

MEDICAL REVIEW

**JOURNAL OF THE SOCIETY OF PHYSICIANS OF VOJVODINA OF THE
MEDICAL SOCIETY OF SERBIA**
THE FIRST ISSUE WAS PUBLISHED IN 1948

Editor-in-Chief

LJILJA MIJATOV UKROPINA

Assistant to the Editor-in-Chief for Clinical Branches: PETAR SLANKAMENAC

Assistant to the Editor-in-Chief for Imaging Methods: VIKTOR TILL

Assistants to the Editor-in-Chief

BOJANA KRSTONOŠIĆ

ŽELJKO ŽIVANOVIĆ

EDITORIAL BOARD

OKAN AKHAN, Ankara
ANDREJ ALEKSANDROV, Birmingham
STOJANKA ALEKSIĆ, Hamburg
VLADO ANTONIĆ, Baltimor
ITZHAK AVITAL, Bethesda
KAREN BELKIĆ, Stockholm
JEAN-PAUL BEREGI, Lille Cedex
HELENA BERGER, Ljubljana
MILAN BREBERINA, Novi Sad
RADOVAN CVIJANOVIĆ, Novi Sad
VLADIMIR ČANADANOVIĆ, Novi Sad
IVAN DAMJANOV, Kansas City
DRAGAN DANKUC, Novi Sad
OMER DEVAJA, Meidstone
PETAR DRVIŠ, Split
TATJANA ĐURĐEVIĆ MIRKOVIĆ, Novi Sad
ZORAN GOJKOVIĆ, Novi Sad
IRENA HOČEVAR BOLTEŽAR, Ljubljana
MARINA JOVANOVIĆ, Novi Sad
ALEKSANDAR KIRALJ, Novi Sad
DRAGAN KOVAČEVIĆ, Novi Sad
DUŠKO KOZIĆ, Novi Sad
DUŠAN LALOŠEVIĆ, Novi Sad
JORGE MANUEL COSTA LAINS, Coimbra
VELJKO MARIĆ, Foča
VLADIMIR MARTINEK, Bad Aibling
SINIŠA MASLOVARA, Osijek

JASNA MIHAILOVIĆ, Novi Sad
LJILJA MIJATOV UKROPINA, Novi Sad
MIROSLAV MILANKOV, Novi Sad
OLGICA MILANKOV, Novi Sad
IGOR MITIĆ, Novi Sad
NADA NAUMOVIĆ, Novi Sad
ALEKSANDRA NOVAKOV MIKIĆ, Novi Sad
AVIRAM NISSAN, Ein Karem
JANKO PASTERNAK, Novi Sad
ĐORĐE PETROVIĆ, Novi Sad
LJUBOMIR PETROVIĆ, Novi Sad
MIHAEL PODVINEC, Basel
JOVAN RAJS, Danderyd
PETAR E. SCHWARTZ, New Haven
MILAN SIMATOVIĆ, Banja Luka
TOMAŠ SKRIČKA, Brno
PETAR SLANKAMENAC, Novi Sad
EDITA STOKIĆ, Novi Sad
ALEXANDER STOJADINOVIĆ, Glen Alen
GORAN STOJILJKOVIĆ, Novi Sad
VIKTOR TILL, Novi Sad
TIBOR TOT, Falun
TAKASHI TOYONAGA, Kobe
KONSTANTIN VIKTOROVIĆ SUDAKOV, Moskva
NADA VUČKOVIĆ, Novi Sad
ZORAN VUJKOVIĆ, Banja Luka
PETAR VULEKOVIĆ, Novi Sad

Proof-reading for English Language: Marija Vučenović

Proof-reading for Serbian Language: Dragica Pantić

Technical Secretary: Vesna Šaranović

Technical Support: "Grafit" Novi Sad

UDC and descriptors prepared by: the Library of the Faculty of Medicine, Novi Sad

MEDICAL REVIEW is published bimonthly (six issues per year) with a circulation of 1.000 copies. The annual payment fee in 2018, for individuals from the territory of Serbia, is 3,000.00 dinars (the value-added tax included), 4,000.00 dinars for individuals from Serbia who are not members of the Society of Physicians of Vojvodina of the Medical Society of Serbia, 60 Euros for members outside the territory of Serbia, and 8,000.00 dinars (+ VAT) for institutions. The payment account is: 340-1861-70 or 115-13858-06, "Annual membership fee for Medical Review".

Copyright © Društvo lekara Vojvodine Srpskog lekarskog društva Novi Sad 1998

**The manuscripts are submitted at: asestant.ceon.rs/index.php/medpreg/. Editorial Office Address:
Društvo lekara Vojvodine Srpskog lekarskog društva, 21000 Novi Sad, Vase Stajica 9,
Tel. 021/521-096; 063/81 33 875, E-mail: dlv@sbb.rs; Website: www.dlv.org.rs**

MEDICINSKI PREGLED

ČASOPIS DRUŠTVA LEKARA VOJVODINE SRPSKOG LEKARSKOG DRUŠTVA
PRVI BROJ JE ŠTAMPAN 1948. GODINE.

Glavni i odgovorni urednik
LJILJA MIJATOV UKROPINA

Pomoćnik urednika za kliničke grane: PETAR SLANKAMENAC

Pomoćnik urednika za imidžing metode: VIKTOR TILL

Pomoćnici urednika:
BOJANA KRSTONOŠIĆ
ŽELJKO ŽIVANOVIĆ

REDAKCIJSKI ODBOR

| | |
|-------------------------------------|---------------------------------------|
| OKAN AKHAN, Ankara | JASNA MIHAILOVIĆ, Novi Sad |
| ANDREJ ALEKSANDROV, Birmingham | LJILJA MIJATOV UKROPINA, Novi Sad |
| STOJANKA ALEKSIĆ, Hamburg | MIROSLAV MILANKOV, Novi Sad |
| VLADO ANTONIĆ, Baltimor | OLGICA MILANKOV, Novi Sad |
| ITZHAK AVITAL, Bethesda | IGOR MITIĆ, Novi Sad |
| KAREN BELKIĆ, Stockholm | NADA NAUMOVIĆ, Novi Sad |
| JEAN-PAUL BEREGI, Lille Cedex | ALEKSANDRA NOVAKOV MIKIĆ, Novi Sad |
| HELENA BERGER, Ljubljana | AVIRAM NISSAN, Ein Karem |
| MILAN BREBERINA, Novi Sad | JANKO PASTERNAK, Novi Sad |
| RADOVAN CVIJANOVIĆ, Novi Sad | ĐORĐE PETROVIĆ, Novi Sad |
| VLADIMIR ČANADANOVIĆ, Novi Sad | LJUBOMIR PETROVIĆ, Novi Sad |
| IVAN DAMJANOV, Kansas City | MIHAEL PODVINEC, Basel |
| DRAGAN DANKUC, Novi Sad | JOVAN RAJS, Danderyd |
| OMER DEVAJA, Meidstone | PETAR E. SCHWARTZ, New Haven |
| PETAR DRVIŠ, Split | MILAN SIMATOVIĆ, Banja Luka |
| TATJANA ĐURĐEVIĆ MIRKOVIĆ, Novi Sad | TOMAŠ SKRIČKA, Brno |
| ZORAN GOJKOVIĆ, Novi Sad | PETAR SLANKAMENAC, Novi Sad |
| IRENA HOČEVAR BOLTEŽAR, Ljubljana | EDITA STOKIĆ, Novi Sad |
| MARINA JOVANOVIĆ, Novi Sad | ALEXANDER STOJADINOVIĆ, Glen Alen |
| ALEKSANDAR KIRALJ, Novi Sad | GORAN STOJILJKOVIĆ, Novi Sad |
| DRAGAN KOVAČEVIĆ, Novi Sad | VIKTOR TILL, Novi Sad |
| DUŠKO KOZIĆ, Novi Sad | TIBOR TOT, Falun |
| DUŠAN LALOŠEVIĆ, Novi Sad | TAKASHI TOYONAGA, Kobe |
| JORGE MANUEL COSTA LAINS, Coimbra | KONSTANTIN VIKTOROVIĆ SUDAKOV, Moskva |
| VELJKO MARIĆ, Foča | NADA VUČKOVIĆ, Novi Sad |
| VLADIMIR MARTINEK, Bad Aibling | ZORAN VUJKOVIĆ, Banja Luka |
| SINIŠA MASLOVARA, Osijek | PETAR VULEKOVIĆ, Novi Sad |

Lektor za engleski jezik: Marija Vučenović

Lektor za srpski jezik: Dragica Pantić

Tehnički sekretar: Vesna Šaranović

Tehnička podrška: „Grafit“, Novi Sad

Izrada UDK i deskriptora: Biblioteka Medicinskog fakulteta, Novi Sad

MEDICINSKI PREGLED izlazi dvomesečno (šest dvobroja godišnje), u tiražu od 1000 primeraka. Pretplata za pojedince sa teritorije Srbije za 2018. godinu iznosi 3.000,00 dinara (sa uračunatim PDV-om), a 4.000,00 dinara za pojedince iz Srbije koji nisu članovi DLV-SLD, 60 eura za članove van Srbije, a za ustanove 8.000,00 dinara (uz dodavanje PDV-a). Uplate se vrše na račun broj 340-1861-70 ili 115-13858-06, s naznakom „Dodatna članarina za Medicinski pregled“.

Copyright © Društvo lekara Vojvodine Srpskog lekarskog društva Novi Sad 1998.

Prijem rukopisa vrši se u elektronskoj formi na stranici: asestant.ceon.rs/index.php/medpreg/.

Adresa Redakcije: Društvo lekara Vojvodine Srpskog lekarskog društva,

21000 Novi Sad, Vase Stajića 9, Tel. 021/521-096; 063/81 33 875

E-mail: dlv@sbb.rs; Web: www.dlv.org.rs

CONTENTS

EDITORIAL

- Petar Slankamenac and Željko Živanović
THE SIGNIFICANCE OF COLLATERAL CIRCULATION IN ACUTE ISCHEMIC STROKE 213-216

ORIGINAL STUDIES

- Vladimir Čanadanović, Nikola Babić, Sofija Davidović, Aleksandar Miljković, Stefan Brunet and Sava Barišić
OUTCOME OF CATARACT SURGERY IN DIABETIC PATIENTS 217-221
- Aleksandra Jakovljević, Vojkan Nestorović, Mirjana Dejanović, Zoran Bukumirić, Aleksandar Jakovljević and Novica Đoković
EVALUATION OF THE COGNITIVE AND AFFECTIVE STATUS IN HEMODIALYSIS PATIENTS WITH CHRONIC RENAL FAILURE 222-226
- Branka Protić Gava, Ksenija Bošković, Miroslav Smajić, Dušica Simić Panić and Nada Naumović
WORK WITH CHILDREN WITH DISABILITIES – THE TEACHERS’ ATTITUDES TOWARDS INCLUSION 227-234
- Milica Gojković, Arsen Uvelin, Milanka Tatić, Vladimir Vrsjakov, Dunja Mihajlović and Aleksandra Lučić Prokin
PREDICTORS OF HYPOTENSION DURING SURGICAL MANAGEMENT OF FEMORAL FRACTURES IN SPINAL ANESTHESIA 235-240

REVIEW ARTICLES

- Jadranka Dejanović, Anastazija Stojšić Milosavljević, Miloš Trajković, Tanja Popov and Aleksandra Ilić
ATYPICAL ELECTROCARDIOGRAPHIC PRESENTATIONS OF MYOCARDIAL INFARCTION WITH ST ELEVATION – ST ELEVATION MYOCARDIAL INFARCTION EQUIVALENTS 241-246

PROFESSIONAL ARTICLES

- Sanja Panchevska, Sasho Elenchevski, Nadica Janeva and Aneta Mijoska
SATISFACTION OF COMPLETE DENTURE WEARERS 247-249
- Radmila Perić, Bojana Krstonošić and Ivana Starčević
MORPHOMETRIC STUDY OF THE POSTERIOR ARCH OF ATLAS VERTEBRA IN THE SERBIAN POPULATION... 250-255

CASE REPORTS

- Tomislav Pejčić, Vladimir Vasić, Vladan Dimitrijević, Milomir Tufegdžić, Tihomir Vejnović and Jovan Hadžidokić
SPONTANEOUS URINOMA DIAGNOSED BEFORE RADICAL CYSTECTOMY – A CASE REPORT 257-260
- Biljana Lazović, Ivana Blažić, Mirjana Zlatković Svenda, Vesna Đurić, Rade Milić and Vladimir Žugić
SPONTANEOUS PNEUMOTHORAX INDUCED BY HIGH ALTITUDE – A CASE REPORT 261-264

SEMINAR FOR PHYSICIANS

- Igor Ivanov, Anastazija Stojšić Milosavljević, Vladimir Ivanović, Miloš Trajković, Aleksandra Vulin and Milenko Čanković
ST ELEVATION MYOCARDIAL INFARCTION EQUIVALENT – DE WINTER T-WAVE ELECTROCARDIOGRAPHY PATTERN 265-269

SADRŽAJ

UVODNIK

- Petar Slankamenac i Željko Živanović
ZNAČAJ KOLATERALNE CIRKULACIJE KOD AKUTNOG ISHEMIJSKOG MOŽDANOG UDARA 213-216

ORIGINALNI NAUČNI RADovi

- Vladimir Čanadanović, Nikola Babić, Sofija Davidović, Aleksandar Miljković, Stefan Brunet i Sava Barišić
ISHOD HIRURŠKOG LEČENJA KATARAKTE KOD PACIJENATA SA DIJABETESOM 217-221

- Aleksandra Jakovljević, Vojkan Nestorović, Mirjana Dejanović, Zoran Bukumirić, Aleksandar Jakovljević i Novica Đoković
PROCENA OŠTEĆENJA KOGNITIVNOG I AFEKTIVNOG STATUSA KOD BOLESNIKA SA HRONIČNOM BUBREŽNOM INSUFICIJENCIJOM NA HEMODIJALIZI 222-226

- Branka Protić Gava, Ksenija Bošković, Miroslav Smajić, Dušica Simić Panić i Nada Naumović
RAD SA DECOM SA SMETNJAMA U RAZVOJU – STAVOVI NASTAVNIKA O INKLUZIJI..... 227-234

- Milica Gojković, Arsen Uvelin, Milanka Tatić, Vladimir Vrsjakov, Dunja Mihajlović i Aleksandra Lučić
PREDIKTORI HIPOTENZIJE TOKOM OPERATIVNOG ZBRINJAVANJA PRELOMA BUTNE KOSTI U SPINALNOJ ANESTEZIJI 235-240

PREGLEDNI ČLANCI

- Jadranka Dejanović, Anastazija Stojšić Milosavljević, Miloš Trajković, Tanja Popov i Aleksandra Ilić
ATIPičNI ELEKTROKARDIOGRAFSKI PRIKAZI INFARKTA MIOKARDA SA ST ELEVACIJOM – EKVIVALENTI INFARKTA MIOKARDA SA ELEVACIJOM ST SEGMENTA 241-246

STRUČNI ČLANCI

- Sanja Panchevska, Sasho Elenchevski, Nadica Janeva i Aneta Mijoska
ZADOVOLJSTVO PACIJENATA TOTALNOM ZUBNOM PROTEZOM..... 247-249

- Radmila Perić, Bojana Krstonošić i Ivana Starčević
MORFOMETRIJSKA STUDIJA ZADNJEG LUKA ATLASA U SRPSKOJ POPULACIJI 250-255

PRIKAZ SLUČAJA

- Tomislav Pejčić, Vladimir Vasić, Vladan Dimitrijević, Milomir Tufegdžić, Tihomir Vejnović i Jovan Hadžidokić
SPONTANI URINOM DIJAGNOSTIKOVAN PRE RADIKALNE CISTEKTOMIJE – PRIKAZ SLUČAJA..... 257-260

- Biljana Lazović, Ivana Blažić, Mirjana Zlatković Svenda, Vesna Đurić, Rade Milić i Vladimir Žugić
SPONTANI PNEUMOTORAKS INDUKOVAN VELIKOM NADMORSKOM VISINOM – PRIKAZ SLUČAJA..... 261-264

SEMINAR ZA LEKARE U PRAKSI

- Igor Ivanov, Anastazija Stojšić Milosavljević, Vladimir Ivanović, Miloš Trajković, Aleksandra Vulin i Milenko Čanković
EKVIVALENTI INFARKTA MIOKARDA SA ELEVACIJOM ST SEGMENTA – ELEKTROKARDIOGRAM DE VINTEROVIH T-TALASA..... 265-269

EDITORIAL

UVODNIK

Clinical Center of Vojvodina, Clinic of Neurology, Novi Sad¹
University of Novi Sad, Faculty of Medicine Novi Sad²

Editorial
Uvodnik
UDK 616.831-005.4-08
<https://doi.org/10.2298/MPNS1808213S>

THE SIGNIFICANCE OF COLLATERAL CIRCULATION IN ACUTE ISCHEMIC STROKE

ZNAČAJ KOLATERALNE CIRKULACIJE KOD AKUTNOG ISHEMIJSKOG MOŽDANOG UDARA

Petar SLANKAMENAC^{1,2} and Željko ŽIVANOVIĆ^{1,2}

The human brain accounts for about 2% of the total body weight, but it consumes about 15% of cardiac output and about 20% of the total body energy at rest [1]. The neurovascular coupling in the brain is a mechanism that increases the blood flow in the part of the brain where neurons are the most active [1]. If, for whatever reason, the blood flow drops below the threshold and there is a loss of ionic homeostasis and anoxic depolarization, consequent neuronal necrosis, i.e. brain infarction develops. Complete arrest of blood supply, or inadequate supply of neurons with glucose and oxygen, leads to metabolic and neuronal disorders (within 30 seconds), then functional disorders occur (after 1 minute), and finally (after 5 minutes) irreversible changes and neuronal death occur; this leads to brain infarction, which clinically manifests as ischemic stroke [2]. If the flow of oxygenated blood is re-established quickly enough, the neuronal damage is reversible.

Acute ischemic stroke

Stroke is one of the leading causes of morbidity and mortality in the world [3]. Ischemic stroke occurs due to sudden occlusion of a cerebral artery, usually as a result of progressive atherosclerosis or embolization [3, 4]. The attitude towards the treatment of patients with acute ischemic stroke (AIS) was predominantly nihilistic till 1993, when, based on the results of the National Institute of Neurological Disorders and Stroke rt-PA (NINDS) study, stroke was defined as an emergency medical condition of the utmost importance [5]. At the end of the twentieth century, intravenous thrombolysis was introduced in the treatment of AIS and now it is a standard treatment of patients within the first 4.5 hours after the onset of symptoms [6]. The last decade was marked by studies employing the endovascular treatment of intrac-

ranial and extracranial occlusions, and it was only recently that several studies confirmed that mechanical thrombectomy following the endovascular approach is superior to standard treatment with or without intravenous thrombolysis [7]. However, the outcomes after these treatments are still variable and do not depend only on the method, but also on specific biological characteristics of the patient [8].

The main goal of the treatment of patients with AIS is recanalization of the previously occluded artery, but sometimes, even despite treatment, patients do not have a favorable outcome. In patients with AIS, one of the most significant and independent factors in the prediction of the clinical outcome is the status of the collateral circulation [9, 10]. In the daily clinical practice and the need to start the treatment for AIS as quickly as possible, vascular neurologists and intervention radiologists often have insufficient time to thoroughly evaluate the pretreatment status of the patient's collateral blood flow. Subsequent analyses showed that a favorable clinical response could not be expected even despite a successful recanalization in patients with poorly developed collaterals [11]. Collateral cerebral circulation is a physiological pathway of specific endogenous connections of blood vessels that protect the brain parenchyma from damage in case of ischemia [12]. The degree of development of collateral circulation also affects the size of the infarct lesion. All these findings have put the relationship between collaterals and the possibility of predicting the evolution of infarction and clinical outcome after AIS in the focus of scientific interest in recent years [8, 13].

Collateral cerebral blood flow

Collateral cerebral blood flow includes the establishment of arterio-arterial anastomosis, which

Abbreviations

| | |
|-------|---|
| AIS | – acute ischemic stroke |
| NINDS | – National Institute of Neurological Disorders and Stroke |
| DSA | – digital subtraction angiography |
| CTA | – computed tomography angiography |
| MRA | – magnetic resonance angiography |
| CT | – computed tomography |
| FLAIR | – fluid attenuation inversion recovery |
| TOF | – time of flight |
| ASL | – arterial spin-labeling |
| TCD | – transcranial Doppler |

supplies oxygen and nutrients to the part of the brain where the primary source of blood supply was interrupted [14]. Two main pathways of the collateral circulation are extra- and intracranial pathways [15]. The extracranial sources consist of a large number of branches of the external carotid artery that develop in case of a chronic, atherosclerotic steno-occlusive disease of the internal carotid artery, in most cases through the ophthalmic artery; however, facial, maxillary, middle meningeal, occipital, as well as unnamed dural vessels may take part in the supply of endocranial arteries [16]. Intracranial collaterals can be divided into primary and secondary. Primary collateral circulation is actually a continuously active part of the arterial network at the base of the brain, i.e. the circle of Willis, which connects the anterior and posterior circulations. Secondary collateral circulation consists of non-linear leptomeningeal anastomoses, which connect distal areas of large cerebral arteries and become extremely significant in case of acute cerebral artery occlusion [14]. In cerebral arterial occlusion, leptomeningeal collaterals are recruited to remodel small cortical arterioles, whereas in chronic occlusions there is also neo-collateralization [17]. Depending on the metabolic activity of neurons, different regions of the brain have different blood flow rates at different times. In acute brain infarction, when cerebral arterial occlusion occurs, the cerebral blood flow decreases significantly, and neuronal death occurs in a few minutes, while in case of hypoperfusion and a slightly greater cerebral flow, neurons become dysfunctional but still viable [18, 19]. This actually takes place in the penumbra, i.e. the brain tissue surrounding the acute infarction, which can potentially be saved if there is timely reperfusion, either following recanalization or due to the collaterals [19, 20]. The degree of collateral formation affects the size of the penumbra, as well as the time needed for its adequate perfusion.

Digital subtraction angiography (DSA) is a gold standard for the anatomic evaluation of collateral circulation [8]. This technique enables spatial and temporal visualization of collateral circulation, providing also feedback about dilatation and phases of filling collaterals. However, it has drawbacks in terms of invasiveness, application of contrast, radiation, inability to show the brain parenchyma, and the additional time needed to perform it, which is some-

times crucial in the treatment of patients with AIS [17, 21]. In contrast to DSA, non-invasive techniques have a limited resolution in the assessment of leptomeningeal or other secondary collaterals [8]. Computed tomography angiography (CTA), a non-invasive, fast, simple and available method is most frequently used today, both in the detection of occlusion site or in the assessment of collateral cerebral circulation in AIS [8, 21]. It implies the application of intravenous contrast, spiral computed tomography (CT) imaging and subsequent three-dimensional reconstruction. Evaluation of collateral circulation using magnetic resonance angiography (MRA) is limited to proximal segments of arteries of the circle of Willis [21, 22]. Slow flow velocity at the site of occlusion, a hyperintense signal in collateral blood vessels, can also be visualized using fluid attenuation inversion recovery (FLAIR) sequences, but without the possibility to quantify the flow [21]. Contrast MRA shows slower flow in the distal branches better, while post-contrast time of flight (TOF) sequences can enhance the retrograde supply/filling through the leptomeningeal arteries [22]. The dynamic, contrast MRA provides precise information on both the occlusion site and the development of collateral circulation and its hemodynamic status; therefore, it can be used as a non-invasive method in the assessment of patients with AIS who are candidates for endovascular interventions [23]. Arterial spin-labeling (ASL) MRI sequence encompasses elements of collaterals quantification and ischemic tissue perfusion through leptomeningeal collaterals, which makes it very useful in the outcome prediction after AIS [22, 23]. Transcranial Doppler (TCD) provides data on cerebral circulation and cerebral autoregulation [8, 21]. Transcranial Doppler has been used primarily in the evaluation of collateral pathways via the arteries of the circle of Willis [24]. Assessment of cerebral vasomotor reactivity using TCD provides information on autoregulation and the collateral status. The main disadvantage of TCD, as well as of other ultrasonography methods, is that the interpretation of findings depends on the examiner [21, 24].

