses, prolonged sneezing, use of oral contraceptives or cocaine abuse have been reported as precipitating factors [2, 3,11].

Angiographic findings of dissection in patients with SCAD can be classified according to the classification system of the National Heart, Lung and Blood Institute developed by the Coronary Angioplasty Registry. This classification has been used in everyday practice of percutaneous coronary interventions. Type A and B dissections demonstrate filling defects on contrast injection but have no or minimal persistence of contrast after the dye has cleared, type C dissections appear as dye staining in an extraluminal cap, type D as a spiral luminal defect, type E as persistent luminal defects and type F as total luminal occlusion [8].

Clinical presentation of SCAD is also variable. Sudden cardiac death occurs frequently, and it has been reported in around 75% of patients [17]. On the other hand, a recent "A Western Denmark Heart Registry Study" did not identify patients with SCAD that died suddenly, although the LAD was the predominant site of dissection [6]. Other clinical presentations include the entire spectrum of acute coronary syndromes. There are few reports on patients with SCAD who are entirely asymptomatic [18].

The optimal treatment strategy for SCAD remains unknown. In large angiographic cohorts, patients are treated with either percutaneous or surgical, but many patients are also treated with medical therapy only. The role of thrombolytic therapy is debatable. There are evidence for both successful and deleterious effects of thrombolytic therapy [19–21]. In series of Vanzetto et al. [7], only 4 patients presenting with ST segment elevation acute coronary syndrome underwent prehospital thrombolysis, which failed to achieve successful reperfusion in three of the cases. However, the severity and extent of coronary dissection was not found to be greater in patients treated with thrombolysis. In earlier studies, patients were mostly treated with medical therapy or coronary artery bypass grafting (CABG) [12–14]. CABG is challenging since grafting of the arterial "true lumen" is not always achievable, especially if dissection extends distally. With the development of percutaneous coronary interventions (PCI) more patients are treated with coronary angioplasty and stenting [6, 7, 11]. In the study by Hering et al. [11], the use of intravascular ultrasound (IVUS) lead to more PCI procedures (74%). There are case reports on patients with SCAD complicated by end- stage heart failure treated successfully with mechanical support devices or heart transplantation [22, 23].

Long-term prognosis in patients with SCAD is generally good. One-year survival in a large series ranges from 76% to 100% [3, 10–14]. In the study by Mortensen et al. [6] the mean follow-up time was 2.9 + 2.5 years, with major adverse cardiac event (MACE) free survival of 81% after 2 years. Meta-analysis by Thompson et al. [24] of the pooled data of 222 patients with SCAD, finds that after 2 years follow-up 95% of patients are still alive.

The largest registry of patients with SCAD has been recently reported by Tweet et al. [25] Their cohort consists of 87 patients with angiographically confirmed SCAD. The mean age was 42.6 years, and most of them were women (82%) while the initial presentation in 49% was ST elevation myocardial infarction. Conservative management was the treatment of choice in 31 patients and was associated with an uncomplicated in-hospital course, the same is true for coronary artery bypass grafting (7 of 87). Percutaneous coronary intervention was initially performed in 43 patients and technical success was achieved in only 28 (65%) and one patient died. During an average follow-up of 47 months (intequartile range 18–106) 5 persons developed heart failure, 16 had myocardial infarction and 3 had died at 10 years. Notably, from the group treated by CABG, 8 patients underwent repeated CAG. Of the 15 bypass grafts that had been placed, 11 were found to be occluded, 6 arterial and 5 venous grafts. This study found an unexpected association between fibromuscular dysplasia in non-coronary arterial trees and SCAD, which warrants further investigation.

Lately, patients with atherosclerotic risk factors presenting with coronary artery dissection are excluded from the group of patients with SCAD. Patients with associated atherosclerosis tend to be older, more frequently male, and have a higher prevalence of coronary risk factors. The reason for this division is different pathophysiological mechanism causing dissection [26].

There are some details regarding the patient in this case report that should be clarified. The patient was initially treated with thrombolysis. In our opinion, it might have preserved coronary blood flow and stabilized patients haemodynamics, allowing for transfer to the hospital with cardiac catheterization laboratory for further diagnostics. On the other hand, thrombolytics or therapy for acute coronary syndrome consisting of aspirin, clopidogrel and enoxaparine could have caused the spread of dissection into Cx by preventing occlusion of the false lumen. In our opinion, the possibility of atherosclerotic coronary artery lesion causing myocardial infarction is less likely, due to patient's profile without atherosclerotic risk factors and previous delivery 10

months ago. On the same track with this, would be a possibility of dissection caused by thrombolytic agent.

A decision to initiate medical therapy has been primarily based on the fact that the patient was asymptomatic, without signs of persistent ischemia, heart failure or arrhythmias, which would probably lead us to consider revascularization procedures. Furthermore, the extent of dissection would make PCI complex because of LM involvement, with the possibility of unsuccessful "wiring" of the true arterial lumen, and the need for stent implantation in very long coronary artery segments. All the mentioned imply a poor long-term outcome. Most importantly, TIMI III coronary blood flow secures perfusion of the myocardium, despite SCAD.

A decision to proceed with medical therapy after follow-up visits after 6 months and 2 years after initial event was based on the facts that the patient remained asymptomatic, with improvement of cardiac function assessed by TTE, despite CAG findings (regression, or "sealing" of dissection in LM and Cx, but persistent dissection in LAD causing aneurysmatic changes, coronary blood flow of TIMI II, and occlusion of diagonal branch).

Conclusion

Spontaneous coronary artery dissection is an infrequent cause of acute coronary syndrome. It affects mostly patients that do not have traditional risk factors for coronary atherosclerosis. Despite the presence of symptoms, coronary angiography is essential in making the diagnosis, as well as in initiating proper treatment strategy. The use of thrombolytic therapy is debatable, because it may preserve blood flow in the infarct related artery, but on the other hand, it may promote spreading of dissection into distal segments of coronary arteries. Depending on angiographic findings, short dissections probably should be treated by revascularization procedures, preferably PCI that can be preceded by imaging modalities like intravascular ultrasound or optical coherence tomography which should help in defining the extent of dissection into the coronary artery. Dissections that extend into distal segments of the coronary arteries may be treated with medical therapy only since the success of revascularisation procedures in these cases is highly uncertain.