Evaluation of collaterals in the outcome prediction after AIS

In the last two decades, numerous published data have emphasized the importance of the status of collateral circulation in the outcome assessment after AIS [14]. Considerations about the role of collateral circulation in perfusion of ischemic tissue and consequent replacement and bridging of occlusion sites have become an essential part of the assessment of the vascular status of every patient with AIS [25]. The American Society of Interventional and Therapeutic Neuroradiology and the Association of Interventional Radiology differentiated five degrees of collaterals, based on the DSA findings [10]. Grades 0 and 1 indicate only marginal flow, grade 2 indicates partial filling of the ischemic zone, while

grades 3 and 4 indicate well-developed collaterals with varying degrees of perfusion of the whole vascular territory of the occluded vessel. Assessment of collaterals has become crucial in the prediction of treatment outcome in patients with AIS [17]. Patients with well-developed collaterals were shown to have smaller infarctions after treatment [15, 17], as opposed to patients with poorly developed collaterals, who had worse outcomes [26, 27], leading to the conclusion that the initiation of AIS treatment may have lower impact on the outcome than the collateral status. Micro-vascular parenchymal perfusion [15] is also important for complete restoration of the ischemic tissue. In physiological conditions, the diameter of the blood vessel is the main regulator of cerebral blood flow, while in blood vessel occlusion most of the penumbra perfusion originates from collaterals, which enables retrograde perfusion of the penetrating arterioles of the ischemic penumbra after AIS [28]. Determination of the capillary index score using DSA may enable estimation of the degree of perfusion [29]. To determine the capillary index score, the ischemic area is divided into three identical parts, and each is scored 0 or 1, depending on whether there is no capillary network in that part, or the capillary network is normal. The sum of points for the three parts gives the capillary index score, which can be 0–3 [29]. Scores 2 and 3 indicate that a larger ischemic region is potentially viable for recovery after a successful recanalization. A recently published meta-analysis showed that patients with AIS who underwent endovascular treatment and had a higher capillary index also had higher rates of favorable neurological outcome and significantly lower rates of intracranial bleeding after treatment [29].

All of these findings show that adequate assessment of collaterals and hypoperfused tissue may extend the therapeutic window for administration of either intravenous systemic (thrombolytic) therapy or endovascular treatment [30]. Therefore, the well-developed collaterals slow down the loss of penumbra tissue, that is, they “buy time” for the administration of therapy in patients with AIS [31].

Sometimes, even without a successful recanalization, complete reperfusion can occur due to collateral circulation [32]. On the other hand, poorly developed collaterals, even in case of rapid recanalization and reperfusion, may be predictors of poor outcome and a potential cause of hemorrhagic transformation [33]. Although time is the most important factor in terms of AIS treatment, the status of collateral circulation affects the time-dependent treatment efficacy [14]. Generally, the outcome for patients with poor collaterals is directly dependent on the time of initiation of the endovascular treatment, while in patients with good collaterals, the time of initiation of the treatment bears no such significance [34]. On the other hand, the capacity of collateral circulation in AIS has been shown to weaken with time, i.e. it is more likely that patients with AIS will have good collaterals if they are treated within a shorter time interval from the onset of symptoms [35]. All this leads to the conclusion that if enhanced involvement of collaterals in AIS was possible, the time for initiation of reperfusion treatment could be extended [14].

Today, it is clear that well-developed collateral blood flow in patients with AIS slows down the cascade of metabolic degeneration in the penumbra tissue and is associated with smaller brain infarctions, better reperfusion of ischemic tissue and more favorable outcomes after intravenous thrombolysis and/or mechanical thrombectomy [10, 18]. However, collateral blood flow in AIS is dynamic and over time can become insufficient (collapse of collateral blood flow); therefore, it is still recommended that the therapy should not be delayed but started as soon as possible. Determination of the occlusion site is now a standard in the diagnostic protocol for patients with AIS, and for the purpose of selecting patients for endovascular procedures it is also necessary to evaluate the collateral status of cerebral blood flow, which provides higher probability of predicting favorable outcome, as well as patients at risk for hemorrhagic complications [9, 33, 36].

References

1. Attwell D, Buchan AM, Charpak S, et al. Glial and neuronal control of brain blood flow. *Nature*. 2010;468:232-43.
2. Astrup J, Siesjö BK, Symon L. Thresholds in cerebral ischemia - the ischemic penumbra. *Stroke*. 1981;12:723-5.
3. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45(7):2160-236.
4. Truelsen T, Piechowski-Józwiak B, Bonita R, Mathers C, Bogousslavsky J, Boysen G. Stroke incidence and prevalence in Europe: a review of available data. *Eur J Neurol*. 2006;13:581-98.
5. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *The New England journal of medicine*. 1995;333(24):1581-7.
6. Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013;44(3):870-947.
7. Wahlgren N, Moreira T, Michel P, et al. Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN. *International journal of stroke : official journal of the International Stroke Society*. 2016;11(1):134-47.
8. Alves HC, Pacheco FT, Rocha AJ. Collateral blood vessels in acute ischemic stroke: a physiological window to predict future outcomes. *Arq Neuropsiquiatr*. 2016;74(8):662-70.
9. Liebeskind DS, Jahan R, Nogueira RG, Zaidat OO, Saver JL; SWIFT Investigators. Impact of collaterals on successful revascularization in Solitaire FR with the intention for thrombectomy. *Stroke*. 2014;45(7):2036-40.

10. Leng X, Fang H, Leung TW, et al. Impact of collaterals on the efficacy and safety of endovascular treatment in acute ischaemic stroke: a systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry*. 2016;87(5):537-44.

11. Bang OY, Saver JL, Kim SJ, et al. Collateral flow predicts response to endovascular therapy for acute ischemic stroke. *Stroke*. 2011;42(3):693-9.

12. Faber JE, Chilian WM, Deindl E, Royen N, Simons M. A brief etymology of the collateral circulation. *Arterioscler Thromb Vasc Biol*. 2014;34(9):1854-9.

13. Verma RK, Gralla J, Klinger-Gratz PP, et al. Infarction Distribution pattern in acute stroke may predict the extent of leptomeningeal collaterals. *PLoS One*. 2015;10(9):e0137292.

14. Ginsberg MD. The cerebral collateral circulation: Relevance to pathophysiology and treatment of stroke. *Neuropharmacology*. 2017 Aug 9. pii: S0028-3908(17)30370-2.

15. Liebeskind DS. Collateral lessons from recent acute ischemic stroke trials. *Neurol Res*. 2014;36(5):397-402.

16. Krishnaswamy A, Klein JP, Kapadia SR. Clinical cerebrovascular anatomy. *Catheter Cardiovasc Interv* 2010;75(4):530-9.

17. Sheth SA, Liebeskind DS. Collaterals in endovascular therapy for stroke. *Curr Opin Neurol*. 2015;28(1):10-5.

18. Sakoh M, Ostergaard L, Gjedde A, et al. Prediction of tissue survival after middle cerebral artery occlusion based on changes in the apparent diffusion of water. *J Neurosurg*. 2001;95(3):450-8.

19. Sobesky J, Zaro Weber O, Lehnhardt FG, et al. Which time-to-peak threshold best identifies penumbral flow? A comparison of perfusion weighted magnetic resonance imaging and positron emission tomography in acute ischemic stroke. *Stroke* 2004;35(12):2843-7.

20. Hammer MD, Schwamm L, Starkman S, et al. Safety and feasibility of NeuroFlo use in eight- to 24-hour ischemic stroke patients. *Int J Stroke*. 2012;7(8):655-61.

21. Martinon E, Lefevre PH, Thouant P, Osseby GV, Ricolfi F, Chavent A. Collateral circulation in acute stroke: assessing methods and impact: a literature review. *J Neuroradiol*. 2014;41(2):97-107.

22. Ernst M, Forkert ND, Brehmer L, et al. Prediction of infarction and reperfusion in stroke by flow- and volume-weighted collateral signal in MR angiography. *AJNR Am J Neuroradiol*. 2015;36(2):275-82.

23. Hernández-Pérez M, Puig J, Blasco G, et al. Dynamic Magnetic Resonance Angiography Provides Collateral Circulation and Hemodynamic Information in Acute Ischemic Stroke. *Stroke*. 2016;47(2):531-4.

24. Prokin AL, Slankamenac P, Kovačević P, Kaloci SR, Živanović ŽD. Cerebral Vasomotor Reactivity and Apnea Test in Symptomatic and Asymptomatic High-Grade Carotid Stenosis. *Srp Arh Celok Lek*. 2015;143(9-10):520-4.

25. Wintermark M, Sanelli PC, Albers GW, et al. Imaging recommendations for acute stroke and transient ischemic attack patients: A joint statement by the American Society of Neuro-radiology, the American College of Radiology, and the Society of NeuroInterventional Surgery. *AJNR Am J Neuroradiol*. 2013;34(11):E117-27.

26. Maas MB, Lev MH, Ay H, et al. Collateral vessels on CT angiography predict outcome in acute ischemic stroke. *Stroke*. 2009;40(9):3001-5.

27. Menon BK, Smith EE, Modi J, et al. Regional leptomeningeal score on CT angiography predicts clinical and imaging outcomes in patients with acute anterior circulation occlusions. *AJNR Am J Neuroradiol*. 2011;32(9):1640-5.

28. Beard DJ, McLeod DD, Logan CL, et al. Intracranial pressure elevation reduces flow through collateral vessels and the penetrating arterioles they supply. A possible explanation for 'collateral failure' and infarct expansion after ischemic stroke. *J Cereb Blood Flow Metab*. 2015 May;35(5):861-72.

29. Jagani M, Brinjikji W, Murad MH, Rabinstein AA, Cloft HJ, Kallmes DF. Capillary Index Score and Correlation with Outcomes in Acute Ischemic Stroke: A Meta-analysis. *J Vasc Interv Neurol*. 2017;9(3):7-13.

30. Cheng-Ching E, Frontera JA, Man S, et al. Degree of collaterals and not time is the determining factor of core infarct volume within 6 hours of stroke onset. *AJNR Am J Neuroradiol*. 2015;36(7):1272-6.

31. Jung S, Gilgen M, Slotboom J, et al. Factors that determine penumbral tissue loss in acute ischaemic stroke. *Brain*. 2013;136(12):3554-60.

32. Soares BP, Chien JD, Wintermark M. MR and CT monitoring of recanalization, reperfusion, and penumbra salvage: everything that recanalizes does not necessarily reperfuse! *Stroke*. 2009;40(3 Suppl 1):S24-7.

33. Bang OY, Saver JL, Kim SJ, et al. Collateral flow predicts response to endovascular therapy for acute ischemic stroke. *Stroke*. 2011;42(3):693-9.

34. Hwang YH, Kang DH, Kim YW, Kim YS, Park SP, Liebeskind DS. Impact of time-to-reperfusion on outcome in patients with poor collaterals. *AJNR Am J Neuroradiol*. 2015; 36(3):495-500.

35. Liebeskind DS, Jahan R, Nogueira RG, Jovin TG, Lutsep HL, Saver JL. Early arrival at the emergency department is associated with better collaterals, smaller established infarcts and better clinical outcomes with endovascular stroke therapy: SWIFT study. *J Neurointerv Surg*. 2016;8:553-8.

36. Sheth SA, Sanossian N, Hao Q, et al. Collateral flow as causative of good outcomes in endovascular stroke therapy. *J Neurointerv Surg*. 2016;8:2-7.

Rad je primljen 30. IV 2018.

Prihvaćen za štampu 30. IV 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:213-216.

ORIGINAL STUDIES

ORIGINALNI NAUČNI RADOVI

Clinical Center of Vojvodina, Eye Clinic, Novi Sad¹
University of Novi Sad, Faculty of Medicine Novi Sad
Department of Ophthalmology²

Original study
Originalni naučni rad
UDK 617.741-004.1-08:616.379-008.64
<https://doi.org/10.2298/MPNS1808217C>

OUTCOME OF CATARACT SURGERY IN DIABETIC PATIENTS

ISHOD HIRURŠKOG LEČENJA KATARAKTE KOD PACIJENATA SA DIJABETESOM

Vladimir ČANADANOVIĆ^{1,2}, Nikola BABIĆ^{1,2}, Sofija DAVIDOVIĆ^{1,2}, Aleksandar MILJKOVIĆ^{1,2}, Stefan BRUNET¹ and Sava BARIŠIĆ¹

Summary

Introduction. The association between diabetes and cataract formation has been shown in many clinical studies. Development of cataract occurs more frequently and at an earlier age in diabetic patients. Due to the increasing prevalence of diabetes worldwide, the incidence of diabetic cataracts steadily rises. While the overall outcomes of cataract surgery are excellent, patients with diabetes may have poorer vision outcomes than those without diabetes. The objective of this study was to evaluate the visual outcomes (visual acuity and visual function), intraoperative and postoperative complications of cataract surgery, and to assess the final surgical outcomes. **Material and Methods.** The prospective study included 128 patients (133 eyes) with cataract and diagnosis of diabetes mellitus type 2 at least 5 years prior to cataract surgery, operated at the Eye Clinic, Clinical Center of Vojvodina, Novi Sad. A full medical history included patients' age, the time since the diagnosis of diabetes, current management of diabetes, blood pressure and assessment of glycemic control using glycosylated hemoglobin. All patients underwent complete ophthalmological examination before cataract surgery, and were re-examined 7 days, one and six months after the surgery. **Results.** The mean age of patients at the time of surgery was 63.5 years (SD ± 6.5, range 57–70 years) with mean duration of diabetes 8.5 years. The glycosylated haemoglobin level in the group treated with insulin was 6.8 vs. 8.2 in patients on oral medications ($p < 0.05$). Diabetes mellitus was accompanied by other systemic diseases in 81 patients (63.28%), whereas 45 of 133 operated eyes (33.83%) had other ocular diseases. Intraoperative complications occurred in 20 of 133 operated eyes (15%): posterior capsular rupture with vitreous loss, intraoperative miosis, iris hemorrhage and suprachoroidal hemorrhage. **Conclusion.** Cataract surgery with intraocular lens implantation is an effective and safe surgical procedure in diabetic patients, and sight threatening complications are rare. Our study confirmed that visual acuity after surgery in diabetic patients depends on the severity of diabetic retinopathy at the time of surgery. **Key words:** Diabetes Mellitus; Cataract; Vision Disorders; Visual Acuity; Cataract Extraction; Treatment Outcome; Postoperative Complications; Phacoemulsification; Hemoglobin A, Glycosylated; Diabetic Retinopathy

Sažetak

Uvod. Udruženost šećerne bolesti i katarakte je dokazana u mnogim istraživanjima a razvoj katarakte kod ovih pacijenata je učestaliji i u ranijem životnom dobu. Porast obolelih od šećerne bolesti dovodi do porasta broja pacijenata sa dijabetesnom kataraktom. Cilj ovog rada bio je da se izvrši procena vida (vidna oština i vidna funkcija), intraoperativnih i postoperativnih komplikacija operacije katarakte i da se sagleda krajni ishod hirurškog lečenja. **Materijal i metode.** Ova prospektivna studija obuhvatila je 128 pacijenata (133 oka) sa kataraktom i šećernom bolešću tipa II u trajanju od najmanje pet godina pre izvršene operacije na Klinici za očne bolesti, Kliničkog centra Vojvodine. Evaluirani su prosečna starost, način regulacije šećerne bolesti, visina krvnog pritiska i vrednosti glikoliziranog hemoglobina. Pacijenti su praćeni preoperativno, a zatim sedam dana, jedan mesec i šest meseci nakon operativnog lečenja. **Rezultati.** Prosečna starost pacijenata u ovoj studiji iznosila je 63,5 godina (SD ± 6,5, raspon 57–70 godina) sa prosečnim trajanjem šećerne bolesti 8,5 godina. Vrednosti glikoliziranog hemoglobina u grupi na insulinskoj terapiji u odnosu na peroralnu iznosile su 6,8 vs. 8,2 ($p < 0,05$). Kod 81 pacijenta (63,28%) dijabetes melitus je bio udružen sa drugim sistemskim bolestima a kod 45, od 133 operisana oka (33,83%), postojala su i druga očna oboljenja. Intraoperativne komplikacije iznosile su 15%: rupture zadnje kapsule sočiva sa gubitkom staklastog tela, intraoperativno suženje zenice, krvarenje iz dužice i suprahoroidalno krvarenje. **Zaključak.** Operacija katarakte sa ugradnjom intraokularnog sočiva kod pacijenata obolelih od šećerne bolesti je bezbedna procedura sa niskim rizikom u pogledu nastanka komplikacija koje bi mogle dovesti do gubitka vida. Ova studija potvrđuje da postoperativna vidna funkcija pacijenata sa šećernom bolešću zavisi od preoperativnog stepena dijabetesne retinopatije. **Gljučne reči:** dijabetes melitus; katarakta; poremećaji vida; vidna oština; ekstrakcija katarakte; ishod lečenja; postoperativne komplikacije; fakoemulzifikacija; glikozilizirani hemoglobin; dijabetesna retinopatija

Abbreviations

| | |
|-------|--------------------------------|
| DM | – diabetes mellitus |
| HbA1C | – glycosylated hemoglobin |
| CME | – cystoid macular edema |
| DR | – diabetic retinopathy |
| BCVA | – best corrected visual acuity |

Introduction

Cataract is a common cause of visual impairment. The prevalence of all types of cataract increases with age, from 4.5% among persons in their 40s to 40–60% in those aged 70 years and over [1]. Senile cataract is one of the most common causes of reversible vision loss in elderly persons. Visual impairment caused by cataract affects the patient in several ways, leading to perceived difficulties in performing vision related everyday activities and decreasing the quality of life [2–4]. It is estimated that by the year 2021, the number of people affected by cataract will increase by 63%, due to population aging [5].

Cataract has a multifactorial etiology and seems to be caused by accumulation of risk factors [6, 7]. Osmotic stress caused by sorbitol accumulation in the ocular lens has long been suggested to be the major cause of this complication, since sorbitol was found to be accumulated to a substantially high level in cataractous lenses in diabetic patients. Under hyperglycemic conditions, sorbitol is formed from the reduction of glucose by the enzyme aldose reductase. The conversion of sorbitol to fructose via sorbitol dehydrogenase has also been suggested to contribute to redox imbalance in diabetes. It has been suggested that glucose autooxidation and nonenzymatic glycation, together termed glycoxidation, are the major contributors to the increase in free radicals in diabetic lenses. During diabetes, the lens antioxidant system may also be compromised. A loss of antioxidants, like vitamin C, vitamin E, and glutathione, were found in lenses under hyperglycemic condition.

The association between diabetes and cataract formation has been shown in many clinical studies, and development of cataract occurs more frequently and at an earlier age in diabetic patients [8, 9]. Two types of cataract may be associated with diabetes mellitus (DM). True diabetic cataract appears as bilateral white punctate or snowflake posterior or anterior opacities. It is the result of osmotic overhydration of the lens. In some diabetic patients cataract has the characteristics of typical senile cataract but progresses more rapidly [8].

Due to increasing numbers of diabetics worldwide, the incidence of diabetic cataracts steadily rises. It has been estimated that up to 15% of cataract surgery is performed on diabetics. Cataract extraction is the most frequent surgical procedure in ophthalmology and continues to be one of the most commonly performed elective surgical procedures in medicine [10]. Advances in new technology have led to the development of small incision phaco surgery. This technique has increased the efficacy of surgery with faster rehabilitation and reintegration in daily life activities. The high success rate of cataract surgery has created high expectations

regarding the vision outcome and improvement in vision related everyday activities [11]. The main indications for cataract surgery are the same as for non-diabetic patients. The goal of cataract extraction and intraocular lens implantation is to improve visual acuity and visual function, with an assumption that this will improve overall quality of life [2, 13]. Cataract surgery in diabetic patients is also indicated if the lens opacity prevents fundus examination or produces excessive light scattering during laser therapy. While the overall outcomes of cataract surgery are excellent, patients with diabetes may have poorer vision outcomes than those without diabetes.

Diabetic eyes may have a bigger lens and a shallower anterior chamber in comparison with non-diabetic patients, especially in eyes with diabetic retinopathy (DR) [14, 15]. The lens capsule is more fragile, with higher rate of rupture and vitreous loss [16]. Cataract surgery changes the physiology of the eye and stimulates the release of inflammatory cytokines, fluctuations of intraocular pressure which cause the alterations of ocular perfusion and the function of barrier between the anterior and the posterior segment may be compromised after surgery. The diabetic eye is more susceptible to surgical trauma due to longer duration of surgery, more pronounced miosis and a transient elevation of intraocular pressure [17, 18]. These eyes may have a higher incidence of cystoid macular edema (CME) and more pronounced postoperative inflammation than the non-diabetic eyes [19, 20].

In some patients surgery may cause acceleration of DR, induce rubeosis iridis or lead to macular changes. The worst outcomes may occur in operated eyes with active proliferative retinopathy and/or preexisting macular edema.

Material and Methods

This prospective study included 128 patients (133 eyes) with cataract and diagnosis of DM type 2 at least 5 years prior to cataract surgery, operated at the Eye Clinic, Clinical Center of Vojvodina, Novi Sad.

All diabetic patients included in this study underwent complete ophthalmological examination before cataract surgery: best corrected distance visual acuity (BCVA) testing using Snellen chart, intraocular pressure measurement using applanation tonometer, slit lamp examination of anterior and posterior segment of the eye in artificial mydriasis. All patients were re-examined 7 days, one and six months after surgery. A full medical history included the patients' age, time

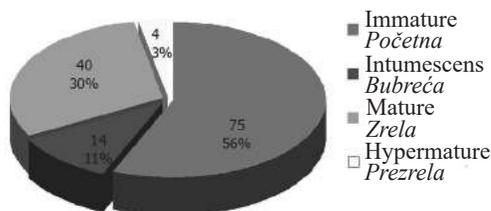


Figure 1. Maturity of cataracts
Slika 1. Zrelost katarakte

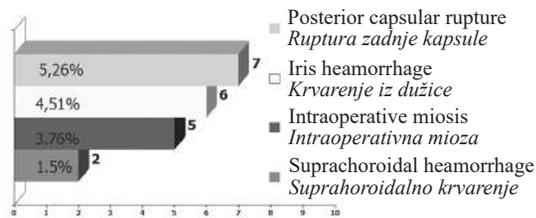


Figure 2. Intraoperative complications
Slika 2. Intraoperativne komplikacije

from diabetes diagnosis and current management of diabetes, blood pressure and glycemic control assessed by glycosylated hemoglobin (HbA1C) measurement. All patients included in this study were without clinical significant diabetic or CME. If present before surgery, DR was mild and non-proliferative. Patients with other ophthalmic conditions (history of any ophthalmic surgery, laser treatment, anti-vascular endothelial growth factor therapy, uveitis etc.) that might have influenced the onset and course of diabetic eye disease were excluded.

Results

A total of 128 diabetic patients (133 eyes) were enrolled in this study, 70 (55%) females and 58 (45%) males. The mean age of patients at the time of surgery was 63.5 years (SD ± 6.5, range 57 – 70 years) with mean duration of diabetes 8.5 years. The treatment of diabetes included insulin therapy in 35% and oral medications in 65%. Assessment of HbA1C values between patients receiving different diabetic therapy revealed statistically significantly higher values of HbA1C in the group treated with insulin in comparison to patients on oral medications (6.8 vs. 8.2, p < 0.05). DM was accompanied with other systemic diseases in 81 patients (63.28%) hypertension (67 pts), renal insufficiency (8 pts) and cardiovascular disorders (6 pts). Other ocular diseases accompanying cataract were found in 45 from 133 operated eyes (33.83%): DR (24.06%), macular degeneration (2.25%), degenerative myopia (3.01%) and glaucoma (4.51%). According to maturity, immature cataract was present in 75 (56%), intumescent cataract in 14 (11%), mature cataract in 40 (30%), and hypermature cataract in 4 (3%) eyes (Figure 1).

Intraoperative complications were found in 20 of 133 operated eyes (15%): posterior capsular rupture with vitreous loss in 7 (5.26%), intraoperative miosis in 5 (3.76%), iris hemorrhage in 6 (4.51%) and suprachoroidal hemorrhage in 2 (1.5%) (Figure 2).

Seven days after cataract surgery, CME was found in 44 (33.08%), retinal detachment in 2 (1.5%), fibrin exudation in 12 (9.02%) and corneal decompensation in 14 (10.5%) operated eyes. The main postoperative complications one month after the cataract surgery were CME in 34 (25.6%), opacification of the posterior capsule in 7 (5.26%), retinal detachment in 2 (1.5%), fibrin exudation in 8 (6%) and corneal decompensation in 4 (3%) operated eyes.

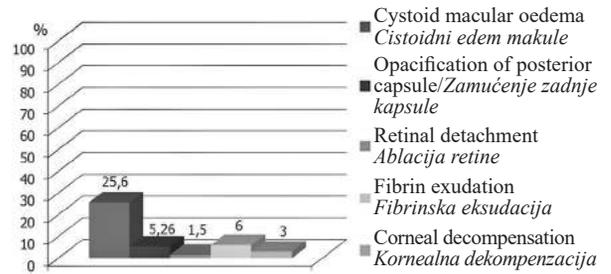


Figure 3. Postoperative complications (1 month)
Slika 3. Postoperativne komplikacije (jedan mesec)

The main postoperative complications one month after cataract surgery are shown in Figure 3.

Six months after cataract surgery, the main postoperative complications were opacification of the posterior capsule in 22 (16.54%), persistent CME in 14 (10.52%), and corneal decompensation in 3 (2.25%) operated eyes. The main postoperative complications six months after cataract surgery are shown in Figure 4.

At the time of surgery, BCVA was 0.4 or less in 121 (90.97%) eyes. Only 12 (9.02%) had BCVA of 0.5 or better. After surgery, the BCVA was significantly

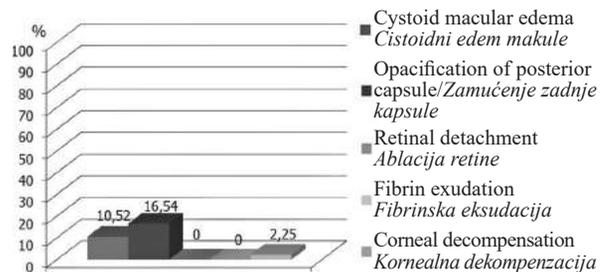


Figure 4. Postoperative complications (6 months)
Slika 4. Postoperativne komplikacije (šest meseci)

better; 94 (70.76%) eyes achieved a BCVA of 0.5 or better (median 0.7; range 0.5 – 1.0). The remaining 31 (23.3%) eyes had a BCVA of 0.2 or better (median 0.3; range 0.2 – 0.4) and 8 (6.01%) had BCVA of 0.1 or less due to persistent macular edema and corneal decompensation. The main preoperative and postoperative BCVA are shown in Figure 5.

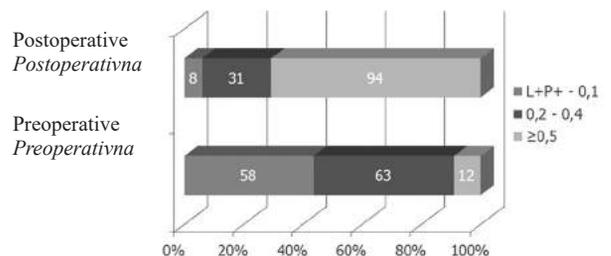


Figure 5. Preoperative and postoperative best corrected visual acuity
Slika 5. Preoperativna i postoperativna najbolje korigovana vidna oštrina

Discussion

The incidence of diabetes is increasing due to many factors, but the most significant are the increasing incidence of obesity and the prevalence of sedentary lifestyle. Many epidemiological and clinical studies documented a higher prevalence of cataract in diabetic patients [21, 22]. Association between diabetes and cataract is shown in the Beaver Dam Eye Study, the Blue Mountains Eye Study and the Visual Impairment Project [23, 24]. The Wisconsin Epidemiologic Study of Diabetic Retinopathy documented a direct relationship between HbA1C and cataract [25]. In our study increased level of HbA1C was found in 43.6% of diabetic patients with cataract.

In study of Raman et al. [26] the prevalence of cataract was higher in women, patients with diagnosed diabetes, and those with longer duration of diabetes. The risk factors for any type of cataract were older age and increasing HbA1C. The mean age of patients enrolled in our study was 63.5 years (range 57–70 years) with average value of HbA1C 7.4%. In 52.34% of operated patients diabetes was accompanied with hypertension. Patients with diabetes require regular follow-up to optimize their glycemic status, blood pressure and lipid control to prevent development and progression of DR and other diabetes-related complications [27, 28]. It is known that diabetic eyes have more complications during and after cataract surgery than nondiabetic eyes.

According to previous studies, the prevalence of posterior capsular rupture and vitreous loss varies from 1.92–7% [29, 30]. Interestingly, the rate of 4.4% has been reported in a study from the United Kingdom [31]. In our study, the rate of posterior capsule rupture and vitreous loss was 5.26%.

The effects of cataract surgery on the postoperative course of DR and how lens removal may affect diabetic retinal changes in operated eye is still unclear. Williams et al. [32] showed that lens extraction can inhibit endothelial proliferation and may induce vascular alterations resulting in neovascularisation. Jaffe and Burton reported development of severe exudative forms of diabetic macular edema following cataract extraction [33].

In the study of Pollac et al. on 44 operated eyes, 50% of eyes presented with CME 6 weeks after surgery and in 25% it was still present 1 year later. The CME occurred postoperatively only in 32% of eyes

without pre-existing DR and in 81% of eyes with pre-existing DR [34]. In our study, the incidence of clinically significant CME, detectable on ophthalmoscopic examination one month after the cataract surgery, was 25.6%. Patients with DR prior to surgery are at higher risk for poor visual outcome after surgery [35, 36]. Aiello et al. found that patients with or without background retinopathy were at higher risk for developing vitreous hemorrhage [37]. In contrast, other authors found that cataract surgery was not associated with the progression of DR and reported similar progression in the unoperated fellow eye [38]. A considerable proportion of eyes with aggravation of retinopathy would reflect the natural course of the disease, systemic factors or both, rather than the effects of cataract surgery [39]. In our study, at the time before surgery DR was of mild non-proliferative type. Six months after the cataract surgery we found no progression of DR. The findings of our study should be interpreted with caution, due to the small number of diabetic patients with cataract and short follow up period.

In our study, after phacoemulsification, the visual acuity was improved in the majority of operated eyes. The largest group with good visual results after cataract surgery (70.67% of operated patients with BCVA > 0.5) included patients with good glycemic control at the time of cataract surgery. Our results are similar to those reported by other researches [40].

Conclusion

The results of numerous previous clinical studies and the results of our study showed that cataract surgery with intraocular lens implantation in diabetic patients is an effective and safe surgical procedure and sight threatening complications are rare. Our study confirmed that visual acuity after surgery in diabetic patients depends on the severity of diabetic retinopathy at the time of surgery. The preoperative status of diabetic retinopathy may be a significant prognostic factor for the postoperative visual outcome. The risk of intraoperative and postoperative complications is related to duration of diabetes, accompanied eye diseases, maturity of cataract and increased serum level of glycosylated hemoglobin. These patients should be monitored postoperatively for early screening of diabetic retinopathy progression, and if necessary laser treatment should be considered.

References

1. Shrestha LB. Population aging in developing countries. *Health Aff (Millwood)*. 2000;19(3):204–12.
2. Lundström M, Stenevi U, Thorburn W. The Swedish National Cataract Register B. A 9-year review. *Acta Ophthalmol Scand*. 2002;80(3):248–57.
3. Čanadanović V, Latinović S, Babić N, Babović S, Žikić Z, Lješević Lj, et al. Quality of life in patients with cataract - VQOL Study Group report. *Patients Reported Outcomes Newsletter*. 2005;34:23–4.
4. Finger RP, Fenwick E, Marella M, Dirani M, Holz FG, Chiang PP, et al. The impact of vision impairment on vision specific quality of life in Germany. *Invest Ophthalmol Vis Sci*. 2011;52(6):3613–9.
5. Ročtchina E, Mukesh BN, Wang JJ, McCarty CA, Taylor HR, Mitchell P. Projected prevalence of age-related cataract and cataract surgery in Australia for the years 2001 and 2021: pooled data from two population-based surveys. *Clin Exp Ophthalmol*. 2003;31(3):233–6.
6. Zorić L, Elek-Vlajić S, Jovanović M, Kisić B, Đokić O, Čanadanović V, et al. Oxidative stress intensity in lens and

aqueous depending on age-related cataract type and brunescence. *Eur J Ophthalmol*. 2008;18(5):669-74.

7. Čanadanović V, Latinović S, Barišić S, Babić N, Jovanović S. Age related changes of vitamin C levels in aqueous humour. *Vojnosanit Pregl*. 2015;72(9):823-6.

8. Bowling B, editor. *Kanski's clinical ophthalmology: a systematic approach*. 8th ed. London: Elsevier; 2016.

9. Peterson SR, Silva PA, Murathi TJ, Sun JK. Cataract surgery in patients with diabetes: management strategies. *Semin Ophthalmol*. 2018;33(1):75-82.

10. Rana M, Shah S. Modern-day cataract surgery: can we match growing expectations? *Br J Ophthalmol*. 2014;98(10):1313-4.

11. Čanadanović V, Latinović S, Babić N, Miljković A, Grković D, Barišić S. Vision related problems after cataract surgery. *Med Pregl*. 2017;70(9-10):307-11.

12. Lundström M, Stenevi U, Thorburn W. Quality of life after first- and second-eye cataract surgery. Five-year data collected by the Swedish National Cataract Register. *J Cataract Refract Surg*. 2001;27(10):1553-9.

13. Tan A, Tay TW, Zheng FY, Tan AG, Wang JJ, Mitchell P, et al. The impact of bilateral or unilateral cataract surgery on vision function when does second eye surgery benefit patients. *Br J Ophthalmol*. 2012;96(6):846-51.

14. Brown N, Hungerford J. The influence of the size of the lens in ocular disease. *Trans Ophthalmol Soc UK*. 1982;102 Pt 3:359-63.

15. Sparrow JM, Bron AJ, Phelps Brown NA, Neil HA. Biometry of the crystalline lens in late onset diabetes: the importance of diabetic type. *Br J Ophthalmol*. 1992;76(7):428-33.

16. Kuchle M, Schonherr U, Dieckmann U. Risk factors for capsular rupture and vitreous loss in extracapsular cataract extraction. *Fortschr Ophthalmol*. 1989;86(5):417-21.

17. Zaczek A, Zetterström C. Cataract surgery and pupil size in patients with diabetes mellitus. *Acta Ophthalmol Scand*. 1997;75(4):429-32.

18. Antcliff RJ, Poulson A, Flanagan DW. Phacoemulsification in diabetics. *Eye (Lond)*. 1996;10(Pt 6):737-41.

19. Menchini U, Bandello F, Brancato R, Camesasca FI, Galdini M. Cystoid macular oedema after extracapsular cataract extraction and intraocular lens implantation in diabetic patients without retinopathy. *Br J Ophthalmol*. 1993;77(4):208-11.

20. Zaczek A, Zetterström C. Aqueous flare intensity after phacoemulsification in patients with diabetes mellitus. *J Cataract Refract Surg*. 1998;24(8):1099-104.

21. Mukesh BN, Le A, Dimitrov PN, Ahmed S, Taylor HR, McCarty CA. Development of cataract and associated risk factors: the Visual Impairment Project. *Arch Ophthalmol*. 2006;124(1):79-85.

22. Chang JR, Koo E, Agron E, Hallak J, Clemons T, Azar D, et al. Risk factors associated with incident cataracts and cataract surgery in the Age-related Eye Disease Study (AREDS): AREDS report number 32. *Ophthalmology*. 2011;118(11):2113-9.

23. Rowe NG, Mitchell PG, Cumming RG, Wans JJ. Diabetes, fasting blood glucose and age-related cataract: the Blue Mountains Eye Study. *Ophthalmic Epidemiol*. 2000;7(2):103-14.

24. Klein BE, Klein R, Wang Q, Moss SE. Older-onset diabetes and lens opacities: the Beaver Dam Eye Study. *Ophthalmic Epidemiol*. 2005;2(1):49-55.

25. Klein BE, Klein R, Moss SE. Incidence of cataract surgery in the Wisconsin Epidemiologic Study of Diabetic Retinopathy. *Am J Ophthalmol*. 1995;119(3):295-300.

26. Raman R, Pal SS, Adams JS, Rani PK, Vaitheeswaran K, Sharma T. Prevalence and risk factors for cataract in diabetes: Sankar Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study, report No. 17. *Invest Ophthalmol Vis Sci*. 2010;51(12):6253-61.

27. Ting DS, Cheung GC, Wong TY. Diabetic retinopathy: global prevalence, major risk factors, screening practices and public health challenges: a review. *Clin Exp Ophthalmol*. 2016;44(4):260-77.

28. Keenum Z, McGwin G Jr, Witherspoon CD, Haller JA, Clark ME, Owsly C. Patients' adherence to recommended follow-up eye care after diabetic retinopathy screening in a Publicly Funded County Clinic and factors associated with follow-up eye care use. *JAMA Ophthalmol*. 2016;134(11):1221-8.

29. Abbasoğlu OE, Hoşal B, Tekeli O, Gürsel E. Risk factors for vitreous loss in cataract surgery. *Eur J Ophthalmol*. 2000;10(3):227-32.

30. Lai FH, Lok JY, Chow PP, Young AL. Clinical outcomes of cataract surgery in very elderly adults. *J Am Geriatr Soc*. 2014;62(1):165-70.

31. Desai P, Minassian DC, Reidy A. National cataract surgery survey 1997-8: a report of the results of the clinical outcomes. *Br J Ophthalmol*. 1999;83(12):1336-40.

32. Williams GA, Eisenstein R, Schumacher B, Hsiao KC, Grant D. Inhibitor of vascular endothelial cell growth in the lens. *Am J Ophthalmol*. 1984;97(3):366-71.

33. Jaffe GJ, Burton TC. Progression of nonproliferative diabetic retinopathy following cataract extraction. *Arch Ophthalmol*. 1988;106(6):745-9.

34. Pollack A, Leiba H, Bukelman A, Oliver M. Cystoid macular oedema following cataract extraction in patients with diabetes. *Br J Ophthalmol*. 1992;76(4):221-4.

35. Cheour M, Mazlout H, Falfoul Y, Chakroun I, Marrakchi A, Skhiri M, et al. Progression of diabetic retinopathy after cataract surgery by phacoemulsification. *J Fr Ophthalmol*. 2013;36(1):62-5.

36. Haddad NM, Sun JK, Abujaber S, Schlossman DK, Silva PS. Cataract surgery and its complication in diabetic patients. *Semin Ophthalmol*. 2014;29(5-6):329-37.

37. Aiello LM, Wand M, Liang G. Neovascular glaucoma and vitreous hemorrhage following cataract surgery in patients with diabetes mellitus. *Ophthalmology*. 1983;90(7):814-20.

38. Sebstyten JG. Intraocular lenses and diabetes mellitus. *Am J Ophthalmol*. 1986;101(4):425-8.

39. Kato S, Fukada Y, Hori S, Tanaka Y, Oshika T. Influence of phacoemulsification and intraocular lens implantation on the course of diabetic retinopathy. *J Cataract Refract Surg*. 1999;25(6):788-93.

40. Zaczek A, Olivestedt G, Zetterström C. Visual outcome after phacoemulsification and IOL implantation in diabetic patients. *Br J Ophthalmol*. 1999;83(9):1036-41.

Rad je primljen 2. VII 2018.

Recenziran 8. VII 2018.

Prihvaćen za štampu 9. VII 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:217-221.

University of Priština, Faculty of Medicine, Institute of Physiology,
Kosovska Mitrovica¹
University of Belgrade, School of Medicine,
Institute for Medical Statistics and Informatics, Belgrade²
Health Center Kosovska Mitrovica, Kosovska Mitrovica³

Original study
Originalni naučni rad
UDK 616.61-78-052:159.94/95.072
<https://doi.org/10.2298/MPNS1808222J>

EVALUATION OF THE COGNITIVE AND AFFECTIVE STATUS IN HEMODIALYSIS PATIENTS WITH CHRONIC RENAL FAILURE

PROCENA OŠTEĆENJA KOGNITIVNOG I AFEKTIVNOG STATUSA KOD BOLESNIKA SA HRONIČNOM BUBREŽNOM INSUFICIJENCIJOM NA HEMODIJALIZI

**Aleksandra JAKOVLJEVIĆ¹, Vojkan NESTOROVIĆ¹, Mirjana DEJANOVIĆ¹,
Zoran BUKUMIRIĆ², Aleksandar JAKOVLJEVIĆ³ and Novica ĐOKOVIĆ³**

Summary

Introduction. Hemodialysis patients with chronic renal failure, suffer from affective dysfunction to a variable extent. The aim of our study was to evaluate the cognitive and affective status in patients before and after hemodialysis. Apart from this, the goal of the study was to examine and compare the cognitive status of patients on dialysis in relation to the control group, but also in relation to laboratory parameters. **Material and Methods.** This research was a prospective study including 30 hemodialysis patients with chronic renal failure treated at the Department of Nephrology of the Health Center in Kosovska Mitrovica. The cognitive status of the subjects was evaluated by determining the simple reaction time to auditory and visual stimuli before and after hemodialysis sessions and using the Mini Mental Status Examination, while the affective status was evaluated by using the Beck Depression Inventory. **Results.** The analysis of the obtained results showed a statistically significantly lower auditory and visual simple reaction times ($p = 0.014$) after dialysis ($p = 0.023$). The results have confirmed a statistically significantly decreased simple reaction time to visual stimuli ($p = 0.001$), while a statistical significance ($p = 0.137$) was not obtained for the auditory stimuli when compared to the control group. The Mini Mental Status Examination and the Beck Depression Inventory did not indicate a significant cognitive status damage or presence of depression. **Conclusion.** The importance of hemodialysis in the improvement of cognitive function is clearly evident, even though the general state of cognitive status in patients on hemodialysis is lower compared to the healthy population. Evaluation of the cognitive and affective status using simple reaction time, Folstein's Mini Mental State Examination and the Beck Depression Inventory, should be used on daily basis in hemodialysis patients.

Key words: Renal Insufficiency, Chronic; Cognitive Dysfunction; Affective Symptoms; Reaction Time; Neuropsychological Tests; Renal Dialysis; Treatment Outcome

Introduction

Unrecognized and untreated chronic renal diseases lead to chronic renal failure (CRF) and terminal renal failure, and their incidence has in-

Sažetak

Uvod. Kod pacijenata sa hroničnom bubrežnom insuficijencijom podvrgnutih hemodijalizi kognitivna i afektivna disfunkcija je prisutna u varijabilnom intenzitetu. Cilj istraživanja je procena kognitivnog statusa pacijenata pre hemodijaliznog tretmana i nakon njega, kao i afektivnog statusa. Jedan od ciljeva istraživanja je i sagledati kognitivni status pacijenata na dijalizi u odnosu na kontrolnu grupu, kao i u odnosu na laboratorijske parametre. **Materijal i metode.** Istraživanje je koncipirano kao prospektivna studija koja je obuhvatila 30 pacijenata sa dijagnozom hronične bubrežne insuficijencije hemodijaliziranih na odeljenju nefrologije Zdravstvenog centra u Kosovskoj Mitrovici. Kognitivna funkcija ispitanika procenjena je određivanjem prostog reakcionog vremena na auditivni i vizuelni stimulus pre i nakon hemodijalizne seanse i primenom mini mental testa, dok je afektivni status procenjen primenom Bekovog testa depresije. **Rezultati.** Analizom dobijenih rezultata registrovane su statistički značajno niže vrednosti prostog reakcionog vremena na auditivni ($p = 0,014$) i vizuelni stimulus nakon dijalize ($p = 0,023$). Dobijeni rezultati ukazuju na statistički značajno smanjenje vrednosti reakcionog vremena na vizuelni stimulus ($p = 0,001$), dok za auditivni stimulus nije postignuta statistička značajnost ($p = 0,137$) u poređenju sa kontrolnom grupom. Mini mental test i Bekov test depresije nisu ukazali na signifikantno oštećenje kognitivnog statusa i prisustvo depresije. **Zaključak.** Značaj dijalize u poboljšanju kognitivnih funkcija je jasno evidentan iako je opšte stanje kognitivnog statusa pacijenata na hemodijalizi oštećeno u odnosu na zdravu populaciju. Procena kognitivnog i afektivnog statusa određivanjem prostog reakcionog vremena, primenom Folsteinovog i Bekovog testa depresije, treba da nađe veću zastupljenost u svakodnevnom kliničkom radu sa pacijentima na dijalizi.

Ključne reči: hronična bubrežna insuficijencija; kognitivni poremećaji; afektivni poremećaji; reakciono vreme; neuropsihološki testovi; hemodijaliza; ishod lečenja

creased exponentially over the past two decades. Consequently, more than two million patients in the world are currently treated with one of the three methods of renal replacement therapy – hemodialysis (HD), peritoneal HD and kidney transplantation

Abbreviations

| | |
|------|---------------------------------|
| CRF | – chronic renal failure |
| HD | – hemodialysis |
| SRT | – simple reaction time |
| MMSE | – Mini Mental State Examination |
| BDI | – Beck Depression Inventory |

[1, 2]. The very nature of CRF affects the incidence of cognitive impairment, most often due to uremia, but this may be attributed to any other metabolic disorder caused by the loss of renal function [3]. The presence of global cognitive impairment in people with CRF compared to healthy individuals from the similar or same age group is evident [3, 4]. Among the laboratory parameters that deviate from the reference values, in correlation with cognitive impairment, the indicators of anemia, serum levels of nitrogenous substances and the elevated potassium levels have been established. Patients with good dialysis efficiency have mild cognitive deficits, progressing to moderate impairments associated with lower HD efficiency. Anemia is a crucial factor and its correction may improve the patient's cognitive status. In patients with different stages of CRF, cognitive impairment shows variable intensity, but its incidence is also observed in individuals undergoing HD treatment [4].

Some studies suggest that there is a proportional correlation between the degree of cognitive impairment and the stage of CRF [5]. Patients with elevated urea and other harmful metabolic products in the blood show poor performance on tests, shorter attention span, and lower levels on working memory tasks [6]. In addition, it should be noted that HD treatment can positively impact the cognitive status in patients with end-stage CRF. The comparison of these results with the results of transplant patients in one of the studies showed that HD does not delay the repair of cognitive functions [7, 8]. The research has also shown a significant influence of low hematocrit values, in other words anemia, on the decline in cognitive function [6, 9]. The synergy of several factors that affect the onset of cognitive impairment and its incidence in dialysis patients requires attention as it can be an indicator of HD efficacy, complications related to the treatment itself, as well as the engagement of other factors including comorbid diseases. Cognitive impairment can significantly reduce patients' quality of life, which in turn leads to inadequate medical care due to the patient's difficulty in following the advice on necessary lifestyle, and may also affect the quality of interpersonal relationships, reduce the ability of social adaptation, and partly lead to the decline in quality of life [5, 9, 10].

The very nature of CRF is associated with the prevalence of psychiatric disorders. The multisystemic involvement with a mass of symptoms leads to patients' inadequate mental response. Symptoms from the domain of mental functions are manifested, over time, by the presence of smaller intellectual deficiencies, fatigue, concentration difficulties and apathy. Mood and character disorders also develop during the progression of the disease. During the treatment of CRF by HD, anxi-

ety and depression are only the most frequent manifestations followed by a decreasing libido and insomnia. A kind of "handicap" is being formed, often influenced by an attachment to the apparatus being used at a certain time. In relation to patients' response to medical personnel performing the HD treatment, the reactions range from an apparent cooperation with the ultimate regression to constant demands and conflicts with the rules. Sometimes, even a suicidal behavior may occur [11]. Psychiatric disorders are more frequent in patients with CRF than in the general population. Although depression significantly affects the survival rate of HD patients, a more accurate incidence rate of depression and other psychiatric disorders has not been fully defined [12].