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CASE REPORT

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Disseminated *Rhodococcus equi* infection in a patient with Hodgkin lymphoma

Diseminovana *Rhodococcus equi* infekcija kod bolesnice sa Hočkinovim limfomom

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Abstract

Introduction. *Rhodococcus (R) equi* is an opportunistic, uncommon human pathogen that causes mainly infection in immunocompromised hosts. The disease is usually presented as subacute pneumonia that is mostly cavitary and sometimes bacteremic. **Case report.** We reported the extremly rare case of a 43-year-old woman with Hodgkin lymphoma, who developed *R. equi* pulmonary infection after recieving multiple courses of chemotherapy. Secondary, the patient developed bacteremia, leading to sepsis and dissemination of *R. equi* infection in many extrapulmonary sites. At addmission the patient was febrile, tachypnoic, tachycardic, hypotensive, with facial edema, splenomegaly, positive meningeal signs, left hemiparesis and paraparesis. Laboratory data included erythrocyte sedimentation rate (ESR) > 140 mm/h, C-reactive protein (CRP) 143.0 mg/L, red blood cells (RBC) 2.14 × 10^{12}/L, whyite blood cells (WBC) 2.8 × 10^{9}/L, lactate dehydrogenase (LDH) 706 U/L, serum albumin 26 g/L, sodium 127 mmol/L and potassium 2.7 mmol/L. Blood culture and culture of sputum and empyema were positive for *R. equi.* Imaging studies demonstrated a large right cavitary pneumonia and abscess, empyema, pericarditis, mediastinal and intra-abdominal lymphadenopathy, brain and psoas abscesses, osteomyelitis and spondylodiscitis. The patient recovered completely after a 12-month treatment with combinations of parenteral and oral antibiotics (meropenem, vancomycin, teicoplanin, ciprofloxacin, rifampicin, macrolides etc), including drainage of abscesses and empyema. Eight years after completition of the treatment the patient was without recurrence of *R. equi* infection and lymphoma. **Conclusion.** Since the eradication od *R. equi* is very difficult, it is very important to make the diagnosis and initiate appropriate antibiotic therapy as soon as possible.

Key words:
rhodococcus equi; hodgkin disease; immunologic deficiency syndromes; infection; sepsis; anti-bacterial agents; drug therapy, combination.

Apstrakt

Uvod. *Rhodococcus (R) equi* je oportuni patogen koji retko uzrokuje oboljenje u humanoj populaciji, uglavnom kod imunokompromitovanih domaćina. Oboljenje se obično ispoljava kao subakutna pneumonija koja je često kavitarna i neretko praćena bakterijemijom. **Prikaz bolesnika.** Prikazujemo veoma redak slučaj bolesnice stare 43 godina sa Hočkinovim limfomom, kod koje je došlo do razvoja *R. equi* pneumonije u toku primene hemoterapije. Kasnije, kod bolesnice je došlo do razvoja bakterijemije i sepse uz diseminaciju *R. equi* infekcije u brojna ekstrapulmonalna tkiva. Na prijemu bolesnica je bila febrilna, tahipnoična, tahikardična, hipotenzivna, sa otokom lica, splenomegalijom, pozitivnim meningealnim znacima, levostranom hemiparezom i paraparezom. U laboratorijskim nalazima sedimentacija eritrocita (SE) bila je > 140 mm/h, C-reaktivni protein (CRP) 143,0 mg/L, eritrociti 2,14 × 10^{9}/L, leukociti 2,8 × 10^{12}/L, lektat dehidrogenaza (LDH) 706 U/L, serumski albumin 26 g/L, natrijum 127 mmol/L i kalijum 2,7 mmol/L. Hemokulturom i kulturom sputuma i empijema izolovan je *R. equi.* Radiološke metode registrovale su veliku kavitarnu pneumoniju i apsces pluća, empijem pleure, perikarditis, medijastinalnu i abdominalnu limfadenopatiju, apsces mozga i psoasa, osteomijelitis i spondilodiscitis. Bolesnica se potpuno oporavila nakon 12 meseci terapije kombinacijama parenteralnih i peroralnih antibiotika, uz primenu drenaže apscesnih kolekcija i empijema. Osam godina po završenoj terapiji kod bolesnice nije zabeležen recidiv *R. equi* infekcije niti limfoma**. Zaključak.** S obzirom na to da je eradikacija *R. equi* veoma teška, od velike je važnosti što ranije postaviti dijagnozu i otpočeti adekvatnu antibiotsku terapiju.

Ključne reči:
rhodococcus equi; hodžkinova bolest; imunitet, sindromi nedostatka; infekcija; sepsa; antibiotici; lečenje, kombinovano.

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Introduction

Rhodococcus equi R. equi is an opportunistic, gram-positive, weak acid-fast aerobic *coccobacillus* that primarily causes zoonotic infections and is usually present in soil and feces of horses [1, 2]. Although natural exposure to *R. equi* is frequent, the first infection by this organism in humans was described in 1967 [3]. Overall, a few hundred cases of *R. equi* infections in humans have been reported till now. The disease is typically described in immunocompromised hosts, especially in patients with acquired immunodeficiency syndrome (AIDS), and less than 15% of the patients have hematopoietic and other malignancies [4–13]. The most often, *R. equi* causes a subacute, cavitary and bacteriemic pneumonia which is characterised by frequent relapses and a high mortality rate. Extrapulmonary disease is usually a late manifestation of the initial pulmonary infection [4–9, 14–18].

We reported an extremely rare case of disseminated *R. equi* infection in a patient with Hodgkin lymphoma who was successfully treated with antibiotics and drainage of abscesses. To the best of our knowledge, this is the first documented case of *R. equi* infection in Serbia.

Case Report

A 43-year-old woman was admitted to the Clinic for Infectious and Tropical Diseases of Military Medical Academy, Belgrade due to disseminated *R. equi* infection on April 8, 2004. She became ill on February 2001 with the appearance of fever, malaise and enlarged lymph nodes in the right inguinal region. At that period of time, the patient worked hard as a lawyer, for several months, at a farm near the village she lived in. One year later, a generalized lymphadenopathy occurred and the Hodgkin lymphoma was diagnosed. After 7 cycles of chemotherapy, in October 2002, the patient developed high fever, chills, cough, and severe pain in the right hemithorax. On chest radiography loose shadow in the right lung with pleural effusion was registered. Despite the implementation of various parenteral and peroral antibiotics in a multiple short courses, the progression of acquired pneumonia in the right lung was registered and the permanent deterioration of general condition.

Chemotherapy was discontinued in March 2003. In order to maintain intra-abdominal lymphadenopathy radiotherapy was performed. In the following period, in addition to high temperature and expectoration of the purulent sputum, a pain in the left hip occurred. Computed tomography showed the presence of a large abscess and pneumonia in the right lung, pleural effusion on the right side and paraaortic lymphadenopathy of more than 2 cm. Magnetic resonance imaging registered progressive spondylodiscitis L2/L3 and psoas abscess at the left side (Figure 1).

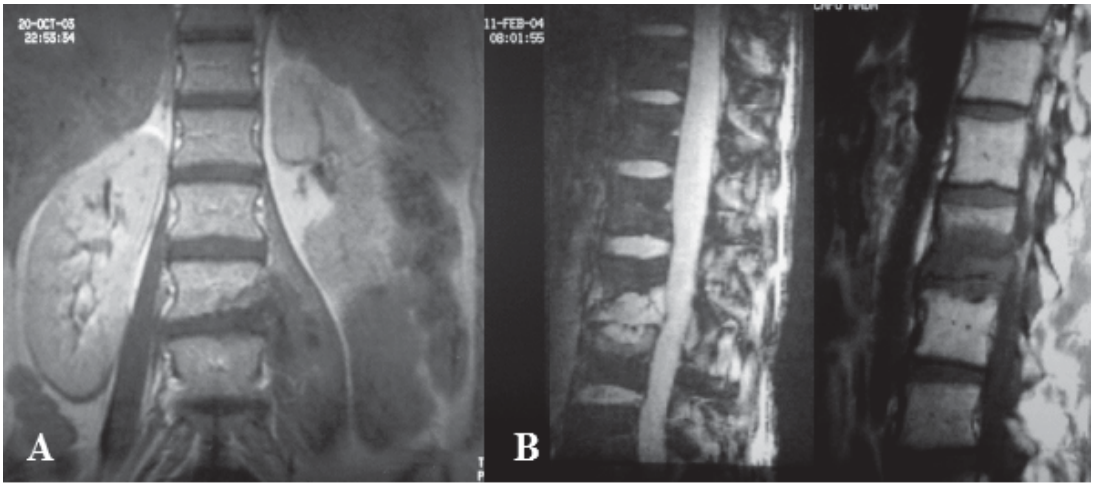

Fig. 1 – Magnetic resonance imaging of the lumbar spine in the presented patient with disseminated *R. equi* infection: progressive spondylodiscitis L2/L3 and psoas abscess of the left side.