Neurophysiological and neuropsychological methods, such as cognitive evoked potentials (P300) and reaction time, are objective markers of the readiness levels of cognitive mechanisms. Therefore, their registration and analysis are logical steps in assessing the cognitive state of both healthy subjects and those with different pathological conditions. The reaction time is increasingly used as a quantitative method and technique in examining the speed of information processing in humans, during an experimental process. The time interval between the moment of simple or complex stimuli introduction and the subsequent motor response reflects the speed of neurophysiological, cognitive and information processes that result from the effect of the stimulus on subjects' sensory system. Information perceiving and processing, decision making, and responding by motor action are processes that follow one another and comprise what we call reaction time [13, 14]. A simple reaction time (SRT) is a reaction to an already known stimulus, where the same response is expected in all subsequent attempts, so the subject is able to program the movement in advance [15]. In testing, the reaction time method reflects the readiness level of nervous and cognitive mechanisms, making them valid in studying the reaction rate in various situations in subjects on HD.

The cognitive status of CRF patients on HD expressed through the mean value of SRT is not the same before and after dialysis treatment, and it is affected by the values of biochemical laboratory parameters characteristic for CRF. The more pronounced the parameters of anemia, electrolyte imbalance, and elevated levels of nitrogenous substances, the poorer the achievement in tasks requiring preserved writing ability and constructive activity, which in turn can be estimated by using Mini Mental State Examination (MMSE) by Folstein, 1975 [4, 16–18].

The aim of this study was to determine the cognitive and affective status of patients with CRF on HD treatment by examining SRT before and after dialysis treatment using the neuropsychological MMSE test, as well as the Beck Depression Inventory (BDI). One of the objectives of the study was to evaluate the cognitive status of patients with CRF on HD treatment compared to the control group, in relation to laboratory parameters.

The study was based on the assumption that HD treatment contributes to the improvement of cogni-

Table 1. Auditory and visual SRTs before and after hemodialysis**Tabela 1.** Vrednosti prostog reakcionog vremena na vizuelni i auditivni stimulus pre i posle hemodijalize

| Simple reaction time/Prosto reakciono vreme | Before HD/Pre HD | Post HD/Posle HD | p - value/p - vrednost |
|---|------------------|------------------|------------------------|
| Auditory stimuli/Auditivni stimulus | 332.9 ± 94.1 | 313.8 ± 67.1 | 0.014 |
| Visual stimuli/Vizuelni stimulus | 429.2 ± 147.8 | 385.1 ± 121.8 | 0.023 |

HD - hemodijaliza

Table 2. Mean auditory and visual reaction times compared to the control group**Tabela 2.** Prikaz srednjeg reakcionog vremena na auditivni i vizuelni stimulus u odnosu na kontrolnu grupu

| Simple reaction time/Prosto reakciono vreme | Post HD/Posle HD | Control group/Kontrolna grupa | p - value/p - vrednost |
|---|------------------|-------------------------------|------------------------|
| Auditory stimuli/Auditivni stimulus | 313.8 ± 67.1 | 293.8 ± 34.7 | 0.137 |
| Visual stimuli/Vizuelni stimulus | 385.1 ± 121.8 | 300.9 ± 50.5 | 0.001 |

HD - hemodijaliza

tive and affective status of patients and that the cognitive and affective status of patients with CRF differs from the one of the patients without CRF.

Material and Methods

This prospective study included a total of 30 volunteer patients (22 men and 8 women) aged 29 to 75 (54.3 ± 14.51), with 4 to 16 years of formal education, suffering from CRF on hemodialysis in the period from May to July 2017 at the Department of Nephrology of the Health Center in Kosovska Mitrovica. The subjects were treated by hemodialysis about four hours, three times a week. The study included a control group of 50 healthy volunteers (20 men and 30 women), aged 35 to 69 (56.1 ± 9.5), with 8 to 16 years of formal education.

Using a special computer program, SRT testing was performed in each patient individually, before and immediately after HD treatment. The SRT was measured using a combination of two tasks, one including visual and the other auditory stimuli.

The MMSE (Folstein, 1975) was used as a screening test for the assessment of cognitive decline, that is the existence and the severity of dementia, while BDI (Beck, 1996) was used for assessing the affective status, i.e. the severity of depression.

The obtained data were processed using the Statistical package for the social sciences (SPSS) (version 25) (IBM Corporation, Armonk, NY, USA). The data are shown as percentages and mean values with standard deviation. The T-test was used for testing statistical hypotheses for two dependent and two independent samples. The correlation between the variables was estimated by Pearson's and Spearman's correlation coefficient. Statistical hypotheses were tested at the level of statistical significance (alpha level) of 0.05.

The study was conducted with the approval of Ethics Committee of Health Center Kosovska Mitrovica.

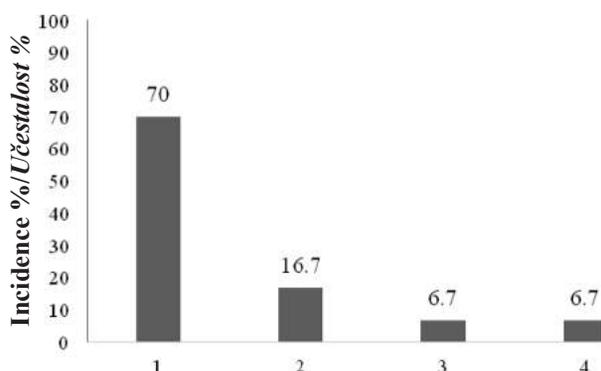
Results

The most common causes of CRF in our subjects were chronic glomerulonephritis (26.7%) and diabetic nephropathy (20.0%). The average duration of

HD treatment was 4.25 ± 4.09 years, with a range of 0.07 to 14.57. In the survey sample, the highest incidence of subjects on HD (56.3%) was recorded in four municipalities of the northern part of Kosovo and Metohija (Kosovska Mitrovica, Leposavić, Zvečan and Zubin Potok). Patients from municipalities in the south of the province had a lower incidence (43.7%).

The mean SRT to auditory stimuli before HD was 332.9 ± 94.1 and post HD treatment it was 313.8 ± 67.1 , which shows a statistically significant difference ($p = 0.014$). There was a significant reduction in the mean SRT to the auditory stimuli post HD treatment. The mean SRT to visual stimuli before HD was 429.2 ± 147.8 , while post HD treatment it was 385.1 ± 121.8 , which also shows a statistically significant difference ($p = 0.023$). There was a significant reduction of SRT to visual stimuli post HD (**Table 1**).

The mean SRT to auditory stimuli in subjects with CRF after HD treatment was 313.8 ± 67.1 , while in the control group it was 293.8 ± 34.7 , which was not a statistically significant difference ($p = 0.137$). The mean SRT to visual stimuli in subjects after HD treatment was 385.1 ± 121.8 while in the control group it was 300.9 ± 50.6 , which was a statistically significant difference ($p = 0.001$) (**Table 2**).

**Graph 1.** Beck Depression Inventory in the studied group of patients**Grafikon 1.** Bekov indikator depresije kod ispitivane grupe pacijenata

Based on the results of our study, the incidence of patients with CRF on HD examined by the Folstein's MMSE showed no statistically significant predictive value affecting their cognitive status. The total score reported normal functioning in 27 patients (90%), and a minimal cognitive deficit in 3 patients (10%).

The BDI was used to examine the degree of depression in patients with CRF on HD, or the lack thereof. The results of examination showed 9 positive cases, 2 patients with severe, 2 with moderate, and 5 with mild depression, while no depression was detected in 21 patients. The statistical analysis of the obtained data revealed that there was no correlation between depression and mean SRT (**Graph 1**).

Laboratory indicators of anemia in patients on HD showed decreased mean erythrocyte (3.4 ± 0.6), hemoglobin (104.7 ± 18.2) and hematocrit (316 ± 55.04), while the mean value of iron was 11.8 ± 6.5 . The level of glycemia in patients undergoing HD was 6.02 ± 2.8 .

By reviewing the average range of laboratory parameters that indicate serum levels of nitrogenous substances, in patients with CRF on HD, there were significant increases of urea (26.14 ± 5.75), creatinine (1111.55 ± 1327.88) and uric acid (403.17 ± 73.21) before HD, while the values of azotemia were, as expected, within the reference values (urea: 11.25 ± 3.13 , creatinine: 444.16 ± 124.88 , uric acid: 165.8 ± 59.25) after HD treatment. The review of the electrolyte status before HD indicated an electrolyte imbalance, which contributes to hyperkalemia, a mild elevation of phosphorus before HD treatment, as well as calcium after HD treatment, with approximate reference values for serum concentrations of other electrolytes (Na^+ , Cl^-). The parameters of hepatic parenchymal damage, aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyl transpeptidase, were within the reference values, whereas the average leukocyte and sedimentation values did not indicate an inflammatory disease.

Using the correlation tests, we found that there was a statistically significant, medium negative association between the levels of urea before HD and the values of SRT to auditory stimuli before HD ($r = -0.399$; $p = 0.029$). Also, there was a statistically significant medium negative correlation between post HD creatinine values and post HD values of SRT to auditory stimuli ($r = -0.448$; $p = 0.013$).

The correlation between the duration of dialysis and the values of SRT to auditory and visual stimuli did not prove to be statistically significant.

Discussion

During our study, we have performed two separate measurements of SRT (before and after HD) in patients with CRF on HD treatment. The analysis of the results clearly indicated a longer reaction time prior to HD treatment, both to visual and auditory stimuli, and the difference was statistically significant ($p < 0.001$). A statistically significant difference was also found when comparing the mean SRT to visual stimuli in the control and the HD group (after

HD), but the difference did not reach the statistical significance for the auditory stimuli.

Longer reaction times to visual stimuli were clearly noticeable compared to auditory stimuli. This is probably caused by the fact that auditory stimuli require only 8 to 10 ms to reach the temporal lobe, while visual stimuli require 20 – 40 ms to reach the occipital cerebral lobe [19].

Among patients undergoing HD treatment, the cognitive changes were clearly reversible after HD, transplantation, or introduction of erythropoietin therapy [10]. Due to kidney's inability to maintain the homeostasis of the body fluids and biochemical composition, accumulation of nitrogenous substances and other decomposition products occurs. One of the effects of uremia is the deficit of cognitive strategy. In cases where transplantation is not an option, HD is the main therapeutic method that keeps patients alive. It is a proven fact that HD improves the cognitive status of patients, but the fluctuations of cognitive status related to HD duration, HD type, the frequency of dialysis sessions, including the period between two HD sessions, are slightly less known [20–22]. The parameters for anemia indicate its clear presence in a group of patients on HD, which is supported by lower mean levels of erythrocytes, hemoglobin, and hematocrit. The effects of hematocrit and anemia on neurocognitive performance in patients with CRF on conservative or HD treatment have been investigated in many studies [9, 23–25].

The MMSE is a rapid mental status test which is a good predictor of possible disorders of serum electrolytes [17]. In our study, serum levels of electrolytes indicated a predominantly elevated level of potassium, with no statistically significant correlation. Therefore, the isolated hyperkalemia cannot be a predictor of cognitive dysfunction, which is reflected in the extended SRT values to visual and auditory stimuli prior to HD treatment. Since other relevant electrolytic parameters that are characteristic for HD patients with CRF are within approximate reference ranges, the potassium values are most likely a reflection of the failure of patients on HD to follow the recommended nutritional-hygienic regimen [26]. Our research has shown a correlation between the urea levels before HD and values of SRT to auditory stimuli before HD, as well as a correlation between the creatinine levels after HD and values of SRT to auditory stimuli after HD, while no statistical significance was noted for anemia and electrolyte status parameters.

In our study, we obtained statistically significant values by determining SRTs before and after dialysis and compared them to the results of the MMSE test, which confirmed that determination of SRTs to auditory and visual stimuli is a more sensitive indicator of cognitive deficit.

Patients on HD often feel and look "chronically tired", which means that the fluctuations in memory resources and reaction time are interpreted differently. Specifically, serotonin levels are reduced in patients with CRF, and serotonin is known for its

effects on the affective status and working memory [27]. Psychiatric disorders are more common in patients with CRF than in the general population. A more precise incidence rate of depression and other psychiatric disorders has not been fully defined [12].

Conclusion

Our study showed that there was a significant reduction in the mean simple reaction time to the auditory and visual stimuli post hemodialysis treatment. The importance of hemodialysis in the im-

provement of cognitive functions is clearly evident, even though the general state of cognitive status in patients with chronic renal failure on hemodialysis is impaired compared to a healthy population.

There is a correlation between the levels of urea before hemodialysis as well as creatinine levels post hemodialysis and simple reaction time to auditory stimuli.

Sporadic cases that indicate an impaired affective status and depression of hemodialysis patients require application of preventive psychiatric tests and assessments.

References

- Lysaght MJ. Maintenance dialysis population dynamics: current trends and long-term implications. *J Am Soc Nephrol.* 2002;13 Suppl 1:S37-40.
- Bello AK, Nwankwo E, El Nahas AM. Prevention of chronic kidney disease: a global challenge. *Kidney Int Suppl.* 2005;98:S11-7.
- Graham JE, Rockwood K, Beattie BL, Eastwood R, Gauthier S, Tuokko H, et al. Prevalence and severity of cognitive impairment with and without dementia in an elderly population. *Lancet.* 1997;349(9068):1793-6.
- Kopitović A. Algoritam za rano otkrivanje poremećaja više nervne delatnosti kod bolesnika na hroničnoj hemodijalizi [dissertation]. Novi Sad: Univerzitet u Novom Sadu; 2009.
- Kurella M, Chertow G, Luan J, Yaffe K. Cognitive impairment in chronic kidney disease. *J Am Geriatr Soc.* 2004;52(11):1863-9.
- Hart RP, Pederson JA, Czerwinski AW, Adams RL. Chronic renal failure, dialysis, and neuropsychological function. *J Clin Neuropsychol.* 1983;5(4):301-12.
- McKee DC, Burnett GB, Raft DD, Batten PG, Bain KP. Longitudinal study of neuropsychological functioning in patients on chronic hemodialysis: a preliminary report. *J Psychosom Res.* 1982;26(5):511-8.
- Kiolbasa T. Adequacy of hemodialysis compared to kidney transplantation: A neuropsychological perspective [dissertation]. Chicago: University of Illinois; 1998.
- Lee SY, Lee HJ, Kim YK, Kim SH, Kim L, Lee MS, et al. Neurocognitive function and quality of life in relation to hematocrit levels in chronic hemodialysis patients. *J Psychosom Res.* 2004;57(1):5-10.
- Pereira AA, Weiner DE, Scott T, Sarnak MJ. Cognitive function in dialysis patients. *Am J Kidney Dis.* 2005;45(3):448-62.
- Porot A, Adamović V, Beštić M. Enciklopedija psihijatrije. Beograd: Nolit; 1990.
- Kimmel PL, Weihs K, Peterson RA. Survival in hemodialysis patients: the role of depression. *J Am Soc Nephrol.* 1993;4(1):12-27.
- Pachela RG. The interpretation of reaction time in information-processing research. In: Kantowitz BH, editor. Human information processing tutorials in performance and cognition. Hillsdale: Lawrence Erlbaum Associates; 1974. p. 41-82.
- Mišolić M, Ivetić V, Nestorović V, Milanović Z, Radović D, Biševac B, et al. Uticaj funkcionalnog stanja organizma na vreme reakcije studenata. *Praxis Medica.* 2008;36(3-4):53-6.
- Kohfeld DL. Simple reaction as a function of stimulus intensity in decibels of light and sound. *J Exp Psychol.* 1971;88(2):251-7.
- Folstein MF, Folstein SE, McHugh P. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189-98.
- Todorovski Z, Salević-Obradović J, Slankamenac P. Mini Mental State Examination (MMSE) – valjanost prema kriterijumu patoloških promena u endokranijumu definisanih kompjuterskom tomografijom. In: 54. Naučno stručni skup psihologa Srbije – Sabor, Izazovi za primenjenu psihologiju u Srbiji: knjiga rezimea; 2006 maj 24-27; Zlatibor, Srbija. Beograd: Društvo psihologa Srbije; 2006. p. 46.
- Rondanelli M, Solerte SB, Ferrari E. Electrolytes and cognitive function in the elderly: relationship between serum sodium and chloride concentrations and psychometric test scores. *Panminerva Med.* 1998;40(3):191-5.
- Kemp BJ. Reaction time of young and elderly subjects in relation to perceptual deprivation and signal-on versus signal-off conditions. *Dev Psychol.* 1973;8(2):268-72.
- Kutlay S, Nergizoglu G, Duman N, Atli T, Keven K, Ertürk S, et al. Recognition of neurocognitive dysfunction in chronic hemodialysis patients. *Ren Fail.* 2001;23(6):781-7.
- Evans JD, Wagner CD, Welch JL. Cognitive status in hemodialysis as a function of fluid adherence. *Ren Fail.* 2004;26(5):575-81.
- Pliskin NH, Yurk HM, Ho LT, Umans JG. Neurocognitive function in chronic hemodialysis patients. *Kidney Int.* 1996;49(5):1435-40.
- Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, et al. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. *N Engl J Med.* 1998;339(9): 584-90.
- Drucke TB, Eckardt KU, Frei U, Jacobs C, Kokot F, McMahon LP, et al. Does early anemia correction prevent complications of chronic renal failure? *Clin Nephrol.* 1999;51(1):1-11.
- Martin-Lester M. Cognitive function in dialysis patients: case study of the anemic patients. *ANNA J.* 1997;24(3):359-66.
- Harrison T, Kasper D, Braunwald E, Fauci A. Harrison's principles of internal medicine. New York: McGraw-Hill; 2008.
- Oaksford K, Oaksford M, Ashraf M, Fitzgibbon G. Comparing neuropsychological function before and during haemodialysis: a habituating selective deficit for prose recall. *Br J Health Psychol.* 2008;13(Pt 2):273-89.

Rad je primljen 16. III 2018.

Recenziran 30. V 2018.

Prihvaćen za štampu 15. VI 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:222-226.

University of Novi Sad, Faculty of Physical Education, Novi Sad¹
 University of Novi Sad, Faculty of Medicine Novi Sad²
 Clinical Center of Vojvodina, Department of Medical Rehabilitation, Novi Sad³
 University of Novi Sad, Faculty of Medicine Novi Sad,
 Department of Physiology⁴

Original study
Originalni naučni rad
 UDK 371.3::796:376 i 37.043.2-056.26/36
<https://doi.org/10.2298/MPNS1808227P>

WORK WITH CHILDREN WITH DISABILITIES – THE TEACHERS’ ATTITUDES TOWARDS INCLUSION

RAD SA DECOM SA SMETNJAMA U RAZVOJU – STAVOVI NASTAVNIKA O INKLUZIJI

Branka PROTIĆ GAVA¹, Ksenija BOŠKOVIĆ^{2,3}, Miroslav SMAJIĆ¹,
 Dušica SIMIĆ PANIĆ^{2,3} and Nada NAUMOVIĆ⁴

Summary

Introduction. The aim of this paper was to determine the attitudes of physical education teachers and primary school teachers towards inclusive physical education in Serbia. **Material and Methods.** The research included 132 examinees of both genders: 59.09% females and 40.91% males. Data were collected using an anonymous questionnaire with a 4-point Likert scale. The questionnaire dealt with teachers’ previous experience, their qualifications for implementation of inclusive physical education, support and additional training for realization of inclusive physical education. Data were processed using Statistical Package for the Social Sciences 20. Normality distribution was tested by Kolmogorov-Smirnov and Shapiro-Wilk test, whilst the differences between groups (sexual dimorphism, environment, professional orientation) were examined using Mann-Whitney and Kruskal-Wallis tests at the significance level of $p \leq 0.05$. **Results.** The findings showed that the average scores were inclined towards positive attitudes to inclusive physical education. The findings also showed that there was no statistically significant gender-related difference of attitudes between physical education teachers and primary school teachers. However, there was a statistically significant difference related to geographical background in terms of qualification levels ($p = 0.02$) for work with children with disorders and disabilities, as well in terms of additional training ($p = 0.02$) and professional orientation, since physical education teachers have less experience working with students with developmental disorders. **Conclusion.** Both physical education teachers and primary school teachers have positive attitudes towards inclusion. Physical education teachers have less experience working with challenged students than primary school teachers, therefore additional training programs may be required.

Key words: Attitude to Health; School Teachers; Disabled Children; Mainstreaming (Education); Physical Education and Training; Surveys and Questionnaires

Introduction

Teachers’ attitudes are considered to be the most important factor for successful inclusive education, including inclusive physical education [1]. Researches show that positive attitudes of teachers are af-

Sažetak

Uvod. Cilj ovoga rada bilo je utvrđivanje stavova nastavnika fizičkog vaspitanja i učitelja o inkluzivnoj nastavi fizičkog vaspitanja u Srbiji. **Materijal i metode.** Uzorak ispitanika činilo je 132 ispitanika oba pola: 59,09% ženskog i 40,91% muškog. Podaci su prikupljeni anonimnim upitnikom, u kojem je korišćena četvorostepena skala stavova Likertovog tipa. Pitanja se odnose na prethodna iskustva nastavnika, osposobljenost za realizaciju inkluzivne nastave fizičkog vaspitanja, podrški i dodatnoj obuci za realizaciju inkluzivne nastave fizičkog vaspitanja. Podaci su obrađeni u SPSS statističkom programu, verzija 20. Za testiranje normalnosti distribucije, korišćeni su Kolmogorov-Smirnov i Šapiro-Vilk test, a za razlike među grupama (polni dimorfizam, sredina, profesionalana orijentacija) korišćen je Man-Vitnijev i Kruskal-Wallisov test, na nivou značajnosti $p \leq 0,05$. **Rezultati.** Ustanovljeno je da se prosečni skorovi ispitanika grupišu u zoni pozitivnih stavova prema inkluzivnom fizičkom vaspitanju. Rezultati istraživanja pokazuju da ne postoji statistički značajna razlika u stavovima nastavnika i učitelja u odnosu na polnu pripadnost. Međutim, uočena je statistički značajna razlika u odnosu na geografsku pripadnost u pogledu osposobljenosti ($p = 0,02$) za rad sa decom sa smetnjama i invaliditetom i dodatne obuke ($p = 0,02$), kao i profesionalne orijentacije između nastavnika i učitelja ($p = 0,01$) jer nastavnici imaju manje iskustva u radu sa učenicima sa smetnjama u razvoju. **Zaključak.** Nastavnici fizičkog vaspitanja i učitelji imaju pozitivan stav prema inkluziji. Nastavnici fizičkog vaspitanja imaju manje iskustva od učitelja u radu sa decom sa smetnjama i invaliditetom te im je neophodna dodatna obuka.

Gljučne reči: stavovi prema zdravlju; nastavnici; deca ometena u razvoju; inkluzivno obrazovanje; fizičko obrazovanje; ankete i upitnici

ected by extensive and inclusive education training during schooling, more experience in teaching students with disorders/disabilities and more positive perception of their own competence when it comes to teaching these students [1–5]. Some studies have shown that women have more positive attitudes

Abbreviations

ATIPE – Attitude towards Inclusive Physical Education
SPSS – Statistical Package for the Social Sciences

[6–8], but in other studies this was not the case [9, 10]. When it comes to the correlation between the teachers' age and attitudes towards inclusion, some previous studies suggest that older teachers have less positive attitudes [11], however, it was not confirmed by other studies.

Teachers often experience inclusive education as a source of difficulties and frustration, predicting negative impact on regular students due to inclusive classes and complaining of extra burdens and lack of professional support [12, 13]. The burnout syndrome is positively related to the number of students with disabilities in the inclusive class, poor material conditions and lack of professional support [14]. The combination of teachers' adverse attitudes towards inclusion and insufficient training to work in an inclusive class often result in failure of inclusive physical education [15]. In the research conducted by Đorđić et al. [16], the majority of teachers (58.3%) said that they did not have confidence when it comes to teaching children with developmental disorders/disabilities and only 9.1% of them attended a seminar on inclusive physical education. Teachers who had teaching experience with such children and who had the opportunity to get to know people with developmental disorders/disabilities more closely are more positive about their own competence. Since the credentials and attitudes of teachers change to the greatest extent through practical experiences and participation in effective professional development programs [17], this can undoubtedly be the priority direction for the further development of inclusive physical education in our environment.

The inclusive model of education in the Republic of Serbia has been implemented over the recent ten years in accordance with the national and international strategic documents, such as the Universal Declaration of Human Rights [18], the Convention on the Rights of the Child [19] and the United Nations Millennium Declaration [20]. The Law on the Foundations of the Education System [21] was brought in 2009 as the umbrella law in education, after which the implementation of a project for the development and implementation of an effective model of inclusive education began in Serbia. Another important document, Regulations on Special Education, Health and Social Support for Children and Students [22], was adopted in 2010, and a coordination and implementation team for inclusive education was established within the Ministry of Education. The Ministry of Education has developed a network of support to teachers and schools for the introduction of inclusive educational practice, while teaching and professional school staff has been trained to strengthen the professional competencies necessary for working in inclusive education.

Certain problems have been observed during the first year of implementation of inclusive education

in terms of organization and implementation of inclusive education in primary and secondary schools in Serbia and the difficulties associated with the daily activity of students and teachers affecting the efficiency of the teaching process. The reported problems are largely coincidental with those present in other countries that have previously started inclusive education. Firstly, a great number of students in the class prevent teachers from paying appropriate attention to the child with disorders/disabilities and there is also a lack of definition of roles in school, in terms of who the person who needs to provide support to teachers is. On the other hand, there is a dilemma whether other children in the class are deprived of attention due to the special treatment that children with disorders/disabilities require and how to adequately prepare them for accepting a child with a specific problem [23].

Although it is obvious that the complexity of education requires a better preparation for inclusion, including work on adaptation and accommodation processes [24], the common denominator of all previous remarks refers to understanding the role of teachers in this process. Teachers often perceive inclusion as a source of their difficulties and frustration, point out the negative consequences of inclusion for other students in the class, as well as the necessity of additional work and lack of professional support. In other words, inclusion imposes the need for changing the teachers' way of work, as well as the need for additional professional development in terms of working with children with special educational needs. Many researchers in this field emphasize that the process and outcome of inclusion depends on the knowledge, skills acquired and, in particular, attitudes and beliefs of teachers towards inclusion and persons with disorders/disabilities [2, 25–27].

Accordingly, the purpose of this research was to determine the attitudes of primary school and physical education teachers towards inclusive physical education, as well as the attitudes towards previous experience, skills, necessary support and additional training for working with certain categories of students in the inclusive class in relation to sex distribution, demographic environment, professional orientation (physical education teachers/primary school teacher) and length of service.

Material and Methods

The cross-sectional study was dealing with the attitudes of physical education teachers and primary school teachers on inclusive physical education in the following Districts of Serbia: South Bačka, Srem, Central Banat, Mačva and Raška.

The research included 132 examinees of both genders: 59.09% females and 40.91% males; 56.82% from the South Bačka, Srem and Central Banat Districts, and 43.18% from Mačva and Raška; there were 52.23% of teachers of physical education and 47.77% of primary school teachers; 11.37% had a working experience of up to 5 years, 31.06% between 6 and 15

Table 1. Differences in the attitudes of physical education teachers and primary school teachers regarding professional orientation**Tabela 1.** Razlike u stavovima nastavnika fizičkog vaspitanja i nastavnika razredne nastave u odnosu na profesionalnu orijentaciju

| Variables <i>Varijable</i> | Professional orientation <i>Profesionalna orijentacija</i> | N | M | SD | M-W | p |
|---|---|----|------|------|--------|------|
| Previous experience in work with students with disorders/disabilities <i>Prethodno iskustvo u radu sa učenicima sa smetnjama u razvoju/invaliditetom</i> | Physical education teachers <i>Profesori fizičkog vaspitanja</i> | 69 | 1.90 | 0.54 | 1583.0 | 0.01 |
| | Primary school teachers <i>Nastavnici razredne nastave</i> | 63 | 1.66 | 0.41 | | |
| Competence for working with students with disorders/disabilities <i>Osposobljenost za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | Physical education teachers <i>Profesori fizičkog vaspitanja</i> | 69 | 1.90 | 0.54 | 1747.5 | 0.07 |
| | Primary school teachers <i>Nastavnici razredne nastave</i> | 63 | 1.66 | 0.41 | | |
| Support for working with students with disorders/disabilities <i>Podrška za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | Physical education teachers <i>Profesori fizičkog vaspitanja</i> | 69 | 3.24 | 0.61 | 1864.0 | 0.15 |
| | Primary school teachers <i>Nastavnici razredne nastave</i> | 63 | 3.36 | 0.67 | | |
| Additional training for teachers working with students with disorders/disabilities <i>Dodatna obuka za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | Physical education teachers <i>Profesori fizičkog vaspitanja</i> | 69 | 3.19 | 0.56 | 2062.5 | 0.61 |
| | Primary school teachers <i>Nastavnici razredne nastave</i> | 63 | 3.14 | 0.80 | | |
| Inclusive physical education <i>Inkluzivno fizičko vaspitanje</i> | Physical education teachers <i>Profesori fizičkog vaspitanja</i> | 69 | 2.56 | 0.34 | 1989.5 | 0.40 |
| | Primary school teachers <i>Nastavnici razredne nastave</i> | 63 | 2.65 | 0.50 | | |

Legend: N – number of examinees; M – arithmetic mean; SD – standard deviation; M-W – Mann-Whitney test; p – statistical significance**Legenda:** N – broj ispitanika; M – aritmetička sredina; SD – standardna devijacija; M-W – Man-Vitnjev test; p – statistička značajnost

years, 34.09% between 16 and 25, and 23.48% worked over 25 years.

The data were collected using an anonymous questionnaire, which provided general data on examinees (gender, employment, length of service, professional orientation - primary school teacher or physical education teacher, geographical affiliation and previous teaching experience in an inclusive setting), their previous working experience and attitudes towards students with disorders/disabilities, the ability to realize inclusive physical education, support and additional training for the implementation of inclusive education. A four-fold Attitude towards Inclusive Physical Education (ATIPE) scale was used to examine attitudes of primary school teachers and physical education teachers towards inclusive physical education [7]. Full agreement with the given claims was expressed by number 1, while complete disagreement with number 4. In order to avoid the unwanted halo effect, the claims were formulated negatively, so that marking the item with number 4 meant the most positive attitude towards the claim, and number 1 implied the most negative attitude.

The data were processed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 20. Absolute and relative frequencies were determined by descriptive statistics. The normality distribution was assessed by Kolmogorov-Smirnov and the Shapiro-Wilk tests, and Mann-Whitney and Kruskal-Wallis tests were used to determine the differences

between groups of examinees, at the significance level $p \leq 0.05$.

Results

The gathered results examining attitudes of physical education teachers' and primary school teachers' towards their previous work experience, work skills, support and additional training for work with students with disorders/disabilities, as well as the attitudes towards inclusive physical education in relation to professional orientation – teachers of physical education or primary school teachers (**Table 1**), show that there is a statistically significant difference only in the past work experience with disabled students in favour of primary school teachers.

The results of gender-related differences in attitudes are shown in **Table 2**. The findings showed that there were no statistically significant gender-related differences in attitudes of teachers of physical education and primary school teachers towards inclusive physical education, in terms of: previous work experience of primary school and teachers of physical education with particular categories of students, their qualifications for realization of inclusive physical education, support for work in inclusive classes, additional training for work in inclusive classes, and the extent of agreement concerning inclusive physical education.

Table 2. Differences in attitudes of physical education teachers and primary school teachers towards inclusion with sex distribution**Tabela 2.** Razlike u stavovima nastavnika fizičkog vaspitanja i nastavnika razredne nastave prema inkluziji u odnosu na pol

| Variables Varijable | Gender Pol | N | M | SD | M-W | p |
|---|---------------|----|------|------|--------|------|
| Previous experience in work with students with disorders/disabilities <i>Prethodno iskustvo u radu sa učenicima sa smetnjama u razvoju/invaliditetom</i> | M | 54 | 1.81 | 0.51 | 2016.5 | 0.68 |
| | F | 78 | 1.77 | 0.48 | | |
| Competence for working with students with disorders/disabilities <i>Osposobljenost za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | M | 54 | 1.81 | 0.51 | 1836.5 | 0.26 |
| | F | 78 | 1,76 | 0,48 | | |
| Support for working with students with disorders/disabilities <i>Podrška za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | M | 54 | 3.26 | 0.63 | 1957.5 | 0.47 |
| | F | 78 | 3.33 | 0.65 | | |
| Additional training for teachers working with students with disorders/disabilities <i>Dodatna obuka za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | M | 54 | 3.12 | 0.64 | 1892.5 | 0.32 |
| | F | 78 | 3.20 | 0.71 | | |
| Inclusive physical education <i>Inkluzivno fizičko vaspitanje</i> | M | 54 | 2.55 | 0.41 | 1869.5 | 0.27 |
| | F | 78 | 2.64 | 0.44 | | |

Legend: N – number of examinees; Gender – M – male, F – female; M – arithmetic mean; SD – standard deviation; M-W – Mann-Whitney test; p – statistical significance of differences ($p \leq 0.05$)

Legenda: N – broj ispitanika; Pol – M – muški, F – ženski; M – aritmetička sredina; SD – standardna devijacija; M-W – Man-Vitnijev test; p – statistička značajnost ($p \leq 0.05$)

Testing the significance of differences between groups of examinees with different length of service showed that among these groups there were no statistically significant differences in the average scores on the assessment scale of attitudes towards inclusive physical education.

Table 3 presents the attitudes of the total sample of examinees towards inclusive physical education with regard to the geographical region where they work. The findings indicated that there was a statistically significant difference between examinees who lived and worked in different regions of Serbia, in terms of qualifications for work with particular categories of students ($p = 0.02$) and the attitudes towards additional training for teachers working in inclusive classes ($p = 0.02$).

The examinees from the administrative Districts of Mačva and Raška (western and south-western part of Serbia) achieved higher scores ($1.84 > 1.74$ and $3.30 > 3.11$) related to qualifications and additional training, suggesting that teachers from South Bačka, Srem and Middle Banat Districts (north of Serbia) were better informed about inclusive education than teachers from the western and south-western parts of Serbia.

Discussion

Every child has unique characteristics, interests, abilities and needs in terms of learning, and has a right to primary education; hence, children must be given the opportunity to achieve and maintain an acceptable level of learning. The education systems and education programs should take into account a wide range of differences in the characteristics and needs of each child [28]. Therefore, the basic idea of inclusive education is that all students differ from one another and

that schools need to be adapted and changed so that they can meet the needs of all students [29, 30].

The results and experiences of previous researches indicate the great significance and determinants of subject teachers' attitudes towards inclusion in education [1–5, 7, 8]. Based on these findings, a survey was conducted with the aim of examining the attitudes of our teachers of physical education and primary school teachers towards inclusive physical education, as well as the attitudes towards previous experience, skills, necessary support and additional training for work with certain categories of students in the inclusive class. The results of the research reflect the current phase in the development of inclusive education in our community.

The results of our research show that there is a statistically significant difference between physical education teachers and primary school teachers only in terms of past experience in work with students with developmental disorders, which is in favour of primary school teachers. This result is expected to a certain extent, since primary school teachers first had the opportunity to work with these children in an inclusive class where they taught physical education as well. This has been expected since primary school teachers in Serbia have longer multi-year work experience with the students with disorders and disabilities than physical education teachers.

Our research showed no statistically significant difference in attitudes between teachers of upper and lower-grade students towards inclusive physical education. The results of other studies have shown that teachers in lower-grades have a more negative attitude than teachers in upper-grades towards inclusive education [30]. The authors explain this by the fact that integration and then inclusion have been rapidly introduced without systemic changes

and adjustments, both by schools and by the teachers in lower-grades [2].

The attitudes of primary school teachers and physical education teachers towards inclusive physical education depend on a variety of factors, such as previous work experience in the inclusive class, additional education, age, seniority, and the level of education [31]. Certain difficulties in the inclusive class are caused by the work experience, the choice of teachers and finally – prejudice. The length of service in the profession was not considered in our research as an important determinant of teachers' attitudes. Unlike our research, Clough and Lindsay [32] reported that younger teachers in upper-grades with several years of experience give greater support to inclusion. A possible explanation can be found in the fact that the development of inclusive education model in our schools is at an early stage, so teachers have had little opportunity to teach students with developmental disorders/disabilities during their professional life. Older lower-grade teachers have more positive attitudes towards partial inclusion, especially in classes that are not part of inclusive education. This can be explained by greater experience they have working with children with disabilities [33, 34]. Karić et al. [35] also concluded that older lower-grade teachers have a more positive attitude towards partial inclusion, although additional analysis shows that this correlation is much higher in those who currently have no inclusion

students in their class, than those who teach in class with at least one inclusion student. The authors attributed this correlation to the fact that older lower-grade teachers are actually more open to new experiences and activities. Roberts and Lindsell [36] reported that teachers working with students with disabilities in their classes have more positive attitudes than those without that experience. However, Boer et al. [37] found that most lower-grade teachers show a neutral or negative attitude towards the inclusion of students with developmental disorders in regular classes, and that none of the 26 examined studies revealed pure positive attitudes.

When it comes to length of service and differences in attitudes between upper-grade and lower-grade teachers, the results of our research show that there is no statistically significant difference. These results do not coincide with the results of other researchers who report that this difference exists. Lower-grade teachers with 14 or less years of service have a statistically significantly higher positive score of their attitudes towards inclusion than those who have more than 14 years of service [38].

Statistically significant gender-related differences in terms of general attitude towards inclusive education were not found in teachers of physical education and primary school teachers. Namely, they have equally positive attitudes. These results are not in accordance with the results of previous researches on the impact of gender on the attitudes

Table 3. Attitude of the total sample towards inclusive physical education in examined regions
Tabela 3. Stavovi ukupnog uzorka ispitanika o inkluzivnom fizičkom vaspitanju u odnosu na region

| Variables <i>Varijable</i> | Administrative region of Serbia <i>Administrativni region Srbije</i> | N | M | SD | M-W | p |
|---|--|----|------|------|------------|---|
| Previous experience in work with students with disorders/disabilities <i>Prethodno iskustvo u radu sa učenicima sa smetnjama u razvoju/invaliditetom</i> | South Bačka, Srem and Middle Banat <i>Južna Bačka, Srem i Srednji Banat</i> | 75 | 1.74 | 0.46 | 1994.50.38 | |
| | Mačva/Mačva Raška/Raška | 57 | 1.84 | 0.53 | | |
| Competence for working with students with disorders/disabilities <i>Osposobljenost za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | South Bačka, Srem and Middle Banat <i>Južna Bačka, Srem i Srednji Banat</i> | 75 | 1.74 | 0.46 | 1576.50.02 | |
| | Mačva/Mačva Raška/Raška | 57 | 1.84 | 0.53 | | |
| Support for work with students with disorders/disabilities <i>Podrška za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | South Bačka, Srem and Middle Banat <i>Južna Bačka, Srem i Srednji Banat</i> | 75 | 3.22 | 0.71 | 1873.00.22 | |
| | Mačva/Mačva Raška/Raška | 57 | 3.40 | 0.52 | | |
| Additional training for teachers working with students with disorders/disabilities <i>Dotatna obuka za rad sa učenicima sa smetnjama u razvoju/invaliditetom</i> | South Bačka, Srem and Middle Banat <i>Južna Bačka, Srem i Srednji Banat</i> | 75 | 3.11 | 0.73 | 1636.50.02 | |
| | Mačva/Mačva Raška/Raška | 57 | 3.30 | 0.60 | | |
| Inclusive physical education <i>Inkluzivno fizičko vaspitanje</i> | South Bačka, Srem and Middle Banat <i>Južna Bačka, Srem i Srednji Banat</i> | 75 | 2.62 | 0.35 | 1875.00.23 | |
| | Mačva/Mačva Raška/Raška | 57 | 2.57 | 0.51 | | |

Legend: N – number of examinees; M – arithmetic mean; SD – standard deviation; M-W – Mann-Whitney test; p – statistical significance of differences ($p \leq 0.05$)

Legenda: N – broj ispitanika; M – aritmetička sredina; SD – standardna devijacija; M-W – Man-Vitnjev test; p – statistička značajnost ($p \leq 0.05$)

about inclusion [2, 16, 32–34, 39–41]. These results are also contrary to the results of Al-Zyoudi [42], who found a minimum difference between male and female teachers, where female respondents had more positive attitudes than male. The explanation should probably be sought in the fact that the research was carried out in a meticulously selected sample of examinees whose schools were involved in inclusion at that time. One of the reasons may also be a higher percentage of female teachers who participated in the research. The authors of other studies also reported more females than males in their studies, up to 87% [43].

During professional work, a number of mechanisms or gender are being developed that make it easier to adapt to specific situations, as a result of which differences in assessments of male and female teachers are also increasing. This interpretation is corroborated by the results of numerous studies conducted in America, which indicate that men are much more conservative and authoritative and that they have stronger orientation towards being coaches than teachers [44]. This orientation can affect and increase intrapersonal conflicts when such an approach prevents a teacher from adequate approach (imposing) to persons with disabilities, which further affect their attitudes towards these persons and their problems.

The lack of additional training and support of professionals who work with students with disorders/disabilities is a major difficulty in the inclusive process [31]. The results of our study point to the fact that all of them need additional training and support from experts in inclusive education; however, the difference in attitudes is not statistically significant. Furthermore, 62.5% of the respondents who analyzed the study conducted by Boric [45], whose results are in line with ours, thought that the first necessary condition for inclusive education was additional education. Teachers working in inclusive schools are aware of their shortcomings in work with children with disabilities [46]. They are interested in new knowledge and skills, which they can gain through their professional development. Professional development of teachers through work with children with disabilities can be a possible solution to some of the problems that occur in inclusive education.

Professional teacher training is an effective way to improve their attitudes towards inclusion [47] as well as more oriented training during schooling, more experience in teaching students with disabilities and more positive perception of their own competence when it comes to teaching these students [16]. Thus, professional teacher training is one of the key factors of successful inclusion [48], and an important factor in improving the attitude of teachers towards inclusion is their knowledge about children with disabilities. This was also supported by the findings of Al-Khatteeb [49] and Beh-Pajooh [50]. Differences between the upper-grade and lower-grade teachers' attitudes in our study, regarding additional training, or training to work with students with disabilities, are not statisti-

cally significant. However, both upper-grade and lower-grade teachers alike feel that they need additional training to work with children with disabilities.

Professional training of teachers who work with children with disabilities is a necessity, because it is a precondition for quality inclusion [51]. The application of current knowledge can lead to the change of interactive processes in the process of inclusion. The knowledge that upper-grade and lower-grade teachers gain in basic studies can be expanded through further training at higher levels of studies - master and PhD studies [52]. Enrichment of existing programs by introducing new contents would enable future experts to be effective, because they would be able to recognize the nature of the disorder and evaluate the child's abilities better and more easily, modify the curriculum and expectations from the child, given the specificity of individual students. In this way, they would be able to clearly define tasks in the learning process.

Conclusion

Essentially, inclusive education is the practice of including all students into mainstream schools and classes in which it is possible to fulfil all their needs, regardless of talents, limitations, socio-economic background and origin.

However, due to substantial ambiguities and fears related to inclusive education, teachers are afraid to work with the students with disorders and disabilities, which may be justified to a certain extent. The curricula of the Faculties of Sport and Physical Education pay insufficient attention to inclusive education which has become a reality. The preparation of teachers for work with children with disorders/disabilities in regular schools is being significantly changed in recent years. One of the most important concerns is the necessary adaptation of teachers to the ever-increasing range of differences among students, i.e. need to prepare for inclusive teaching. The results of previous researches indicate that the preparation must begin during the course of the teachers' education, since the views of university teachers on inclusive education greatly affect the attitudes of future teachers [53, 54].

Inclusive education, therefore, involves the need for adaptation of regular schools in order to accommodate children with disorders and disabilities or create an atmosphere in which any child can develop regardless of his disabilities. These changes include changing values, attitudes, policies and practices within and outside schools, which is strongly corroborated by the fact that literature generally puts emphasis on the role of primary school teachers and course teachers as one of the most important factors for the functional implementation of social inclusion.

To sum up briefly: the results of this study show that both physical education teachers and primary school teachers have positive attitudes towards inclusion. On the other hand, physical education teachers have less experience with challenging students than primary school teachers, and therefore additional training programs may be useful.

References

1. Folsom-Meek SL, Rizzo TL. Validating the physical educators' attitude toward teaching individuals with disabilities III (PEATID III) survey for future professionals. *Adapt Phys Activ Q.* 2002;19(2):141-54.
2. Avramidis E, Bayliss P, Burden R. A survey into mainstream teachers' attitudes towards the inclusion of children with special educational needs in the ordinary school in one local education authority. *Educ Psychol.* 2000;20(2):191-211.
3. Block ME, Rizzo TL. Attitudes and attributes of physical educators associated with teaching individuals with severe and profound disabilities. *J Assoc Pers Sev Handicaps.* 1995;20(1):80-7.
4. Kowalski EM, Rizzo TL. Factors influencing preservice student attitudes toward individuals with disabilities. *Adapt Phys Activ Q.* 1996;13(2):180-96.
5. Rizzo TL, Kirkendall DR. Teaching students with mild disabilities: what affects attitudes of future physical educators? *Adapt Phys Activ Q.* 1995;12(3):205-16.
6. Downs P, Williams T. Student attitudes toward integration of people with disabilities in activity settings: a European comparison. *Adapt Phys Activ Q.* 1994;11(1):32-43.
7. Hutzler Y, Zach S, Gafni O. Physical education students' attitudes and self-efficacy towards the participation of children with special needs in regular classes. *Eur J Spec Needs Educ.* 2005;20(3):309-27.
8. Papadopoulou D, Kokaridas D, Papanikolaou Z, Patsiaouras A. Attitudes of Greek physical education teachers toward inclusion of students with disabilities. *Int J Spec Educ.* 2004;19(2):104-11.
9. Hodge SR, Davis R, Woodard R, Sherrill C. Comparison of practicum types in changing preservice teachers' attitudes and perceived competence. *Adapt Phys Activ Q.* 2002;19(2):155-71.
10. Rizzo TL, Vispoel WP. Physical educators' attributes and attitudes toward teaching students with handicaps. *Adapt Phys Activ Q.* 1991;8(1):4-11.
11. DePauw KP, Karp GG. Attitudes of selected college students toward including disabled individuals in integrated settings. In: Doll-Tepper G, Dahms C, Doll B, Von Selzam H, editors. *Adapted physical activity.* Berlin: Springer Verlag; 1990.
12. Reiter S. Mainstreaming children with special needs in Israel: a major source of stress in schools. In: Swarzer C, Zeidner M, editors. *Stress, anxiety and coping in academic settings.* Tübingen: Francke Verlag; 1996.
13. Scruggs TE, Mastropieri MA. Teacher perception of mainstreaming/inclusion, 1958–1995: a research synthesis. *Except Child.* 1996;63(1):59-74.
14. Talmor R, Reiter S, Feigin N. Factors relating to regular education teacher burnout in inclusive education. *Eur J Spec Needs Educ.* 2005;20(2):215-29.
15. Block ME. Did we jump on the wrong bandwagon? Problems with inclusion in physical education. *Palaestra.* 1999;15(3):30-6.
16. Đorđić V, Tubić T. Učitelji kao nosioci inkluzivnog fizičkog vaspitanja [Teachers as managers of inclusive physical education]. *Sportske nauke i zdravlje.* 2012;2(1):60-4.
17. Ben-Yehuda S, Leyser Y, Last U. Teacher educational beliefs and sociometric status of special educational needs (SEN) students in inclusive classrooms. *International Journal of Inclusive Education.* 2010;14(1):17-34.
18. United Nations. Universal Declaration on Human Rights [Internet]. 1948 [cited 2011 Aug 8]. Available from: <http://www.un.org/en/universal-declaration-human-rights/index.html>.
19. United Nations. Convention on the Rights of the Child [Internet]. 1989 [cited 2011 Aug 8]. Available from: <https://www.ohchr.org/Documents/ProfessionalInterest/crc.pdf>.
20. United Nations. United Nations Millennium Declaration [Internet]. 2000 [cited 2018 Jun 8]. Available from: <http://www.un.org/millennium/declaration/ares552e.htm>.
21. Zakon o osnovama sistema obrazovanja i vaspitanja [Law on Fundamentals of Education System] [Internet]. Beograd: Ministarstvo prosvete; 2009 [cited 2018 Jun 8]. Available from: <http://www.rckanjiza.edu.rs/wp-content/uploads/2013/11/Zakon-o-osnovama-sistema.pdf>. Serbian.
22. Pravilnik o dodatnoj obrazovnoj, zdravstvenoj i socijalnoj podršci detetu i učeniku [The Rulebook on additional education, health and social support to the child and student]. Beograd: Ministarstvo prosvete i nauke; 2010. Serbian.
23. Fejgin N, Talmor R, Erlich I. Inclusion and burnout in physical education. *Eur Phy Educ Rev.* 2005;11(1):29-50.
24. Milačić-Vidojević I, Glumčić N, Đorđević M. Mogućnost inkluzivnog obrazovanja dece s poremećajima autističkog spektra. In: Radovanović D, editor. *U susret inkluziji - dileme u teoriji i praksi* [Possibilities of inclusive education of children with autism spectrum disorders. Embracing inclusion – dilemma in theory and practice] [Monograph on the Internet]. Beograd: Fakultet za specijalnu edukaciju i rehabilitaciju; 2008 [cited 2018 Jun 8] p. 213–27. Available from: http://www.icf.fasper.bg.ac.rs/zbornici/2008-U_SUSRET_INKLUZIJI.pdf. Serbian.
25. Bender WN, Vail CO, Scott K. Teachers attitudes toward increased mainstreaming: Implementing effective instruction for students with learning disabilities. *J Learn Disabil.* 1995;28(2):87-94.
26. Cook BG. A comparison of teachers' attitudes toward their included students with mild and severe disabilities. *J Spec Educ.* 2001;34(4):203-13.
27. Friend M, Bursuck WD. Including students with special needs: a practical guide for classroom teachers. 4th ed [Monograph on the Internet]. Boston: Pearson & Allyn Bacon; 2006 [cited 2018 Jun 8]. Available from: <https://www.amazon.com/Including-Students-Special-Needs-Practical/dp/0132179725>.
28. The Salamanca statement and framework for action on special needs education [Internet]. Paris: UNESCO; 1994 [cited 2018 Jun 8]. Available from: http://www.unesco.org/education/pdf/SALAMA_E.PDF.
29. Kinsella W, Senior J. Developing inclusive schools: a systematic approach. *International Journal of Inclusive Education.* 2008;12(5-6):651-65.
30. Alghazo EM, Naggat Gaad EE. General education teachers in the United Arab Emirates and their acceptance of the inclusion of students with disabilities. *British Journal of Special Education.* 2004;31(2):94–9.
31. Martins CLR. Educação Física inclusiva: atitudes dos docentes. *Movimento.* 2014;20(2):637-56.
32. Clouch P, Lindsay G. Integration and the support service. Berkshire: NFER-Nelson; 1991.
33. Vujačić MB. Uključivanje dece sa smetnjama u razvoju u redovne grupe vrtića: mogućnosti i efekti [magistarski rad]. Beograd: Univerzitet u Beogradu, Filozofski fakultet; 2003.