During July, 2003 pathohistological examination of the material obtained by biopsy of the right pulmonary infiltration showed pulmonary malacoplakia. In late 2003 blood culture and cultures of the sputum and pleural empyema were positive on *R. equi*. Prolonged use of parenteral antibiotics according to the antibiogram with blood transfusions, human albumin and other replacement therapy resulted in improvement of the patient's general condition, normalization of body temperature and marked regression of the right pulmonary infiltration. However, on February 2004 the patient developed to allergic reaction to vancomycin and soon after, hemolytic anemia occured. By the end of March, new relapse was registred. According to high fever, dizziness, headache, nausea, vomiting, cough, expectoration of purulent sputum, hemoptysis and chest pain, a positive meningeal signs were detected. Computerized tomography (CT) scan showed large nodular lesion with cavitation in right lung. This lesion was in a close contact with the vena cava superior, pericard and right hilus. An oval lesion 10 cm in diameter has also been registred in the basal region of the chest, that was in contact with right chest wall and destruction of left ribs 9 and 10 (Figure 2). A lumbar puncture was not performed because of the presence of lumbar spine abscess collection. At that time the patient was addmitted to the

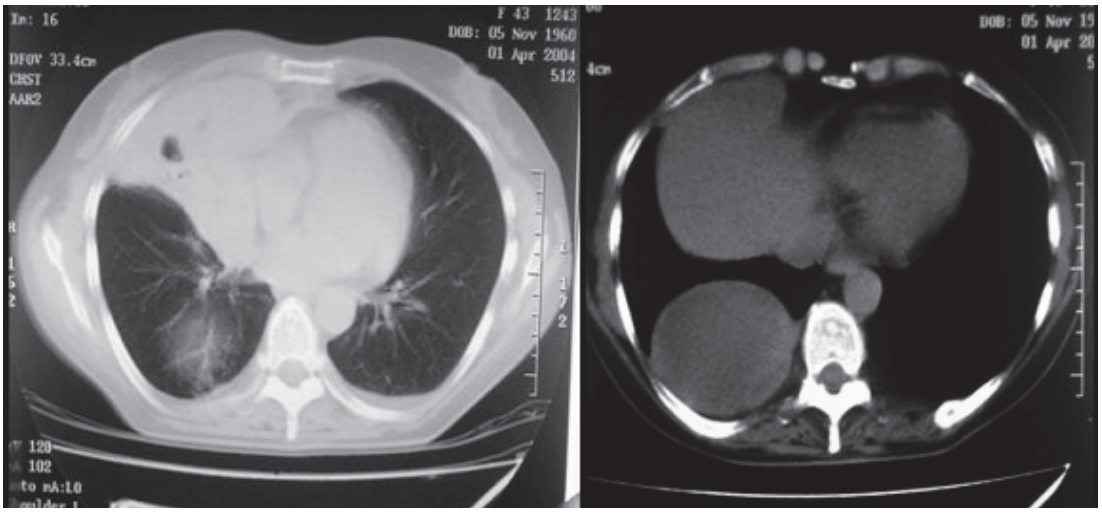

Fig. 2 – Computed tomography of the chest in the presented patient: large cavitary pneumonia and abscess in the right lung.

Clinic for Infectious and Tropical Diseases of Military Medical Academy, Belgrade.

At addmission the patient was in a very bad general condition, febrile (38.5°C), asthenic, hardly moving, with facial edema, tachypnoic, tachicardic and hypotensive. In the physical findings silent breathing in the lower parts of the right lung, splenomegalia, positive meningeal signs, left side hemiparesis and paraparesis were registred.

Laboratory data included ESR > 140 mm/h, fibrinogen 5.8 g/L, CRP 143.0 mg/L, RBC 2.14 × 10^{12}/L, Hb 66 g/L, WBC 2.8 × 10^{9}/L, neutrophils 84.7%, pletelets (PLT) 542 × 10^{9}/L, bilirubin 25 μmol/L, serum protein 54 g/L, serum albumin 26 g/L, gamma GT 80 U/L, LDH 706 U/L, sodium 127 mmol/L, potassium 2.7 mmol/L, iron 5 mmol/L, cholesterol 3.4 mmol/L, γ globulin 19.8%. Direct and indirect Coombs tests were positive. Serological analyses to hepatitis B and C, and human immunodeficiency viruses were negative.

Blood culture and sputum and empyema cultures were positive for *R. equi. R. equi* was sensitive to macrolides, rifampicin, fluoroquinolons, glicopeptids, carbapenems, amikacin and amoxicilin-clavulaxate, but resistentant to cefalosporins, piperacillin-tazobactam, clindamycin, amoxicillin and gentamicin.

Infiltration connected with right hilus and nodular lesion in posterobasal region of the right lung, diameter of 9 cm, were registred on chest radiography examination. Radiography of LS spine showed pathologic fracture of L2 corpus with a wedge-shaped deformation (Figure 3).

Pericardial effusion of 1.4 cm was registred on ehocardiography and splenomegaly of 16 cm on the abdominal ultrasound. CT scan of the brain showed hypodense zones 4 mm in diameter in crus posterior of the right capsula interna and left olive, which did not change their caracteristics after intravenous addmission of the contrast.

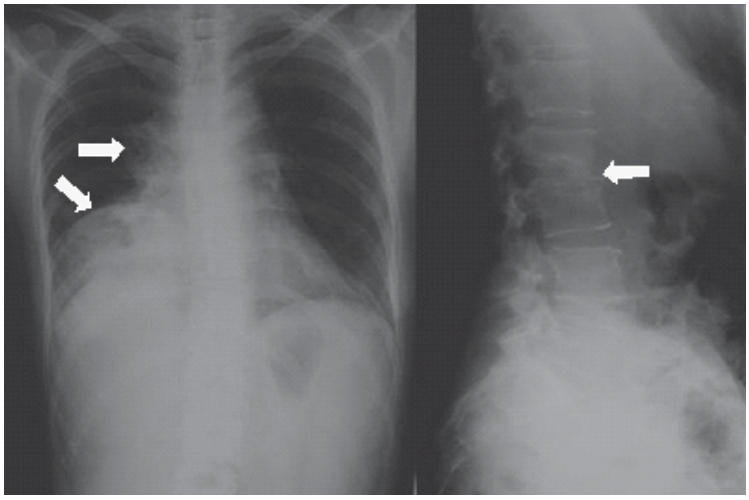

Fig. 3 – Radiography of the chest and lumbar spine in the presented patient at addmission.

Immediately after addmission the therapy with meropenem and rifampicin started. After 7 days ciprofloxacin and amikacin were added. After 14 days amikacin was excluded and teicoplanin was added (Table 1). During the first month the patient recieved immunoglobulins, human albumin, fresh

Table 1

Combined antibiotic therapy in a patient with disseminated *R. equi* infection during the first month of hospitalization in 2004

Antibiotics	Dosage	Application	Therapy duration
Meropenem	1 gr / 8 h / daily	*iv* infusion	April 4 – May 5
Ciprofloksacin	200 mg / 12 h / daily	*iv* infusion	April 15 – Maj 8
Amikacin	1 gr / 24 h /daily	*iv*	April 15 – April 29
Teikoplanin	400 mg / 24 h /daily	*iv* infusion	April 29 – May 15
Rifampicin	600 mg / daily	per os	April 4 – May 12

frosen plasma, cryoprecipitate, filtered erithrocytes and symptomatic therapy which led to normalization of the temperature, improvement of general condition and laboratory values. At control chest CT, regression of lung changes was noticed. In the region of the middle lobe, retrosternally and paracardially, a zone of consolidation of the lung parenchima with cavitation of 5 × 3 cm was registred. Up to the back thoracal wall in the right posterobasal region, incapsulated liquid collection of 6 × 7 cm in diameter was noticed. There was a large number of lymph nodes of about 2 cm in diameter in mediastinum, paratracheally and up to the arcus aortae (Figure 4).

A combined antibiotic treatment was continued also including meropenem, ciprofloxacin, vancomycin, rifampicin, trimethoprim-sulfamethoxazole and lincomycin. By the end of August 2004, drainage of abscess collection diameter of 10 cm in the left psoas was performed (Figure 5). A parenteral antibiotical therapy was continiued for six months more and than was changed with peroral antibiotics (rifampicin, azithromycin, roxithromycin, eritromycin, linkomycin, clarithromycin, ciprofloxacin, trimethoprim-sulfamethoxazole) up to 12 months. At discharge from the Clinic, on February 1, 2005, the patient was in good general condition with lumbar pain and normal laboratory values.

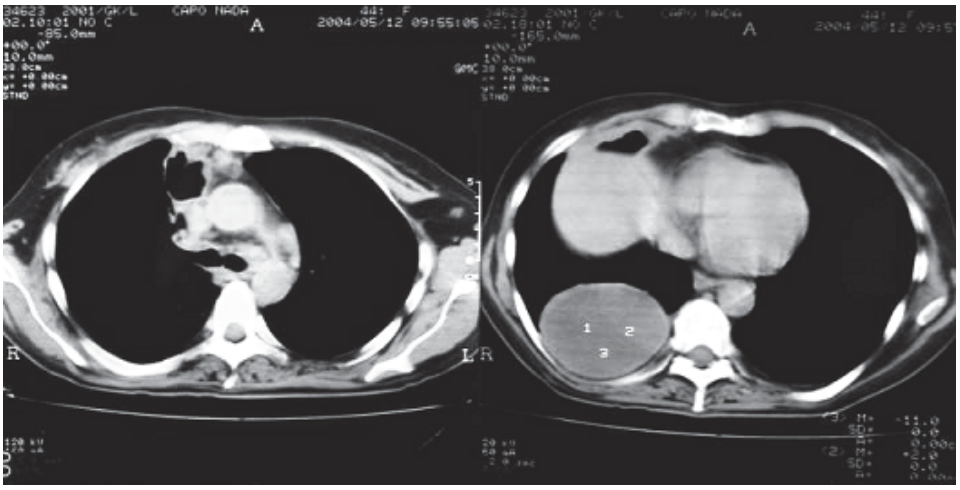

Fig. 4 – Computed tomography of the chest in the presented patient with disseminated *R. equi* infection after a month of combined antibiotic therapy.

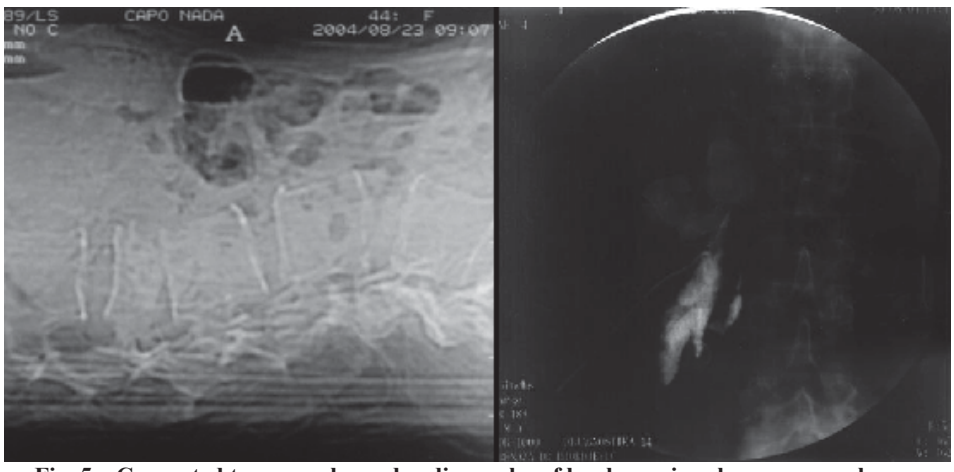

Fig. 5 – Computed tomography and radiography of lumbar spine show a psoas abscess in the presented patient.

Four months later, MRI of the lumbar spine showed cured spondylodiscitis L2/L3 with kyphosis deformity. There were no signs of paravertebral infection (Figure 6).

Five months after therapy cessation, CT scan showed scared lesions in basal paracardial regions of the right lung and incapsulated liquid collection 4 cm in diameter in the posterobasal region of the same lung. Mediastinal lymph nodes were not enlarged (Figure 7).

Eight years after treatment cessation the patient was without recurrence of *R. equi* infection and lymphoma. Meanwhile, fluid collection in the right lung was completely and spontaneously regressed (Figure 8).