34. Vukajlović B. Inkluzivno obrazovanje. Banja Luka: IP Grafid; 2004.
35. Karić T, Mihić V, Korda M. Stavovi profesora razredne nastave o inkluzivnom obrazovanju dece sa smetnjama u razvoju. *Primenjena psihologija*. 2014;7(4):531-48.
36. Roberts CM, Lindsell JS. Children's attitudes and behavioral intentions towards peers with disabilities. *International Journal of Disability, Developmental and Education*. 1997;44(2):133-45.
37. Boer A, Pijl SJ, Minnaert A. Regular primary schoolteachers' attitudes towards inclusive education: a review of literature. *International Journal of Inclusive Education*. 2011;15(3):331-53.
38. Leyser Y, Kapperman G, Keller R. Teacher attitudes toward mainstreaming: a cross-cultural study in six nations. *Eur J Spec Needs Educ*. 1994;9(1):1-15.
39. Ellins J, Porter J. Departmental differences in attitudes to special educational needs in the secondary school. *British Journal of Special Education*. 2005;32(4):188-95.
40. Hutzler Y. Attitudes toward the participation of individuals with disabilities in physical activity: a review. *Quest*. 2003;55(4):347-73.
41. Leyser Y, Tappendorf K. Are attitudes and practices regarding mainstreaming changing? A case of teachers in two rural school districts. *Education*. 2001;121(4):751-60.
42. Al-Zyoudi M. Teachers' attitudes towards inclusive education in Jordanian schools. *Int J Spec Educ*. 2006;21(2):55-62.
43. Sokal L, Sharma U. Canadian in-service teachers' concerns, efficacy, and attitudes about inclusive teaching. *Exceptionality Education International*. 2014;23(1):59-71.
44. Bain LL. Physical education teacher education. In: Houston WR, editor. *Handbook of research on teacher education*. New York: Macmillan, 1990. p. 758-81.
- Rad je primljen 22. VI 2018.
Recenziran 5. VII 2018.
Prihvaćen za štampu 13. VII 2018.
BIBLID.0025-8105:(2018):LXXI:7-8:227-234.
45. Borić S, Tomić R. Stavovi nastavnika osnovnih škola o inkluziji. *Metodički obzori*. 2012;7(3):75-86.
46. Heiman T. Inclusive schooling - middle school teachers' perceptions. *Sch Psychol Int*. 2001;22(4):451-62.
47. Siegel J, Jausovec N. Improving teachers' attitudes toward students with disability. In: *Conference of the International Council on Education and Teaching: Proceedings [Internet]*; 1994 Jul, Istanbul, Turkey. [cited 2018 Jun 8]. [about 21 p.]. Available from: <https://files.eric.ed.gov/fulltext/ED374120.pdf>.
48. Marchesi A. International perspectives on special education reform. *Eur J Spec Needs Educ*. 1998;13(1):116-22.
49. Al-Khatteeb J. Teachers' perceptions of the inclusive school concepts in Jordan. *Educational Journal*. 2002;65:19-39.
50. Beh-Pajooch A. The effect of social contact on college teachers' attitudes towards students with severe mental handicaps and their educational integration. *Eur J Spec Needs Educ*. 1992;7(2):231-6.
51. Golubović Š. Neophodnost profesionalnog osposobljavanja stručnjaka kao jedan od preduslova kvalitetne inkluzije. *Krugovi detinjstva*. 2013;(1):53-8.
52. Golubović Š, Tubić T, Janković P. Teachers' continuing professional development –inclusive education. In: *4th International Conference "Comparative Education in Teachers Training"*; 206 May 1-4; Sofia, Bulgaria. Sofia: Bulgarian Comparative Education Society (BCES); 2006;Vol 4:221-7.
53. Palmer D. Durability of changes in self-efficacy of pre-service primary teachers. *Int J Sci Educ*. 2006;28(6):655-71.
54. Wilczenski FL. Development of a scale to measure attitudes toward inclusive education. *Educ Psychol Meas*. 1995;55(2): 291-9.

Clinical Center of Vojvodina, Novi Sad, Emergency Center¹
 University of Novi Sad, Faculty of Medicine Novi Sad
 Department of Anesthesia and Intensive Care²
 Institute of Oncology of Vojvodina³
 Emergency Center, Department of Emergency Neurology⁴

Original study
Originalni naučni rad
 UDK 616.718.4-001.5-089.5:616.12-008.4
<https://doi.org/10.2298/MPNS1808235G>

PREDICTORS OF HYPOTENSION DURING SURGICAL MANAGEMENT OF FEMORAL FRACTURES IN SPINAL ANESTHESIA

PREDIKTORI HIPOTENZIJE TOKOM OPERATIVNOG ZBRINJAVANJA PRELOMA BUTNE KOSTI U SPINALNOJ ANESTEZIJI

Milica GOJKOVIĆ¹, Arsen UVELIN^{1,2}, Milanka TATIĆ^{2,3}, Vladimir VRSJAKOV¹,
 Dunja MIHAJLOVIĆ^{1,2} and Aleksandra LUČIĆ PROKIN⁴

Summary

Introduction. Femoral fractures are the most common cause of morbidity and mortality in the elderly. The aim of this study was to establish the predictors of hypotension in the elderly patients with femoral fractures during surgery in spinal anesthesia. **Material and Methods.** This retrospective study included 454 patients and investigated the relationship between hypotension and predictive factors for the development of hypotension using binary logistic regression. A paired sample T-test for dependent variables was used to compare the mean arterial pressure before and after the surgical procedure. Three mean arterial pressure values were compared between subjects receiving bupivacaine and subjects who received levobupivacaine: preoperative, the lowest value during the surgery, and the mean arterial pressure at the end of the surgery. **Results.** The age of the subjects ranged from 20 to 93 years (mean = 71.56; standard deviation = 13.26, median = 74). The mean arterial pressure values during the preoperative evaluation (103.2 ± 14.7) were higher than the last mean arterial pressure during surgery (84.8 ± 13.6) and these differences were statistically significant ($p < 0.001$). The group of subjects who received levobupivacaine presented with higher values of median arterial pressure (73.99) than the group receiving bupivacaine (70.76). **Conclusion.** The predictors of hypotension during surgery of patients with femoral fractures in spinal anesthesia are elderly age and preoperative use of beta blockers.

Key words: Hypotension; Anesthesia, Spinal; Femoral Fractures; Orthopedic Procedures; Age Factors; Adrenergic beta-Antagonists; Risk Factors

Introduction

Femoral fractures are the most common cause of morbidity and mortality in elderly patients [1]. Surgical management of femoral fractures may be performed under general or neuraxial block anesthesia [2, 3]. The choice of anesthesia depends on patients' chronic diseases, previous anesthesiological compli-

Sažetak

Uvod. Prelomi butne kosti predstavljaju najčešći uzrok morbiditeta i mortaliteta bolesnika starijeg životnog doba. Cilj rada je utvrđivanje faktora koji imaju prediktivnu moć za nastanak hipotenzije tokom spinalne anestezije za operativno zbrinjavanje preloma butne kosti. **Materijal i metode.** Ispitivanje je sprovedeno po tipu retrospektivne studije, obuhvatilo je 454 bolesnika. Radi ispitivanja povezanosti hipotenzije i faktora koji imaju prediktivni značaj za nastanak hipotenzije primenjena je binarna logistička regresija. Poređenjem vrednosti srednjeg arterijskog pritiska na kraju operativnog zahvata sa inicijalnom vrednosti srednjeg arterijskog pritiska, u perioperativnoj evaluaciji primenjen je t-test za zavisne uzorke. Upoređivane su tri vrednosti srednjeg arterijskog pritiska: preoperativna vrednost, najniža vrednost tokom operativnog zahvata i vrednost srednjeg arterijskog pritiska na kraju operativnog zahvata, između grupe ispitanika koja je dobila bupivakain i grupe ispitanika koja je dobila levobupivakain. **Rezultati.** Starost ispitanika se kretala u opsegu od 20 do 93 godine (srednja vrednost = 71,56; standardna devijacija SD = 13,26; medijana = 74). Pokazano je da su vrednosti srednjeg arterijskog pritiska tokom preoperativne evaluacije ($103,2 \pm 14,7$) više u odnosu na poslednju vrednost srednjeg arterijskog pritiska tokom operacije ($84,8 \pm 13,6$) i ove razlike su statistički značajne ($p < 0,001$). Grupa ispitanika koja je primila levobupivakain imala je više vrednosti medijalnog srednjeg arterijskog pritiska 73,99 od grupe ispitanika koja je primila bupivakain (70, 76). **Zaključak.** Prediktori nastanka hipotenzije tokom operativnog zbrinjavanja preloma butne kosti u spinalnoj anesteziji su starost bolesnika i preoperativna upotreba beta blokatora.

Ključne reči: hipotenzija; spinalna anestezija; frakture butne kosti; ortopedski procedure; faktori starosti; beta blokatori; faktori rizika

cations and potential hemodynamic and respiratory problems. In regard to the accompanying comorbidities, spinal anesthesia may have advantages over general anesthesia. The advantages include lower incidence of respiratory and myocardial depression, better peripheral tissue perfusion due to the sympathetic blockade, decreased intra-operative bleeding and minimal coagulation disorders [4].

Abbreviations

| | |
|-----|---|
| ASA | – American Society of Anesthesiologists |
| SAP | – systolic arterial pressure |
| DAP | – diastolic arterial pressure |
| MAP | – mean arterial pressure |
| SP | – surgical procedure |
| MV | – mean value |

Hypotension is one of the most frequent adverse effects of spinal anesthesia and it may appear in up to one-third of patients undergoing surgery in spinal anesthesia [5]. Sympathetic blockade affects the cardiovascular system by decreasing the vein inflow and systemic vascular resistance [6]. When the level of analgesia overlaps the level of the fourth thoracic vertebra, it blocks cardioaccelerator fibers, causing pulse decrease and cardiac output reduction. Hypotension during spinal anesthesia represents a risk for brain and cardiac ischemia [7]. The elderly patients are more inclined to get hypotension due to difficult adaptation of the cardiovascular system to the changes in circulatory system [8].

Patients who consume alcohol are at higher risk for hypotension, due to neuropathy which is accompanying alcoholism and causes orthostatic hypotension. Patients undergoing urgent surgery present with higher incidence of surgical hypotension than patients who undergo elective surgery [9].

Material and Methods

This retrospective study included 454 patients with femoral fractures who underwent surgery at the Department of Anesthesia and Reanimation of the Emergency Center of the Clinical Center of Vojvodina in the period from 2014 – 2016.

The research was conducted with the approval of the Ethics Committee of the Clinical Center of Vojvodina.

There is little research on predictive factors of hypotension in elderly patients with femoral fractures during surgery in spinal anesthesia.

Medical history data as well as anesthesia cards were analyzed including patient age, sex, diagnosis, type of surgical procedure, preoperative status, American Society of Anesthesiologists (ASA) classification, accompanying comorbidity (ischemic heart disease, hypertension, diabetes, chronic obstructive lung disease), and chronic therapy. Arterial pressure was preoperatively examined in each patient by an internist.

The spinal anesthesia data included the type, dose of local anesthetic, duration of anesthesia and duration of surgery. Initially, noninvasive basal arterial pressure verified the systolic and diastolic pressure prior to spinal anesthesia and then every five minutes after spinal anesthesia. The anaes-

Table 1. Medical history data**Tabela 1.** Anamnestički podaci

| | | Incidence/Učestalost | Percentage/Procenat |
|--|--|----------------------|---------------------|
| Diagnosis <i>Dijagnoza</i> | Fractura colli femoris | 255 | 56.17 |
| | Fractura daipahyseos femoris | 25 | 5.51 |
| | Fractura capitis femoris | 37 | 8.15 |
| | Fractura subtrochanterica femoris | 137 | 30.18 |
| Surgery <i>Operacija</i> | Hemialoarthroplastica coxae sec Moore | 76 | 16.70 |
| | Aloarthroplastica coxae cum proth.totalis | 77 | 16.92 |
| | Osteosynthesis cum cunei Gamma short | 103 | 22.64 |
| | Osteosynthesis cum cunei Gamma long | 42 | 9.23 |
| | Aloarthroplastica coxae partialis | 37 | 8.13 |
| | Osteosynthesis femoris | 119 | 26.15 |
| Accompanying diseases <i>Prpratna oboljenja</i> | Hypertension arterialis/ <i>Arterijska hipertenzija</i> | 303 | 57.50 |
| | Ischemic cardiac diseases/ <i>Ishemijska bolest srca</i> | 45 | 8.54 |
| | Chronic obstructive lung diseases <i>Hronična opstruktivna bolest pluća</i> | 34 | 6.45 |
| | Diabetes mellitus type 2/ <i>Dijabetes melitus tip II</i> | 89 | 16.89 |
| | Without accompanying disease <i>Bez prpratnih oboljenja</i> | 56 | 10.63 |
| Chronic therapy <i>Hronična terapija</i> | Beta blocker/ <i>Beta blokatori</i> | 73 | 16.08 |
| | Angiotensin converting enzyme inhibitors <i>Inhibitori angiotenzin konvertujućeg enzima</i> | 34 | 7.49 |
| | Calcium channel blockers <i>Blokatori kalcijumskih kanala</i> | 13 | 2.86 |
| | Other medications/ <i>Druga terapija</i> | 69 | 15.20 |
| | No therapy/ <i>Bez terapije</i> | 265 | 58.37 |

Table 2. Association between medical history data and hypotension during surgery, multivariable logistic regression
Tabela 2. Povezanost anamnestičkih podataka i hipotenzije tokom operacije, multivarijatna logistička regresija

| | | OR/OV/ KŠ | 95% CI/IP LL/DG UL/GG | | p |
|---|---|--------------|--------------------------|------|-------|
| Age/Godine | | 1.02 | 1.00 | 1.04 | 0.037 |
| ASAC/KAUA | | 0.78 | 0.52 | 1.18 | 0.238 |
| Accompanying diseases Pratna oboljenja | Arterial hypertension/Arterijska hipertenzija | 1.04 | 0.64 | 1.70 | 0.881 |
| | Ischemic cardiac diseases/Ishemijska bolest srca | 1.53 | 0.69 | 3.40 | 0.293 |
| | Chronic obstructive lung disease Hronična opstruktivna bolest pluća | 1.07 | 0.47 | 2.46 | 0.865 |
| | Diabetes Mellitus type II/Dijabetes melitus tip II | 1.27 | 0.72 | 2.25 | 0.413 |
| Chronic therapy Hronična terapija | Beta blockers/Beta blokatori | 3.16 | 1.42 | 7.01 | 0.005 |
| | Angiotensin converting enzyme inhibitors Inhibitori angiotenzin konvertujućeg enzima | 1.23 | 0.49 | 3.14 | 0.659 |
| | Calcium channel blockers/Blokatori kalcijumskih kanala | 0.65 | 0.16 | 2.63 | 0.543 |
| Diagnosis Dijagnoze | Fractura colli femoris | 0.73 | 0.43 | 1.21 | 0.222 |
| | Fractura diaphyseos femoris | 1.22 | 0.38 | 3.93 | 0.735 |
| Surgery Operacija | Hemiarthroplastica coxae sec Moore | 1.05 | 0.52 | 2.09 | 0.899 |
| | Aloarthroplastica coxae cum proth.totalis | 1.14 | 0.58 | 2.24 | 0.709 |
| | Osteosynthesis cum cunei Gamma short | 0.59 | 0.34 | 1.05 | 0.074 |
| | Osteosynthesis cum cunei Gamma long | 0.91 | 0.40 | 2.05 | 0.818 |

Legend: OR – odds ratio. 95%; CI – confidence interval for OR; LL – lower level of confidence interval; UL – upper level of the confidence interval; ASAC – American Society of Anesthesiologists Classification; p - difference between measurements

Legenda: OV - odnos verovatnoće (KŠ – količnik šansi), IP – intervali poverenja za OV; DG – donja granica intervala poverenja. GG – gornja granica intervala poverenja; KAU - Klasifikacija Američkog udruženja anesteziologa, p – nivo razlika među merenjima

thetic card included the systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) in order to verify values of arterial pressure with a precision of up to 5 mmHg. Mean arterial pressure (MAP) was calculated based on the formula $DAP + (SAP - DAP)/3$. Hypotension was defined as the drop of the arterial pressure by 20% under basal conditions.

The integral part of the data analysis was the quantity of crystalloid and colloid solutions, and vasoactive medications that were used in patients with hypotension after spinal anesthesia. Data about blood loss during surgery and the quantity of blood products that were applied in the aim of compensation (resuspended erythrocytes and freshly frozen plasma) were also analyzed.

In order to examine the connection between hypotension during surgery and medical history data, binary logistic regression was applied. The criterion variable was the value of arterial blood pressure prior to surgery, whereas the predictor variables included age, ASA, accompanying diseases, chronic therapy, diagnosis, and type of surgery.

T-test for dependent variables was applied in order to compare the last MAP at the end of surgery with the initial, preoperative MAP. Three mean pressure values were compared in the group that received bupivacaine and the group that received levobupivacaine prior to surgery, at the end of surgery, and the lowest pressure during the procedure, as well as three T-tests for independent samples.

Results

The age of patients ranged from 20 to 93 years (mean age = 71.56; SD = 13.26; median = 74). There were more female than male patients (283; 62.3%). Detailed medical history data are presented in **Table 1**. The duration of surgical procedure (SP) was from 25 to 240 minutes, whereas the average duration was 67.9 minutes. During the SP, 62 patients (13.65%) received an erythrocyte transfusion, whereas the average amount of erythrocytes was 395.9 rml (SD = 56.8).

Transfusion of blood plasma was received by 4 patients (0.08%), and the average blood plasma volume was 217.5 ml (SD = 56.8).

Table 2 presents results of multivariable logistic regression analysis and the model was statistically significant ($\chi^2(15) = 26.45, p < 0.05$). The results suggested that the patients had higher values of MAP during the pre-operative evaluation (mean value (MV) = 103.2; SD = 14.7) in relation to the last value of MAP during surgery (MV = 84.8; SD = 13.6) and these differences were statistically significant ($p < 0.001$). Detailed medical history data are represented in **Table 3**.

The MAP measured upon surgery was by 10% (or more) lower than MAP in the pre-operative evaluation of 305 (66.4%) examined subjects, and by 20% (or more) lower in 204 (44.4%) of examined patients. The gathered results showed that the differences were present only in case of the lowest values of the mean pressure during the SP ($t(425) = 2.04, p < 0.05$). The group of patients who re-

Table 3. Descriptive statistics for mean arterial pressure (MAP)
Tabela 3. Deskriptivna statistika za srednji arterijski pritisak (SAP)

| | MAP – preoperatively (1) SAP – preoperativno (1) | MAP – at the end SP (2) SAP – na kraju OZ (2) | MAP – the lowest during SP (3) SAP – najniži tokom OZ |
|---------|---|--|--|
| Min/Min | 50.00 | 40.00 | 40.00 |
| Max/Max | 163.33 | 120.00 | 113.33 |
| MV/MV | 103.24 | 84.82 | 72.73 |
| SD/SD | 14.6 | 13.60 | 13.61 |
| Sk/Sk | 0.365 | 0.062 | 0.245 |
| Ku/Ku | 1.575 | -0.184 | -0.265 |
| p/p | 1 > 2 (p < 0.001), 1 > 3 (p < 0.001), 2 > 3 (p < 0.001) | | |

Legend: Min – minimum, Max – maximum, MV- mean value, SD – standard deviation, Sk – declivity, Ku – flattening, p - difference between measurements

Legenda: Min – minimum, Max – maksimum, MV – srednja vrednost, SD – standardna devijacija, Sk – zakošenost, Ku – spljoštenost, p – nivo razlika među merenjima, OZ – operativni zahvat

ceived levobupivacaine (MV= 73.99) presented with somewhat higher values of MAP in regard to the group who received bupivacaine (70.76). Detailed medical history data are represented in the **Table 4**.

Column N refers to the number of respondents per group. There were 337 patients in the Marcaine group, and 92 patients in the Chirocaine group.

The two last columns present Skjunis (symmetrical distribution measure) and Kurtosis (statistical measure that describes the tailedness of the probability distribution of the real valued random variable) are important characteristics for the implementation of certain statistical analyses and in all cases they were in the range of acceptable values of ± 2.00 .

Examined subjects who had hypotension during surgery received a greater quantity of solution (MV= 1631.2; SD = 637.9) from those without hypotension during surgery (MV= 1344.4; SD = 489.1) and these differences were statistically significant ($t(301.1) = -5.14$, $p < 0.001$). Of the overall number of 454 patients, 122 (26.6%) received neosynephrine during the SP. The average dosage of neosynephrine was 157.7 micrograms (SD = 130.7). On average, the group of examinees who received neosynephrine was older (MV= 73.53; SD = 11.92) from the group who did not receive neosynephrine (MV = 70.83; SD = 11.12) and these differences were statistically significant ($t(244.6) = -2.04$, $p < 0.005$).