Discussion

R. equi is an opportunistic pathogen well described in veterinary science as a causative agent of pneumonia and sepsis in domestic animals, and a leading cause of chronic pneumonia in foals less than six months of age [1, 2]. However, its role in the etiology of human diseases is much less known. Human *R. equi* infection was described in 1967 for the first time in a patient with autoimmune hepatitis, who suffered from cavitary pneumonia after immunosupressive treatment [3]. In the next 15 years only 12 cases of this illness have been reported. After that, the frequency of *R. equi* in-

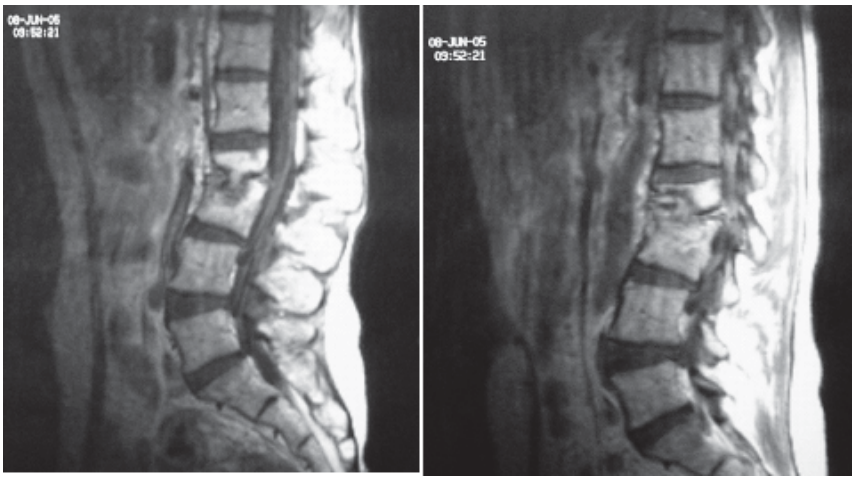

Fig. 6 – Magnetic resonance imaging of the lumbar spine 2 months after antibiotic treatment cessation.

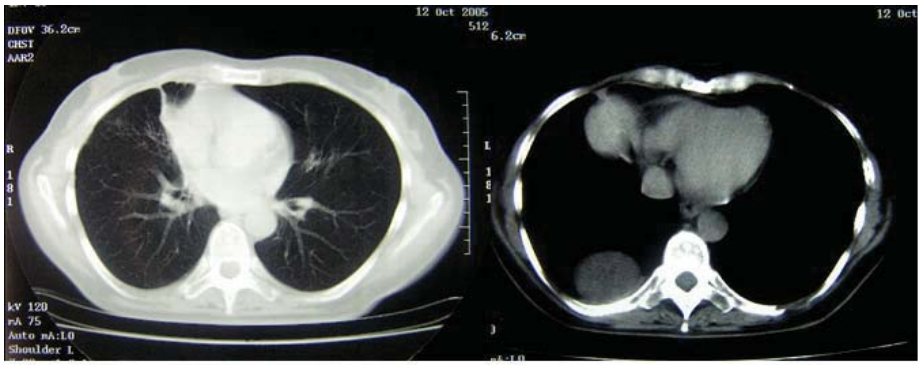

Fig. 7 – Computed tomography of the chest in the presented patient 5 months after the antibiotic therapy completition.

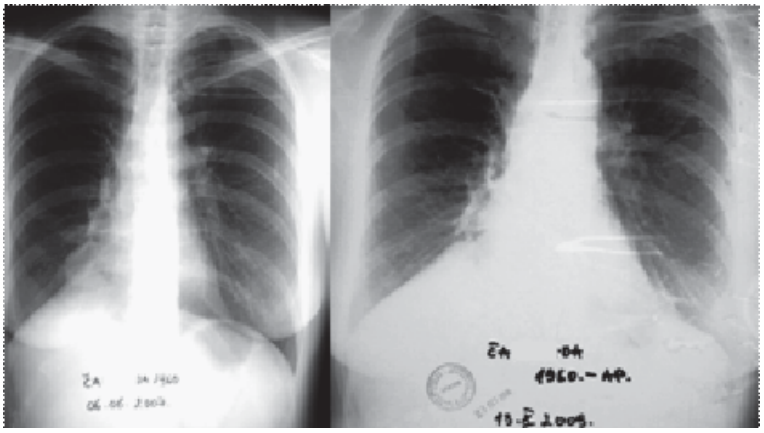

Fig. 8 – Radiography of the chest in the presented patient few years after the antibiotic therapy

fection begins to increase along with the increasing number of immunocompromised hosts, particularly the number of AIDS patients [4, 19–21].

R. equi has been isolated from almost each specimen and tissue of domestic and wild animals. It has been isolated from soil on 50%–90% farms on each continent, except Antarctic. Concentration of *R. equi* is especially high in feces of horses. From that reason direct and indirect contact with domestic animals could have an important role in development of human *R. equi* infection. The infection occurs through inhalation, ingestion and inoculation [1, 2, 22–24]. We assume that the presented patient acquired *R. equi* infection most probably by inhalation, working at the farm of horses. However, we are not sure when the infection actually occurred.

Like the other authors, we assume that regional lymphadenitis was caused by dissemination of *R. equi* infection from the primary focus [20, 25]. However, we are not absolutely sure what was the role of *R. equi* infection in the development of mediastinal and intra-abdominal lymphadenopathy in the presented patient. Namely, chemotherapy of Hodgkin lymphoma was interuppted when the patient had significant mediastinal and intraabdominal lymphadenopathy, and this lymphadenopathy just withdrew after a long-term of a combined antibiotical therapy. This indicates that the most likely cause of lymphadenitis was *R. equi*.

The most important factor in the development of *R. equi* infection is impaired cellular immunity. This is confirmed by the results of the study conducted in HIV positive persons, which showed that *R. equi* infection is more common in patients with blood CD4 + lymphocytes count less than 100/mm^3. For that reason the disease is more frequent in the patients with AIDS and on immunosuppressive therapy after solid organ or bone marrow transplantation, but very rare in healthy immunocompetent persons [6, 7, 8, 20, 26, 27]. This explains why there was continuous impairment of lung inflammatory process in the presented patient and why the dissemination of *R. equi* infection appeared. However, the delayed diagnosis and inadequate antibiotic therapy has also contributed to the frequent relapses and dissemination of the disease. Namely, bacteriemia, relapses and dissemination of the infection also registered after chemotherapy cessation and making the diagnosis. According to data from the literature, relapses, bacteriemia and visceral dissemination of *R. equi* infection rarely occures in HIV negative persons in contrast to the patients with AIDS [4, 14, 16, 27–30].

Clinical manifestations of *R. equi* infection may be different, but the disease is usually manifested with respiratory symptoms and signs. The most frequent form of *R. equi* infection is chronic, progressive, granulomatous and necrotizing inflammation which is cavitary in 2/3 of the patients. The other manifestations of respiratory infection are nodular infiltrates which can be complicated by lung absesses, empyema, pleural effusion and spontaneous pneumothorax [6, 7, 8, 20, 27]. Extrapulmonal *R. equi* infection can be primary and secondary, and usually is a late manifestation of initial lung infection as was the case in our patient. It is a multisistemic or local disease, usually presented as sepsis, fever of unknown origin, cerebral abscess, meningitis, pericarditis, osteomyelitis, subcutaneous abscess, regional lymphadenitis, mastoiditis, or wound infection [18, 25, 27, 31–36]. Because of the delayed diagnosis and treatment, frequent bacteriemias and dissemination of *R. equi* infection, almost all of these manifestations were seen in our patient. However, we should not forget that in such cases disease progression is registred in about 10% of patients, despite adequate therapy [4, 20, 27].