Discussion

Femur fractures are most common in elderly women. The average age of the patients in this retrospective study was 71.5 years, and almost two-thirds were women. The average age of the patients with fractures of the upper femur in the European literature is a bit higher, over 80 years [10].

During spinal anesthesia, hypotension occurs due to the blockage of sympathetic fibers. Vasodilation of the post-arterioles decreases the circulatory volume and the venous inflow into the heart. Dagnino et al. established that due to the degenerative-dystrophic changes that influence the blood vessels, the older

patients are more likely to experience hemodynamic changes during spinal anesthesia. Elderly patients have less functional reserve to cope with hemodynamic changes during spinal anesthesia [11].

In our research, predictors of hypotension during spinal anesthesia for femoral fracture surgical treatment were the age and chronic therapy by beta blockers prior to the surgery. Similar results were reported by Oliveira et al. who pointed out the age over 45 years and female sex are predictors of hypotension during spinal anesthesia; however, these were not just patients with femoral fractures [9]. Beta blockers reduce the sympathetic system activity and decrease the myocardial oxygen consumption. These medications have an impact on the myocardium and decrease the intensity of myocardial activity, the arterial blood pressure and the heart rate. There is no data in the literature showing that chronic treatment with beta blockers may be a predictor of hypotension during spinal anesthesia. This can be interpreted as an indication that generally patients who take beta blockers have slower heart rate; drop of systemic vascular resistance occurs as an effect of blocking the sympathetic nervous system, so they cannot adequately react to increase the heart rate, but experience an intensive drop of the heart rate and arterial pressure.

Our research has established that the examined subjects who received levobupivacaine for spinal anesthesia intraoperatively presented with slightly higher average arterial pressure. Luck JF et al. suggested that levobupivacaine used for spinal anesthesia in the elderly caused lower decrease of arterial blood pressure than bupivacaine [12]. It was also established that the group of patients who received levobupivacaine showed higher average arterial pressure in comparison to those who received bupivacaine. Glaser et al. failed to prove that there was a difference in intraoperative values of arterial pressure between the patients in spinal anesthesia who received levobupivacaine versus those who received racemic bupivacaine. However, in this research, the group of patients was very heterogeneous regarding the age, from 18 to 85 years [13].

Table 4. Descriptive indicators for Medial pressure versus a group of drugs
Tabela 4. Deskriptivni pokazatelji za medijalni pritisak u odnosu na grupu lekova

| | Group/Grupa | N/Broj | MV/SV | SD/SD | Min/Min | Max/Maks | Sk/Sk | Ku/Ku |
|---|-------------|--------|--------|-------|---------|----------|-------|-------|
| MAP preoperatively <i>Medijalni pritisak preoperativno</i> | Marcaine | 333 | 103.01 | 15.31 | 70.0 | 163.33 | 0.45 | 1.12 |
| | Chirocaine | 92 | 104.60 | 12.38 | 80.0 | 146.67 | 0.89 | 1.57 |
| MAP - at the end of SP <i>MP na kraju OZ</i> | Marcaine | 337 | 84.46 | 12.92 | 40.0 | 120.0 | -0.01 | 0.00 |
| | Chirocaine | 92 | 87.27 | 15.52 | 50.0 | 120.0 | -0.61 | 0.50 |
| MAP - the lowest during SP <i>MP najniži tokom OZ</i> | Marcaine | 335 | 70.76 | 13.22 | 40.0 | 113.33 | -0.22 | 0.26 |
| | Chirocaine | 92 | 73.99 | 14.18 | 45.0 | 110.0 | 0.44 | 0.49 |

Legend: Min – minimum, Max – maximum, MV- mean value, SD – standard deviation, MAP – medial arterial pressure, SK – declivity, Ku – flattening, p - level of difference between measurements

Legenda: Min – minimum, Maks – maksimum, SV – srednja vrednost, SD – standardna devijacija, MP – medijalni pritisak, OZ – operativni zahvat, SK – zakošenost, Ku – spljoštenost, p - nivo razlika među merenjima

Gulek et al. established that there was no significant statistical difference between the type or dosage of the local anesthetic (bupivacaine and levopubivacaine) and arterial hypotension during spinal anesthesia in elderly patients [14]. By comparing the preoperative values of average arterial pressure and the values at the end of the SP, it was proved that the patients have higher preoperative MAP in relation to the last value of MAP during surgery. In our research, in more than 44% of examined patients MAP was lower by 20% or more in relation to the preoperative MAP.

Hartmann et al. found that patients who consumed alcohol were at three times higher risk for arterial hypotension. Due to alcoholic neuropathy, the sympathetic nervous system is being attacked, causing orthostatic dysregulation [15].

Patients prone to hypotension during spinal anesthesia received a higher initial and maintenance dose of neosynephrine during the surgical procedure. In our patients, almost one-third received 150 micrograms of phenylephrine for hypotension during the surgery.

Mitra et al. established that application of crystalloid solutions was efficient prior to the surgery in the aim of preventing hypotension. In their research they proved that it was more efficient to apply phenylephrine than ephedrine in the treatment of hypotension in spinal anesthesia [16].

Our research also recognized that it was efficient to use crystalloid and colloid solutions in the aim of filling intravascular volume in the treatment of hypotension in spinal anesthesia. If inadequate therapy response was obtained in regard to correction of volume, neosynephrine was used in the treatment of hypotension.

Our study has pointed out the predictors of hypotension in surgical management of femoral fractures in spinal anesthesia - the patient's age and taking beta blockers. It showed that levobupivacaine caused lower degree of hypotension than bupivacaine. Thus, we suggest special preparation before and during spinal anesthesia in elderly patients, and potential reduction of beta blockers immediately prior to surgery.

The main drawback of our study is its retrospective design. A prospective study should check whether levopubivacaine causes lower degree of hypotension than racemic bupivacaine in elderly patients with femoral fractures treated in spinal anesthesia, and it may represent a better choice in geriatric population.

Conclusion

Predictors of hypotension during surgery of patients with femoral fractures in spinal anesthesia are elderly age and preoperative use of beta blockers.

References

1. Grubor P, Asotić M, Grubor M. Method of choice in the treatment of femoral neck fractures in subjects aged over 65. *Acta Medica Medianae*. 2010;49(3):5-10.
2. Vidić G, Milenković S, Golubović Z, Stojanović S, Antić Z, Antić Z. Treatment of periprosthetic femoral fractures with self-dynamisable internal fixator. *Acta Medica Medianae*. 2017;56(3):31-7.
3. Mladenović M. The role of surgical procedures in prevention and therapy of hip osteoarthritis caused by morphological changes of the femoral neck [dissertation]. Niš: University of Niš, Faculty of Medicine; 2017.
4. Janković D. Spinal anesthesia. In: Janković D. Regional nerve blocks and infiltration therapy of pain. Oxford: Blackwell Publishing; 2004. p. 272-85.
5. Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology*. 1992;76(6):906-16.
6. Klasen J, Junger A, Hartmann B, Benson M, Jost A, Banzhaf A, et al. Differing incidences of relevant hypotension with combined spinal-epidural anesthesia and spinal anesthesia. *Anesth Analg*. 2003;96(5):1491-5.
7. Casati A, Fanelli G, Aldegheri G, Colnaghi E, Casaletti E, Cedrati V, et al. Frequency of hypotension during conventional or asymmetric hyperbaric spinal block. *Reg Anesth Pain Med*. 1999;24(3):214-9.
8. Tarkkila P, Isola J. A regression model for identifying patients at high risk of hypotension, bradycardia and nausea during spinal anesthesia. *Acta Anaesthesiol Scand*. 1992;36(6):554-8.

9. Oliveira Filho GR, Garcia JHS, Goldschmidt R, Dal Mago AJ, Cordeiro MA, Ceccato F. Predictors of early hypotension during spinal anesthesia. *Rev Bras Anesthesiol.* 2001;51(4):298-304.

10. Herrera R, De Andres J, Etan L, Olivas FJ, Martinez-Mir I, Steinfeldt T. Hemodynamic impact of isobaric levobupivacaine versus hyperbaric bupivacaine for subarachnoid anesthesia in patients aged 65 and older undergoing hip surgery. *BMC Anesthesiol.* 2014;14:97.

11. Dagnino J, Prys-Roberts C. Studies of anaesthesia in relation to hypertension. VI: cardiovascular responses to extradural blockade of treated and untreated hypertensive patients. *Br J Anaesth.* 1984;56(10):1065-73.

12. Luck JF, Fettes PD, Wildsmith JA. Spinal anaesthesia for elective surgery a comparison of hyperbaric solution of racemic bupivacaine, levobupivacaine. *Br J Anesth.* 2008;101(5):705-10.

Rad je primljen 9. V 2018.

Recenziran 21. VI 2018.

Prihvaćen za štampu 22. VI 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:235-240.

13. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S, et al. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. *Anesth Analg.* 2002;94(1):194-8.

14. Gulec D, Karsli B, Ertugrul F, Bigat Z, Kayacan N. Intrathecal bupivacaine or levobupivacaine: which should be used for elderly patients? *J Int Med Res.* 2014;42(2):376-85.

15. Hartmann B, Junger A, Klasen J, Benson M, Jost A, Banzhaf A, et al. The incidence and risk factors for hypotension after spinal anesthesia induction: an analysis with automated data collection. *Anesth Analg.* 2002;94(6):1521-9.

16. Mitra JK, Roy J, Bhattacharyya P, Yunus M, Lyngdoh NM. Changing trends in the management of hypotension following spinal anesthesia in cesarean section. *J Postgrad Med.* 2013; 59(2):121-6.

REVIEW ARTICLES

PREGLEDNI ČLANCI

Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica¹
University of Novi Sad, Faculty of Medicine Novi Sad²

Review article
Pregledni članci
UDK 616.127-005.8-073.97
<https://doi.org/10.2298/MPNS1808241D>

ATYPICAL ELECTROCARDIOGRAPHIC PRESENTATIONS OF MYOCARDIAL INFARCTION WITH ST ELEVATION – ST ELEVATION MYOCARDIAL INFARCTION EQUIVALENTS

ATIPIČNI ELEKTROKARDIOGRAFSKI PRIKAZI INFARKTA MIOKARDA SA ST ELEVACIJOM – EKIVALENTI INFARKTA MIOKARDA SA ELEVACIJOM ST SEGMENTA

Jadranka DEJANOVIĆ^{1,2}, Anastazija STOJŠIĆ MILOSAVLJEVIĆ^{1,2},
Miloš TRAJKOVIĆ¹, Tanja POPOV^{1,2} and Aleksandra ILIĆ^{1,2}

Summary

Introduction. Some patients with clinical symptoms and signs of acute myocardial and coronary artery occlusion have atypical electrocardiographic presentations – ST elevation myocardial infarction equivalents. Rapid recognition of these patterns is imperative, because the condition requires prompt reperfusion therapy following actual guidelines. **De Winter pattern.** Diagnostic criteria are: tall, prominent, symmetrical T-waves in the precordial leads, upsloping ST segment depression > 1 mm at the J-point in the precordial leads, absence of ST elevation in the precordial leads, ST segment elevation (0.5 mm – 1 mm) in aVR. **ST Elevation in aVR.** Electrocardiographic criteria include ST segment elevation in aVR ≥ 1 mm, ST segment elevation in aVR ≥ V1, and diffuse ST segment depression in lateral leads. **Wellens syndrome.** Wellens syndrome describes deeply inverted or biphasic T-waves in leads V2 – V3, highly specific for significant stenosis of the left anterior descending artery. **Posterior infarction.** Posterior infarction is confirmed with ST segment depression ≥ 0,5 mm in leads V1 – 3 and ST segment elevation ≥ 0,5 mm in posterior leads (V7 – V9). **Conclusion.** There are many electrocardiographic patterns that physicians should promptly recognize as clinical myocardial infarction with ST segment elevation equivalents in order to perform urgent reperfusion therapy for better prognosis and survival in these patients.

Key words: Electrocardiography; ST Elevation Myocardial Infarction; Early Diagnosis; Signs and Symptoms; Reperfusion; Coronary Occlusion; Acute Coronary Syndrome; Bundle-Branch Block; Coronary Stenosis

Introduction

Acute myocardial infarction (MI) is a clinical manifestation of coronary artery disease which de-

Sažetak

Uvod. Postoji grupa bolesnika koja ima kliničke simptome i znake akutnog infarkta uz prisutnu okluziju koronarne arterije, ali uz nespecifične elektrokardiografske promene – tzv. STEMI ekvivalenti. Imperativ je brzo ih prepoznati i uraditi reperfuzionu terapiju prateći preporuke važećih vodiča. **De Winterov sindrom.** Dijagnostički kriterijumi su: visoki, simetrični T-talasi u prekorodijalnim odvodima, ushodna ST depresija > 1 mm u J-tački u prekorodijalnim odvodima, odsustvo ST elevacije u prekorodijalnim odvodima, ST elevacija (0,5 mm – 1 mm) u aVR odvodu. **Sindrom ST elevacije u aVR odvodu.** Elektrokardiografski kriterijumi su: ST elevacija u aVR ≥ 1 mm, ST elevacija aVR ≥ V1, difuzna ST depresija u lateralnim odvodima. **Velensov sindrom.** Velensov sindrom opisuje duboke negativne ili bifazne T-talase u odvodima V2–V3, a može biti visokospecifičan za kritičnu stenozu prednje nishodne koronarne arterije. **Infarkt miokarda zadnjeg zida.** Infarkt miokarda zadnjeg zida je potvrđen u prisustvu ST depresije ≥ 0,5 mm u odvodima V1–3 i elevacijom ST segmenta ≥ 0,5 mm u zadnjim odvodima (V7–V9). **Zaključak.** Postoji veliki broj nespecifičnih elektrokardiograma koje bi lekari trebalo brzo da prepoznaju kao kliničke ekvivalente akutnog infarkta miokarda sa elevacijom ST segmenta kako bi se dala urgentna reperfuziona terapija i poboljšala prognoza i preživljenje bolesnika.

Ključne reči: elektrokardiografija; STEMI; rana dijagnoza; znaci i simptomi; reperfuzija; koronarna okluzija; akutni koronarni sindrom; blok leve grane Hisovog snopa; koronarna stenozna

velops when a blood vessel is narrowed or occluded leading to irreversible myocardial ischemia [1]. The leading symptom that initiates the diagnostic and treatment cascade in patients with acute coronary

Abbreviations

| | |
|--------|---|
| ECG | – electrocardiogram |
| MI | – myocardial infarction |
| STEMI | – myocardial infarction with ST segment elevation |
| NSTEMI | – non ST elevation myocardial infarction |
| pPCI | – primary percutaneous coronary intervention |
| ESC | – European Society of Cardiology |

syndrome is chest pain. In the United States, 50% of acute coronary syndromes have clinically atypical presentations (e.g. dyspnea, nausea, syncope or pain in the arm, neck or the abdomen) and the 12-lead electrocardiogram (ECG) maintains the gold standard as the first line test [2]. This is the single most important initial clinical test for diagnosing MI and its correct interpretation can be the basis for immediate therapeutic interventions. Based on ECG changes with persistent elevation of ST segment we can distinguish acute MI with ST elevation (STEMI) and non ST elevation MI (NSTEMI). In NSTEMI, the ECG abnormalities may include transient ST segment elevation, persistent or transient ST segment depression, inversion of the T-wave, flat T-waves, pseudo-normalization of the T-wave or it may be completely normal [3]. Sometimes, chest pain with the ECG signs of ischemia and high cardiac-specific enzymes can have origins other than coronary, like in myopericarditis [4].

Current guidelines [3, 5] do not recommend urgent reperfusion therapy in patients with acute MI with ST depression, except in case of suspected isolated posterior MI. Standard STEMI criteria may overlook patients with atypical and recently described ECG patterns that may indicate risk of transmural MI (STEMI-equivalents) with obstructive coronary disease, who would benefit from primary percutaneous intervention (PCI). The European Society of Cardiology (ESC) Guidelines for the management of acute MI in patients with ST segment elevation [6] recognized atypical ECG presentations in patients with ongoing symptoms consistent with myocardial ischemia that should be performed in pPCI: bundle branch block, ventricular paced rhythm, isolated posterior infarction, and ischemia due to left main coronary artery occlusion in the presence of ST depression ≥ 1 mm in eight or more surface leads (inferolateral ST depression), coupled with ST segment elevation in augmented vector right (aVR) and/or V1. These patients have high-risk STEMI equivalent patterns that should be recognized in the emergency department because they have a higher mortality rate compared to other patients with acute MI without ST elevation [7].

Clinical entities that represent the equivalent of acute MI with ST segment elevation described below are:

1. De Winter pattern
2. ST Elevation in aVR
3. Wellens syndrome
4. Isolated posterior MI
5. Presumed new left bundle branch block.

De Winter pattern

In 2008, in their study, Robert J. de Winter and Wellens pointed out the importance of recognizing the equivalents of acute MI with ST elevation and need for emergency reperfusion therapy. After analyzing data obtained from the database of PCIs, ECG on the first contact with the patient, ECG before treatment, findings of coronary angiography, they described ECG pattern found in approximately 2% of patients with angiography proven anterior MI with occlusion of the anterior descending coronary artery [8]. Diagnostic criteria for de Winter pattern are: tall, prominent, symmetrically peaked T-waves in the precordial leads, upsloping ST segment depression > 1 mm at the J-point in the precordial leads, absence of ST elevation in the precordial leads, ST segment elevation (0.5 mm – 1 mm) in aVR. Normal STEMI morphology may precede or follow the de Winter pattern. Unlike the hyper-acute T-waves which occur within minutes of coronary artery occlusion and progress rapidly to classical ST elevation MI, STEMI pattern, de Winter T-waves are not transient findings and remain present in subsequent ECGs (**Figure 1**).

Verounden et al. found de Winter pattern in 35 out of 1890 patients who needed PCI on the proximal left descending artery (in about 2% of patients). Patients with de Winter pattern were younger, more often male and with a higher incidence of hypercholesterolemia compared to classic MI with ST elevation [9]. The

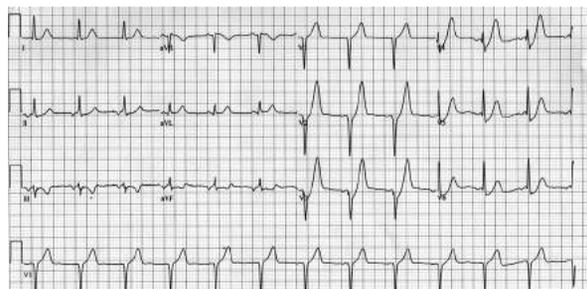


Figure 1. ECG de Winter pattern
Slika 1. Elektrokardiogram De Winterov T-talas

available data suggest that this pattern has a high positive predictive value for acute coronary occlusion [10].

Many case reports confirmed the importance of early recognition of this STEMI equivalent and early reperfusion therapy [11–13].

ST elevation in aVR

Occlusion of the left main coronary artery is a clinical entity that results in the development of acute MI in the anterior or anterolateral region with cardiogenic shock and high mortality rate. Because of the high risk of potential complications and high mortality, early detection of this type of STEMI equivalent and urgent reperfusion is imperative and provides better outcomes [14, 15].

ECG criteria are: ST segment elevation in aVR ≥ 1 mm, ST segment elevation in aVR \geq V1, and diffuse ST segment depression in lateral leads (subendocardial ischemia) [16] (**Figure 2**).

ST segment elevation in aVR is not always specific for the occlusion of the left main coronary artery. It can be indicative for: left main equivalent disease (significant disease of the left anterior descending and left circumflex artery), occlusion of the anterior descending artery, severe three vessel

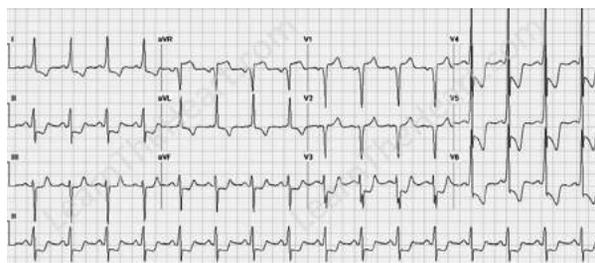


Figure 2. ECG presentation of left main coronary artery stenosis

Slika 2. Elektrokardiogram stenoze glavnog stabla leve koronarne arterije

disease and diffuse transmural ischemia [17, 18]. The absence of ST segment elevation in aVR excludes a significant lesion in the left main coronary artery. American Heart Association/American College of Cardiology recommended this pattern to be read as “ischemia due to multivessel or left main coronary artery obstruction”. When the resting ECG reveals ST segment depression greater than 0.1 mV (1 mm) in 8 or more body surface leads coupled with ST segment elevation in aVR and/or V1, but is otherwise unremarkable, the automated interpretation should suggest ischemia due to multivessel or left main coronary artery obstruction [3].

Some authors argue that the term “occlusion of the left main coronary artery” is incorrect, firstly because most patients with criteria for this clinical entity have at least slight flow through the main trunk of the left coronary artery, and secondly, occlusion quickly leads to acute MI with ST segment elevation, cardiogenic shock and death [19]. The lack of specificity of this pattern is documented by Knotts et al. because only 43% patients with subendocardial ischemia (ST elevation in aVR and diffuse ST depression) who underwent angiography had significant left main stenosis or a triple vessel disease [20]. Nevertheless, current guidelines recommend early reperfusion strategy for patients presenting with this pattern [3, 6].

Wellens syndrome

Wellens syndrome was first described in the 1980s by de Zwaan, Wellens, et al, who identified specific T-wave changes in precordial leads in 14% to 18% of patients with unstable angina who, subsequently, de-

veloped a large anterior wall MI [21]. Some of risk factors for this syndrome are diabetes mellitus, family history of premature heart disease, hypertension, hypercholesterolemia and metabolic syndrome. Wellens syndrome describes ECG changes in T-wave, particularly deeply inverted or biphasic T-waves in leads V2 – V3 that is highly specific for significant proximal stenosis of the left anterior descending artery. Patients with these ECG patterns can be without subjective symptoms at the time of recording ECG and have normal or slightly elevated cardiac enzymes. They are at high risk for developing acute large anterior MI in the next few days or weeks if they are on medical treatment only. As soon as the diagnosis is made or suspected, due to possible critical stenosis of the anterior descending artery, definitive treatment is cardiac catheterization with PCI [22].

Reinhardt et al. [23] described the following diagnostic criteria for Wellens syndrome:

1. ECG: deeply inverted T-waves in leads V2 – V3 (may also be seen in leads V1, V4 – V6) or biphasic T-waves (with initial positivity and terminal negativity) in V2 and V3; isoelectric or minimally elevated ST segment < 1 mm; preservation of precordial R wave progression and no precordial Q waves;

2. Clinical: recent history of angina, ECG pattern present in a pain-free state, normal or slightly elevated cardiac markers.

Wellens syndrome has two patterns of T-waves. In type A, T-waves are biphasic, with initial positivity and terminal negativity, present in approximately 25% of cases. Type B T-waves are deeply and symmetrically negative and are present in approximately 75% of cases. The T-wave abnormalities may be persistent for hours to weeks, even when the patient is pain-free [24] (**Figures 3 and 4**).