Optimal treatment regimen and optimal duration of antibiotic therapy in patients with *R. equi* infection are not exactly defined. Combined antibiotic treatment is the cornerstone of the therapy for *R. equi* infection, but surgical incision and drainage of abscess formation can also be useful. Treatment of severe forms of the disease should start with combined parenteral antibiotics and after clinical and laboratory improvement should switch to a combined peroral antibiotic therapy, we also applied [37–43]. Because of high incidence of bacteriemia and large bacterial inoculum it is necessary to apply adequate combination of antibacterial drugs with bactericidal activity, with simultaneous application of lipophilic antibiotics with good intracellular penetration. It is believed that antibiotics combination which includes carbapenems (meropenem, imipenem), glycopeptides (vancomycin, teicoplanin), macrolides and rifampicin can be optimal [4, 20, 27, 37–43]. That was the way we started and continued antibiotic treatment for exactly one year, that resulted in a complete success. Some authors recommend combinations with two or even more antibiotics with intracellular activity, while the others put accent on the bactericidal antimicrobial agents, especially during the initial phase of treatment [37–43]. We appreciated the views of both authors and conducted the treatment with four antimicrobial drugs, guided by antibiogram, in a long period of time. After careful consideration, we anticipated that there was no allergic reaction to vancomycin in our patient, actually it was "red woman" phenomenon, so we continued the treatment with glycopeptides sucessfully. At the same time great attention was paid to the volume replacement therapy and to the fact that drainage of large abscess collection in those with *R. equi* infection should be done whenever possible.

Conclusion

Human *R. equi* infection is a very rare disease usually affecting those with severe immunodeficiences. The delayed diagnosis is very frequent, despite the advances in knowledge about the causative agent. The most important step in making diagnosis is a clinical suspition of the disease and after that, microbiological analyses from the adeqate specimens. Since it is almost impossible to eradicate *R. equi*, it is very important to make a diagnosis and start therapy as soon as possible. Antimicrobial therapy is based on a combination of antibacterial drugs with bactericidal activity and drugs with good intacellular penetration and applied for a long period of time.

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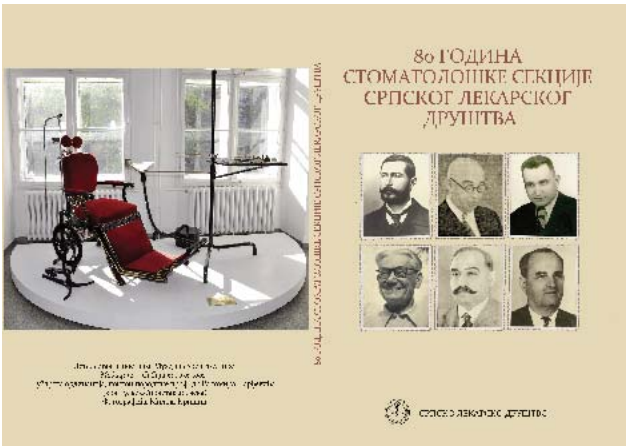
P R I K A Z K N J I G E

80 godina Stomatološke sekcije Srpskog lekarskog društva

Naslov knjige: 80 godina Stomatološke sekcije Srpskog lekarskog društva
Urednici: prof. dr Brana Dimitrijević, dr Zoran Vacić
Izdavač: Srpsko lekarsko društvo, Beograd
Godina izdanja: 2013.



Knjiga od stotinak stranica pod gornjim naslovom objavljena je na dan 21.11. 2013. godine, kada je održan 39. sastanak Sekcije za istoriju medicine Srpskog lekarskog društva (SLD), posvećen 80-godišnjici osnivanja Stomatološke sekcije SLD. U njoj je šezdesetak stranica teksta, i četrdesetak stranica priloga: fotografija i faksimila najrazličitijih dokumenata.

Na osnivanje specijalističkih sekcija SLD dugo se unutar njega samog gledalo s krajnjim nepoverenjem, iz straha (danas vidimo ipak opravdanog) od cepanja jedinstvene medicinske nauke, na niz sve manjih i manjih oblasti, koje će se vremenom udaljavati jedna od druge. Otuda su statutarni uslovi za nastanak specijalističkih sekcija stvoreni tek posle Velikog rata, 1919. godine.

Nasuprot svim ovom bojaznima Stomatološka sekcija nastala je ne zbog izdvajanja, već zbog priključenja ostalim medicinskim disciplinama, budući da u tom trenu (1933) stomatologija još nije bila zastupljena u dodiplomskoj nastavi na Medicinskom fakultetu u Beogradu (osnovanom 1921. godine). Doktori opšte medicine mogli su da specijalizuju bolesti usta i zuba, na istoimenoj poliklinici Opšte državne bolnice u Beogradu, počev od 1923. godine, ali su, osim ove, postojali i mnogi drugi načini zanavljanja zubnolekarskih (bolje reći zubarskih) snaga. Tako je majstor zubni tehničar – što je tada bio zvaničan naziv ovih stručnjaka – posle 14 godina prakse u svojoj radionici (danas laboratoriji), sticao pravo na polaganje ispita „za rad i u ustima pacijenta“, i potom prelazio u „zubare“.

Osnivanje Stomatološke SLD ubrzo je urodilo krupnim plodovima. Na Medicinski fakultet u Beogradu uveden je jednosemestralni predmet Odontostomatologija (1936), a kao nastavna baza poslužila je već pomenuta poliklinika, koja će 1930. godine biti preimenovana u stomatološka. Ovo će biti od ogromnog značaja kada se bude 1948. godine osnivao Stomatološki fakultet, prvi te vrste na Balkanu.

Knjiga obiluje nizom do sada manje poznatih, pa i nepoznatih podataka, koje rasvetljavaju razvoj stomatologije u poslednja dva i po veka u Evropi, SAD i Srbiji. Moderna stomatologija, smatra se, počinje od Fošara (Pierre Fauchard, 1678–1761) koji je svojom knjigom „Zubni hirurg“ (1728) ukazao da zubna hirurgija nije puko vađenje zuba, već da je ona i isceliteljska i obnoviteljska. Hirurgija, da podsetimo, u to doba ne pripada medicini. Ova, nazovimo je njena nova grana zubna-hirurgija, posle Fošara intenzivno će tražiti i nalaziti veze sa mnogim zanatima, što beše prirodno, s obzirom na njeno korišćenje najrazličitijih pomoćnih i gradivnih materijala. Stoga će se tokom čitavog XIX veka stomatologija, na primer u Francuskoj, izučavati i kao zanat, a u Srbiji sve do početka Drugog svetskog rata.

Prva zubarska škola osnovana u Baltimoru, SAD 1846. godine iz pravnih razloga, da bi se znalo ko je (a ko nije) ovlašćen za ovu vrstu poslova. Naziv profesije skovan je po Fošarovoj sintagmi – zubna hirurgija. Njeni pripadnici bili su doktori zubne hirurgije (DDS). Ono ‘doktor’ ukazivalo je na moralne norme kojih se zubni hirurzi moraju držati. Ali, prema medicini beše iskopan dubok rov, u korist zubno hirurške veštine. Reč stomatologija, koja će se tek kasnije pojaviti u Evropi, ni do danas nije se ukorenila u SAD. Model američkih zubarskih škola ubrzo će se raširiti i po Evropi.

Tako će u Parizu već 1857. godine biti osnovana Ecole Dentaire, ali će uskoro biti uvedena i specijalnost zubnog lekarstva za svršene doktore opšte medicine, što će potom dovesti do silnih napetosti (pa i „rata“) između zubara (dentista) i doktora opšte medicine, specijalista zubnog lekarstva.

Ovaj kratak istorijat zubnog lekarstva (zubarstva, zubarije) u globalnim razmerama, iznet u tekstu Brane Dimitrijevića „Zašto je pre osamdeset godina osnovana Stomatološka sekcija Srpskog lekarskog društva“, skladno je (u istom tekstu) dopunjen i nizom podataka o razvoju stomatologije u Srbiji, do osnivanja pomenute sekcije koji se tiču i civilnog i vojnog saniteta. Članak Zorana Vacića „Zubi Laze Ilića“ osvetljava nam jedan malo poznati tekst dr Laze Ilića (poznatog i po svom tragičnom kraju!) iz đačkog lista „Zora“ štampanog u Beču 1875. godine, dok tekst Ljubodraga Popovića „Dr Vladimir Kujundžić (1886–1969) – prilozi za biografiju“, osvetljava, na osnovu pomnog proučavanja arhivske građe, lik prvog predsednika Stomatološke sekcije SLD, priznaćemo, sasvim zaboravljenog i nepoznatog. Vrlo prijatno iznenađenje priredile su dve mlade autorke, „niški đaci“, Miljana Mladenović Petrović i Snežana Mladenović svojim člankom „Dr Dimitrije Zlatanović“, autor prvih nezvaničnih udžbenika iz stomatologije, koji ispravlja dosadašnje shvatanje da su Stomatološku sekciju SLD osnovali isključivo beogradski doktori opšte medicine, specijalisti za bolesti usta i zuba.

Uz dosad nabrojane radove koji su usmeno izloženi, valja pomenuti i one koji su samo štampani u zborniku, a predstavljaju dopunu prethodnih. Tu su tekst Brane Dimitrijevića i Zorana Vacića „Analiza naslova prvih radova referisanih na Stomatološkoj sekciji Srpskog lekarskog društva“ „po pripadnosti“ s ondašnje i današnje tačke gledišta i rad Jelene Jovanović Simić Muzej nauke i tehnike, odeljenje Muzej Srpskog lekarskog društva. Osim toga, u prostorijama samog muzeja priređena je mala izložba posvećena „nekadašnjoj“ stomatologiji.

Najzad, tu su i odlomci dosad neobjavljenog spisa Miloša Đ. Popovića – pisca inače prve knjige o zubnom lekarstvu „Usta i zubi“ (Beograd, 1904), kod nas – a pod naslovom „Istorija zubnog lekarstva u Srbiji“, u odeljku Prilozi, u kome su zatim dati faksimili različitih dokumenata i starih fotografija. Znatan deo priloga posvećen je Zubnoj stanici u Vodeni, koja je osnovana početkom 1917. godine. Za istoriju vojne stomatologije ona je značajna zato što se u njoj prvi put u istoriji srpskog vojnog saniteta vršila i rekonstruktivna stomatologija.

Rečju, vrlo korisna knjiga, koja nam otkriva niz do sada malo poznatih, ili sasvim nepoznatih činjenica, ukazujući i na pravce budućih istraživanja.

dr Milče Čanković Kadijević

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All users of the system: authors, editors and reviewrs have to be registrated users with only one e-mail address. Registration should be made on the web-address:

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VSP publishes: **editorials, original articles**, **short communications**, **reviews**/**meta-analyses, case reports**, from the **medical history** (general or military), personal views, invited comments, letters to the editor, reports from scientific meetings, book reviews, extensive abstracts of interesting articles from foreign language journals, and other contributions. Original articles, short communications, meta-analyses and case reports are published with abstracts in both English and Serbian.

General review papers will be accepted by the Editorial Board only if the authors prove themselves as the experts in the fields they write on by citing not less than 5 self-citations.

Papers should be written on IBM-compatible PC, using 12 pt font, and double spacing, with at least 4 cm left margin. **Bold** and *italic* letters should be avoided. Observational and experimental articles, reviews and meta-analyses, should not exceed 16 pages (including tables and illustrations); case reports – 6; short communications – 5; letters to the Editor, reports on scientific meetings and book reviews – 2.

All measurements should be reported in the metric system in terms of the International System of Units (SI). Standard, internationally accepted terms should be used.

MS Word for Windows (97, 2000, XP, 2003) is recommended for word processing; other programs are to be used only exceptionally. Illustrations should be made using standard **Windows** programs**.** Avoid the use of colors in graphs.

Papers are reviewed anonymously by at least two editors and/or invited reviewers. Remarks and suggestions are sent to the author for final composition. Galley proofs are sent to the first author for corrections that should be returned within 3 days. Manuscripts accepted for publication are not being returned.

Preparation of manuscript

Parts of the manuscript are: **Title page; Abstract with key words; Text; References**.

1. ***Title page***

a) The title should be concise but informative. Subheadings should be avoided;

b) Full name of each author;

c) Name and place of department(s) and institution(s) of affiliation, clearly marked by standard footnote signs.

2. ***Abstract and key words***

The second page should carry a structured abstract with the title for original articles, metanalyses and case reports. The abstract should state the purposes of the study or investigation, basic procedures (selection of study subjects or laboratory animals; observational and analytical methods), main findings (giving specific data and their statistical significance, if possible), and the principal conclusions. It should emphasize new and important aspects of the study or observations. S t r u c t u r e d abstract should contain typical subtitles: *background/aim, methods, results* and *conclusion*. The abstract for metaanalyses and obrginal papers should have up to 450 words, and up to 150 words for case reports (with subtitles *background, case report, conclusion*). Below the abstract authors should provide, and identify as such, 3–10 key words or short phrases that will assist indexers in cross-indexing the article and will be published with the abstract.

3. ***Text***

The text of original articles is divided into sections with the headings: **Introduction**, **Methods**, **Results**, and **Discussion**. Long articles may need subheadings within some sections to clarify their content.

In the **Introduction** repeat the title of the article, excluding the names of authors. State the purpose of the article and summarize the rationale for the study or observation. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

Methods. Describe your selection of the observational or experimental subjects (patients or experimental animals, including controls) clearly. Identify the methods, apparatus (manufacturer's name and address in parentheses), and procedures in sufficient detail to allow other workers to reproduce the results. Give references to established methods, including statistical methods. Identify precisely all drugs and chemicals used, with generic name(s), dose(s), and route(s) of administration. State the approvement of the Ethnics Committe for the tests in humans and enimals.

Results should be presented in logical sequence in the text, tables and illustrations. Emphasize or summarize only important observations.

Discussion is to emphasize the new and important aspects of the study and the conclusions that result from them. Relate the observations to other relevant studies. Link the conclusions with the goals of the study, but avoid unqualified statements and conclusions not completely supported by your data.

References

References should be superscripted and numbered consecutively in the order in which they are first mentioned in the text. **The references must be verified by the author(s) against the original document.** List all authors, but if the number exceeds 6, give 6 followed by et al. Do not use abstracts, secondary publications, oral communications, unpublished papers, official and classified documents. References to papers accepted but not yet published should be designated as ”in press“. Information from manuscripts not yet accepted should be cited in the text as ”unpublished observations“. References are cited according to the ***International Committee of Medical Journal Editors.*** *Uniform Requirements for Manuscripts Submitted to Biomedical Journals. Ann Intern Med 1997; 126: 36–47. Updated October 2001.*

Examples of references:

Jurhar-Pavlova M, Petlichkovski A, TrajkovD, Efinska-Mladenovska O, Arsov T, Strezova A, et al. Influence of the elevated ambient temperature on immunoglobulin G and immunoglobulin G subclasses in sera of Wistar rats. Vojnosanit Pregl 2003; 60(6): 657–612.

DiMaio VJ. Forensic Pathology. 2nd ed. Boca Raton: CRC Press; 2001.

Blinder MA. Anemia and Transfusion Therapy. In: Ahya NS, Flood K, Paranjothi S, editors. The Washington Manual of Medical Therapeutics, 30th edition. Boston: Lippincot, Williams and Wilkins; 2001. p. 413-28.

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: *Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG,* editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [serial on the Internet]. 2002 Jun [cited 2002 Aug 12]; 102(6): [about 3 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm

Tables

Each table should typed double-spaced on a separate sheet, numbered in the order of their first citation in the text in the upper right corner and supplied with a brief title each. Explanatory notes are printed under a table, using the following symbols, in this sequence: ***, †, ‡, §, ||, ¶, **, ††, ...** Each table has to be mentioned in the text. If you use data from another source, acknowledge fully.

Illustrations

Figures are submitted as photos which should be sharp. Letters, numbers, and symbols should be clear and even throughout and of sufficient size that when reduced for publication, each item will still be legible. Each figure should have a label on its back indicating the number of the figure, author's name, and top of the figure. If a figure has been published, acknowledge the original source.

Legends for illustrations are typed on a separate page, with arabic numerals corresponding to the illustrations. Identify and explain each one clearly in the legend symbols, arrows, numbers, or letters used to identify parts of the illustrations. Explain the method of staining in photomicrographs.

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Use only standard abbreviations. Avoid abbreviations in the title and abstracts. The full term for which an abbreviation stands should precede its first use in the text.

Detailed Instructions are available at the web site:
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Rukopis se piše sa proredom 1,5 sa levom marginom od **4 cm**. Koristiti font veličine 12, a načelno izbegavati upotrebu **bold** i *italic* slova, koja su rezervisana za podnaslove. Originalni članci, opšti pregledi i metaanalize ne smeju prelaziti 16 stranica (sa prilozima); aktuelne teme – osam, kazuistika – šest, prethodna saopštenja – pet, a pisma uredniku, izveštaji sa skupova i prikazi knjiga – dve stranice.

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b) Ispisuju se puna imena i prezimena autora.

c) Navode se puni nazivi ustanove i organizacijske jedinice u kojima je rad obavljen i mesta u kojima se ustanove nalaze, sa jasnim obeležavanjem odakle je autor, koristeći standardne znake za fus-note.

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Na drugoj stranici nalazi se strukturisani apstrakt sa naslovom rada. Kratkim rečenicama na srpskom i engleskom jeziku iznosi se **uvod i cilj** rada, osnovne procedure - **metode** (izbor ispitanika ili laboratorijskih životinja; metode posmatranja i analize), glavni nalazi - **rezultati** (konkretni podaci i njihova statistička značajnost) i glavni **zaključak**. Naglasiti nove i značajne aspekte studije ili zapažanja. Strukturisani apstrakt (**250** reči) ima podnaslove: *uvod/cilj, metode, rezultati* i *zaključak*. Za apstrakte na engleskom dozvoljeno je i do **450** reči. Strukturisani apstrakt je obavezan za metaanalize (istog obima kao i za originalne članke) i kazuistiku (do 150 reči, sa podnaslovima *uvod, prikaz slučaja i zaključak*). Ispod apstrakta, pod podnaslovom „Ključne reči“ predložiti 3–10 ključnih reči ili kratkih izraza koji oslikavaju sadržinu članka.

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Tekst sadrži sledeća poglavlja: **uvod**, **metode**, **rezultate** i **diskusiju**. **Zaključak** može da bude posebno poglavlje ili se iznosi u poslednjem pasusu diskusije. U **uvodu** ponovo napisati naslov rada, bez navođenja autora. Navesti hipotezu (ukoliko je ima) i ciljeve rada. Ukratko izneti razloge za studiju ili posmatranje. Navesti samo strogo relevantne podatke iz literature i ne iznositi opširna razmatranja o predmetu rada, kao ni podatke ili zaključke iz rada o kome se izveštava.

Metode. Jasno opisati izbor metoda posmatranja ili eksperimentnih metoda (ispitanici ili eksperimentne životinje, uključujući kontrolne). Identifikovati metode, aparaturu (ime i adresa proizvođača u zagradi) i proceduru, dovoljno detaljno da se drugim autorima omogući reprodukcija rezultata. Navesti podatke iz literature za uhodane metode, uključujući i statističke. Tačno identifikovati sve primenjene lekove i hemikalije, uključujući generičko ime, doze i načine davanja. Za ispitivanja na ljudima i životinjama navesti saglasnost etičkog komiteta.

Rezultate prikazati logičkim redosledom u tekstu, tabelama i ilustracijama. U tekstu naglasiti ili sumirati samo značajna zapažanja.

U **diskusiji** naglasiti nove i značajne aspekte studije i izvedene zaključke. Posmatranja dovesti u vezu sa drugim relevantnim studijama, u načelu iz poslednje tri godine, a samo izuzetno i starijim. Povezati zaključke sa ciljevima rada, ali izbegavati nesumnjive tvrdnje i one zaključke koje podaci iz rada ne podržavaju u potpunosti.

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Primeri referenci:

Đurović BM. Endothelial trauma in the surgery of cataract. Vojnosanit Pregl 2004; 61(5): 491–7. (Serbian)

Balint B. From the haemotherapy to the haemomodulation. Beograd: Zavod za udžbenike i nastavna sredstva; 2001. (Serbian)

Mladenović T, Kandolf L, Mijušković ŽP. Lasers in dermatology. In: *Karadaglić Đ*, editor. Dermatology. Beograd: Vojnoizdavački zavod & Verzal Press; 2000. p. 1437–49. (Serbian)

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: *Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG,* editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [serial on the Internet]. 2002 Jun [cited 2002 Aug 12]; 102(6): [about 3 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm

Tabele

Sve tabele pripremaju se sa proredom 1,5 na posebnom listu. Obeležavaju se arapskim brojevima, redosledom pojavljivanja, u desnom uglu (**Tabela 1**), a svakoj se daje kratak naslov. Objašnjenja se daju u fusnoti, ne u zaglavlju. Za fus-notu koristiti sledeće simbole ovim redosledom: ***, †, ‡, §, ||, ¶, **, ††, ...** Svaka tabela mora da se pomene u tekstu. Ako se koriste tuđi podaci, obavezno ih navesti kao i svaki drugi podatak iz literature.

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