The mechanism of Wellens syndrome remains unclear. It is believed that the changes in T-wave are caused by ischemic changes of anterior myocardial wall after sudden occlusion or subocclusion of the anterior descending artery. Reperfusion of the anterior descending artery relieves the pain and iden-

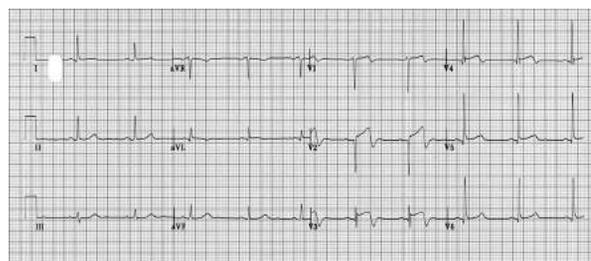


Figure 3. ECG pattern of Wellens syndrome - type A
Slika 3. Elektrokardiogram Velensovog sindroma - Tip A

tified T-wave changes as a reflection of reperfusion, form biphasic or negative T-waves. If the coronary artery remains occluded, acute anterior wall with ST elevation develops [25]. These ECG changes are not characteristic and limited to anterior MI, but

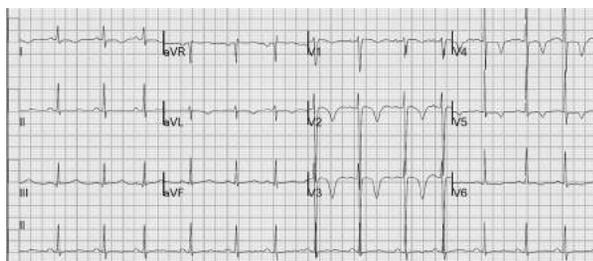


Figure 4. ECG pattern of Wellens syndrome - type B
Slika 4. Elektrokardiogram Velensovog sindroma - Tip B

can be seen in MI of the inferior or lateral wall, with occlusion of the right or circumflex coronary artery or in the vasospasm, and it is described as cocaine-induced vasospasm coronary artery [26].

Differential diagnosis of Wellens syndrome includes: pulmonary thromboembolism, right bundle branch block, left ventricular hypertrophy, right ventricular hypertrophy, hypertrophic cardiomyopathy, Brugada syndrome and hypokalemia [27].

Isolated posterior MI

Posterior MI is a clinical entity that occurs in 15 – 20% of cases of acute MI with ST segment elevation, usually in combination with inferior or lateral MI, while isolated posterior infarction is only found in about 5% of all ST elevation MIs [28], and it is an indication for urgent coronary reperfusion. The ECG findings of a posterior wall MI are different than the typical ST segment elevation seen in other MIs [29]. However, the absence of ST elevation in the standard ECG can lead to missed diagnosis and these patients do not receive reperfusion therapy, the only proper treatment in the acute phase of infarction. About 90% of these patients have critical stenosis or occlusion of the right coronary artery, and 10% of the left coronary artery [30].

There is a high degree of suspicion for posterior MI when the following findings are persisting in the standard ECG: ST segment depression (horizontal, upsloping, downsloping) and prominent upright R wave (> 30 ms) in V1 – V3 leads (can be equal voltage of R and S wave in V1), the R/S ratio > 1.0 in V2 lead, combination of horizontal ST segment depression with a prominent R-waves in leads V1 – V3. Usually, co-existence of acute inferior and/or lateral MI can be seen [31]. To confirm the diagnosis, extra posterior leads can be used (V7 – V9) [32]. Lead V7 is on the left posterior axillary line in the fifth intercostal space, lead V8 on the left side of the back at the tip of the scapula and V9 on the left paraspinal line in the fifth intercostal space) [33]. The use of additional posterior chest wall leads (V7 – V9) in patients with high suspicion of posterior MI (with circumflex occlusion) should be considered, in order to increase the number of diagnosed MIs, leading to better risk assessment, prognosis and survival, due to reperfusion therapy.

From the last ESC guide for acute MI with ST elevation, posterior infarction is confirmed with the

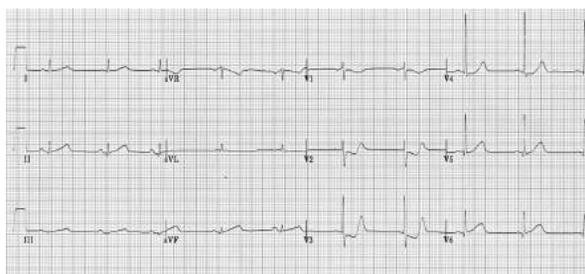


Figure 5. ECG of acute posterior myocardial infarction
Slika 5. Elektrokardiogram akutnog infarkta miokarda zadnjeg zida

presence of ST segment depression ≥ 0.5 mm in leads V1 – V3 and ST segment elevation ≥ 0.5 mm in posterior leads (V7 – V9), and prompt primary percutaneous coronary intervention strategy is recommended in patients with ongoing symptoms consistent with myocardial ischemia [6] (**Figure 5**).

New or presumed new left bundle branch block

ST segment criteria for the diagnosis of acute ischemia are affected by the presence of the left bundle branch block, because of the presented secondary ST changes that occur in this pattern. Left bundle branch block presents a dilemma in the evaluation of chest pain [34]. ECG diagnosis of MI in this pattern is difficult, but possible. The third universal definition of MI [35] gives diagnostic criteria for MI: rise and/or fall of cardiac biomarker values plus symptoms of ischemia, or new or presumed new significant ST segment T-wave changes, or new left bundle branch block. So, new or presumed new left bundle branch block in symptomatic patients is recognized as a STEMI equivalent. Neeland et al. [36] found that only about 40% of patients with presumed new left bundle branch block had a culprit lesion on angiography, and new or presumed new left bundle branch block cannot be a diagnostic criteria “per se”, especially not for prompt percutaneous coronary intervention strategy. The American Heart Association/American College of Cardiology/Heart Rhythm Society Guide [3] recommends to think about the possibility of acute infarction in patients with left bundle branch block who have some of ST segment changes: ST segment elevation ≥ 0.1 mV (1 mm) in leads with a positive ventricular depolarization (QRS), or ST depression ≥ 0.1 mV (1 mm) in leads V1 – V3 (concordant ST segment changes), ST segment elevation ≥ 0.5 mV (5 mm) in leads with negative QRS complex (discordant ST segment changes). The same criteria are used in ESC guidelines for the management of acute MI in patients presenting with ST segment elevation, with a suggestion for patients with a clinical suspicion of ongoing myocardial ischemia and left bundle branch block to be managed in a way similar to STEMI patients [6] (**Figure 6**).

Sgarbossa criteria [37] are a set of ECG findings generally used to identify MI in the presence of a left bundle branch block or a ventricular paced



Figure 6. ECG of acute myocardial infarction in a left bundle branch block

Slika 6. Elektrokardiogram akutnog infarkta miokarda u bloku leve grane Hisovog snopa

rhythm, in order to increase the number of early diagnosed MIs and perform prompt reperfusion. Three included criteria are: ST elevation ≥ 1 mm in a lead with positive QRS complex (concordance) – 5 points, concordant ST depression ≥ 1 mm in leads V1, V2, or V3 – 3 points, and ST elevation ≥ 5 mm in a lead with negative (discordant) QRS complex – 2 points: ≥ 3 points = 90% specificity of STEMI. In the original Sgarbossa criteria, a score < 3 is typically not considered diagnostic of acute MI, but it also does not rule it out. In a review of ventricular-paced ECGs, the most clinically useful Sgarbossa criterion in identifying acute MI was ST segment elevation > 5 mm discordant with the QRS

complex and it is helpful in identifying patients who may ultimately benefit from early aggressive treatment strategies [38].

Smith et al. modified Sgarbossa original criteria replacing the ST elevation measurement ≥ 5 mm in the third component with a ST/S ratio less than -0.25 , greatly improving the diagnostic utility of the rule. Using these criteria resulted in good prediction for acute coronary occlusion: at least one lead with concordant ST elevation ≥ 1 (Sgarbossa criterion 1) or at least one lead of V1 – V3 with concordant ST depression ≥ 1 (Sgarbossa criterion 2) or ST/S ratio ≤ -0.25 and at least 2 mm of ST elevation (replaces Sgarbossa criterion 3) [39].

Conclusion

In everyday clinical practice, especially in emergency room settings, it is very important to think about the possibility of having patients with chest pain and atypical electrocardiographic presentations of myocardial infarction with ST elevation and with coronary artery occlusion. In these patients, with clinical presentation of ongoing myocardial ischemia, a primary percutaneous coronary intervention strategy should be indicated to prevent complications and mortality, because these patients are at higher risk than others with uncomplicated myocardial infarction with ST elevation.

References

- Ostojić M, Beleslin B, Kanjuh V. Kardilogija. Beograd: Zavod za udžbenike i nastavna sredstva; 2012.
- Cervellin G, Rastelli G. The clinics of acute coronary syndrome. *Ann Transl Med.* 2016;4(10):191.
- Wagner GS, Macfarlane P, Wellens H, Josephson M, Gorgels A, Mirvis DM, et al. AHA/ACCF/HRS Recommendations for the standardization and interpretation of the electrocardiogram part VI: acute ischemia/infarction a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol.* 2009;53(11):1003–11.
- Ivanov I, Dejanović J, Ivanov O, Petrović M, Jung R, Panić G. Miopericarditis - diagnostic dilemmas in relation to acute myocardial infarction. *Med Pregl.* 2013;66(9-10):396-400.
- Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2016;37(3):267–315.
- Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39(2):119–77.
- Chung SL, Lei MH, Chen CC, Hsu YC, Yang CC. Characteristics and prognosis in patients with false-positive ST-elevation myocardial infarction in the ED. *Am J Emerg Med.* 2013;31(5):825–9.
- de Winter RJ, Verouden NJ, Wellens HJ, Wilde AA; Interventional Cardiology Group of the Academic Medical Center. A new ECG sign of proximal LAD occlusion. *N Engl J Med.* 2008;359(19):2071–3.
- Verouden NJ, Koch KT, Peters RJ, Henriques JP, Baan J, van der Schaaf RJ, et al. Persistent precordial “hyperacute” T-waves signify proximal left anterior descending artery occlusion. *Heart.* 2009;95(20):1701–6.
- Morris NP, Body R. The De Winter ECG pattern: morphology and accuracy for diagnosing acute coronary occlusion systematic review. *Eur J Emerg Med.* 2017;24(4):236–42.
- Goktas MU, Sogut O, Yigit M, Kaplan O. A novel electrocardiographic sign of an ST-segment elevation myocardial infarction-equivalent: De Winter. *Cardiol Res.* 2017;8(4):165-8.
- Pranata R, Huang I, Damay V. Should de Winter T-wave electrocardiography pattern be treated as ST-segment elevation myocardial infarction equivalent with consequent reperfusion? A dilemmatic experience in rural area of Indonesia. *Case Rep Cardiol.* 2018;2018:6868204.
- Ivanov I, Lovrenski A, Dejanović J, Petrović M, Jung R, Raffay V. Double heart rupture after acute myocardial infarction: a case report. *Vojnosanit Pregl.* 2014;71(12):1151-4.
- Ivanov I, Jaraković M, Dejanović J, Petrović M, Srdanović I, Obradović D. Diagnostic and prognostic utility of aVR lead in electrocardiogram. *Medicinski časopis.* 2014;48(2):104-7.
- Saeed G. Survival after acute and total occlusion of the left main coronary artery. *Asian Cardiovasc Thorac Ann.* 2010;18(6):599.

16. Hennings JR, Fesmire FM. A new electrocardiographic criteria for emergent reperfusion therapy. *Am J Emerg Med.* 2012;30(6):994–1000.

17. Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Nakamura S, et al. Electrocardiographic features in patients with acute myocardial infarction associated with left main coronary artery occlusion. *Heart.* 2004;90(9):1059–60.

18. Hirano T, Tsuchiya K, Nishigaki K, Sou K, Kubota T, Ojio S, et al. Clinical features of emergency electrocardiography in patients with acute myocardial infarction caused by left main trunk obstruction. *Circ J.* 2006;70(5):525–9.

19. Kosuge M, Ebina T, Hibi K, Morita S, Endo M, Maejima N, et al. An early and simple predictor of severe left main and/or three-vessel disease in patients with non-ST-segment elevation acute coronary syndrome. *Am J Cardiol.* 2011;107(4):495–500.

20. Knotts RJ, Wilson JM, Kim E, Huang HD, Birnbaum Y. Diffuse ST depression with ST elevation in aVR: Is this pattern specific for global ischemia due to left main coronary artery disease? *J Electrocardiol.* 2013;46(3):240–8.

21. de Zwaan C, Bär FW, Wellens HJ. Characteristic electrocardiographic pattern indicating a critical stenosis high in left anterior descending coronary artery in patients admitted because of impending myocardial infarction. *Am Heart J.* 1982;103(4 Pt 2):730–6.

22. Rosales-Castillo A, Plaza-Carrera J. Wellens' syndrome. *Rev Clin Esp.* 2017;217(8):491.

23. Rhinehardt J, Brady WJ, Perron AD, Mattu A. Electrocardiographic manifestations of Wellens' syndrome. *Am J Emerg Med.* 2002;20(7):638–43.

24. Hsu YC, Hsu CW, Chen TC. Type B Wellens' syndrome: electrocardiogram patterns that clinicians should be aware of. *Ci Ji Yi Xue Za Zhi.* 2017;29(2):127–8.

25. Sheng FQ, He MR, Zhang ML, Shen GY. Wellens' syndrome caused by spasm of the proximal left anterior descending coronary artery. *J Electrocardiol.* 2015;48(3):423–5.

26. Lin AN, Lin S, Gokhroo R, Misra D. Cocaine-induced pseudo-Wellens' syndrome: a Wellens' phenocopy. *BMJ Case Rep.* 2017;2017.

27. Hayden GE, Brady WJ, Perron AD, Somers MP, Mattu A. Electrocardiographic T-wave inversion: differential diagnosis in the chest pain patient. *Am J Emerg Med.* 2002;20(3):252–62.

28. Oraili S, Maleki M, Tavakolian AA, Eftekharzadeh M, Kamangar F, Mirhaji P. Prevalence and outcome of ST-segment elevation in posterior electrocardiographic leads during acute myocardial infarction. *J Electrocardiol.* 1999;32(3):275–8.

Rad je primljen 3. VII 2018.

Recenziran 6. VII 2018.

Prihvaćen za štampu 9. VII 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:241-246.

29. Ivanov I, Dejanović J, Čurić I, Ivanov M, Čikoš J, Radišić B, et al. Right ventricular infarction. *Medicina danas.* 2003;2(3-4):239-49.

30. van Gorselen EO, Verheugt FW, Meursing BT, Oude Ophuis AJ. Posterior myocardial infarction: the dark side of the moon. *Neth Heart J.* 2007;15(1):16-21.

31. Wung SF, Drew BJ. New electrocardiographic criteria for posterior wall acute myocardial ischemia validated by a percutaneous transluminal coronary angioplasty model of acute myocardial infarction. *Am J Cardiol.* 2001;87(8):970-4.

32. Matetzky S, Freimark D, Chouraqui P, Rabinowitz B, Rath S, Kaplinsky E, et al. Significance of ST segment elevations in posterior chest leads (V7 to V9) in patients with acute inferior myocardial infarction: application for thrombolytic therapy. *J Am Coll Cardiol.* 1998;31(3):506-11.

33. Brady WJ. Acute posterior wall myocardial infarction: electrocardiographic manifestations. *Am J Emerg Med.* 1998;16(4):409-13.

34. Ivanov I, Bugarski S, Dejanović J, Stojšić-Milosavljević A, Radišić-Bosić J, Vujin B. Electrocardiographic signs of acute myocardial infarction in left bundle branch block. *Med Pregl.* 2013;66(11-12):503-6.

35. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. *Eur Heart J.* 2012;33:2551–67.

36. Neeland IJ, Kontos MC, de Lemos JA. Evolving considerations in the management of patients with left bundle branch block and suspected myocardial infarction. *J Am Coll Cardiol.* 2012;60(2):96–105.

37. Sgarbossa EB, Pinski SL, Barbagelata A, Underwood DA, Gates KB, Topol EJ, et al. Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. GUSTO-I (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) Investigators. *N Engl J Med.* 1996;334(8):481-7.

38. Maloy K, Bhat R, Davis J, Reed K, Morrissey M. Sgarbossa criteria are highly specific for acute myocardial infarction with pacemakers. *West J Emerg Med.* 2010;11(4):354-7.

39. Smith SW, Dodd KW, Henry TD, Dvorak DM, Pearce LA. Diagnosis of ST-elevation myocardial infarction in the presence of left bundle branch block with the ST-elevation to S-wave ratio in a modified Sgarbossa rule. *Ann Emerg Med.* 2012;60(6):766–76.

PROFESSIONAL ARTICLES

STRUČNI ČLANCI

”Ss. Cyril and Methodius University”, Faculty of Dentistry,
Skopje, Republic of Macedonia¹
University Dental Clinical Center “St. Pantelejmon”,
Skopje, Republic of Macedonia²

Professional article
Stručni članak
UDK 616.314-089.28-036.8:616-052
<https://doi.org/10.2298/MPNS1808247P>

SATISFACTION OF COMPLETE DENTURE WEARERS

ZADOVOLJSTVO PACIJENATA TOTALNOM ZUBNOM PROTEZOM

Sanja PANCHEVSKA^{1,2}, Sasho ELENČEVSKI^{1,2}, Nadica JANEVA^{1,2} and Aneta MIJOSKA^{1,2}

Summary

Introduction. Conventional complete dentures are still the first choice in the treatment of completely edentulous patients. Dissatisfaction among complete denture wearers is not uncommon. The goal of this study was to determine the causes of patients' dissatisfaction with complete dentures. **Material and Methods.** A total of sixty patients participated in this study, 36 females (60%) and 24 males (40%). Twenty-five patients received their first complete dentures, and fourteen of them had previously worn complete dentures. In patients receiving complete dentures, there are many factors contributing to their adaptation, acceptance and feeling discomfort while wearing them. **Conclusion.** Our study showed that patients' satisfaction was not directly related with the quality of complete dentures.

Key words: Denture, Complete; Patient Satisfaction; Jaw, Edentulous; Surveys and Questionnaires; Treatment Outcome; Mastication; Esthetics, Dental; Quality of Health Care

Introduction

Although dental implants have a lot of functional benefits in completely edentulous patients, conventional complete dentures are often the first choice in the treatment of edentulous patients. Due to inexpensiveness and simplicity, edentulous patients prefer complete dentures over dental implants [1]. It should be noted that complete dentures are preferred by the edentulous patients, as they provide a pleasing appearance (good esthetics) and maintain normal speech, as well as supply occlusal support and mastication of food [2]. Over the years, advancements have been made in complete denture fabrication, and adhesives have been improved for those with high expectations. Still, dissatisfaction among denture wearers is not uncommon.

Researches have pointed out that patient dissatisfaction with medical services exists, and dental treatment is not an exception. Sometimes, there is a discrepancy between the dentists' perceptions and patient expectations [3]. Additionally, a small

Sažetak

Uvod. Konvencionalne totalne proteze još uvek predstavljaju prvi izbor u tretmanu totalne bezubosti. Nezadovoljstvo kod pacijenata koji koriste totalne proteze nije neuobičajeno. Cilj ove studije je da se odrede uzroci nezadovoljstva pacijenata koji koriste totalne proteze. **Materijal i metode.** U ispitivanju je učestvovalo 60 pacijenata od kojih je 36 žena (60%) i 24 muškarca (40%). Kod 25 ispitanika prvi put su bile izrađene totalne proteze, pritom 14 od ovih ispitanika prethodno su koristili fiksne izrade. Kod pacijenata nosilaca totalnih proteza, veliki broj faktora može da utiče na njihovu adaptaciju, prihvatanje totalnih proteza kao i osećaj diskomfora. **Zaključak.** Naše ispitivanje je pokazalo da zadovoljstvo pacijenata nije direktno povezano sa kvalitetom proteze.

Glavne reči: totalna proteza; zadovoljstvo pacijenta; bezuba vilica; ankete i upitnici; ishod lečenja; žvakanje; dentalna estetika; kvalitet zdravstvene usluge

number of patients cannot adapt to the dentures and they are dissatisfied [4].

The goal of this study was to determinate the causes of patient dissatisfaction with their complete dentures.

Material and Methods

A total of sixty patients of both sexes with upper and lower complete dentures, selected on random basis, were included in this study. The complete dentures were made at the Department of Removable Dentures of the University Dental Clinical Center “St. Pantelejmon” in Skopje from September 1st to November 30th, 2017. The patients were scheduled for a check-up after a three month adaptation period. The check-ups were performed by a prosthodontist who was not their dentist. The patients were asked to fill out a questionnaire on their satisfaction with their dentures. Besides questions on their previous experiences with different kinds of den-

Abbreviations

CD – complete dentures
 RPD – removable partial dentures

tures (fixed or mobile) they also had to rate dentures as good, fair or poor, in five categories: 1. Retention; 2. Ability to chew; 3. Appearance; 4. Ability to speak; 5. Comfort.

In order to calculate the Patient Satisfaction Score, each item was scored as: Good = 3, Fair = 2, or Poor = 1. The highest score in all five categories was 15. At the end, all patients were asked to define their main reason for dissatisfaction with complete dentures (CD).

Another questionnaire was prepared for the prosthodontist. The questions about the quality of dentures were divided into 6 categories: 1. Retention and Stability; 2. Centric relation; 3. Vertical dimension; 4. Occlusion; 5. Position of teeth and esthetics, and 6. Mucosal alterations of the supporting tissue. The scoring for retention and stability and occlusion was: Good = 3; Fair = 2, Poor = 1. Both centric relation and vertical dimension were scored: Correct = 2, Incorrect = 1. Mucosal alterations of the supporting tissue were categorised as: without alterations = 3; mucosal hyperemia = 2, decubitus ulcer = 1.

Esthetics was determined by total facial harmony, color, shape and position of the teeth in relation to dental biometric guides:

- Good harmony, appropriate color and shape of the teeth and correct position = 3
- Fair harmony due to inappropriate color or shape of the teeth, correct position = 2
- Incorrect harmony = 1. The highest score was 13.

Results

Sixty patients were included in this study, 36 females (60%) and 24 males (40%), aged 42 - 87 years (average age 68 years). Twenty-five of the patients received their first CD and fourteen of had previously worn CDs. The other thirty-five patients were old denture wearers; 26 of them had CD and 9 removable partial dentures (RPD). Only 12 (34%) of them were dissatisfied with their old dentures. The results of Questionnaire 1 are presented in **Table 1**.

The overall patient satisfaction with CDs after a 3 month adaptation period was 76%: 73% in fe-

males, and 80% among males. Only thirty-seven (61%) patients answered the last question regarding the ability to chew. Twenty-seven (73%) of them answered that they could not chew as easily with the dentures as with natural teeth. The other ten (27%) patients complained about difficulties with speech and general discomfort and insecurity.

The overall quality of the dentures rated by an independent prosthodontist was 76.6%. In the rated categories, the quality of dentures was 72.2% among female and 75.5% among male denture wearers. Results of Questionnaire 2, evaluating the technical quality of dentures are presented in **Table 2**.

Discussion

The main goal of any prosthetic treatment is patient satisfaction. It plays a major role in determining the success of the treatment procedures [5]. There are many factors that pertain to the term "satisfaction". Apart from the therapist's skill and the quality of dentures, subjective factors are very important for the satisfaction [6]. Among these factors, general health, age, gender, personality traits, experiences with previous dentures and patient expectations were evaluated in previous studies [2]. Although some studies performed by Barakat LF et al. [7] found association between these factors and satisfaction of CD wearers, some did not (Maraslioglu CR) [8].

The results of the study show no differences between patient satisfaction with dentures and the specialists' opinion on the quality of dentures. Ellis JS, found that patient satisfaction was unrelated to the denture quality [9]. Studies performed by Jonkman RE and van Waas MA showed that previous experiences and expectations were associated with patient satisfaction [10, 11]. Marchini L, suggested that improving dentist-patient communication was the most useful strategy for improving patient satisfaction with their dentures [12].

Knezović Zlatarić D et al. found that attitude towards dentures was a factor with a great impact on the satisfaction among denture wearers. Patients with positive attitude before getting dentures, more often had positive response after receiving them [6].

In general, patient satisfaction with CD was 76%, which was similar to the opinion of the prosthodontist (76.5%). According to the results of the

Table 1. Patient satisfaction with complete dentures and sex distribution
Tabela 1. Zadovoljstvo pacijenata fiksnim protezama i polna distribucija

| | Male/Muškarci | | | | | | Female/Žene | | | | | |
|-------------------------------------|---------------|----|------------|----|-----------|----|-------------|----|------------|----|-----------|----|
| | Good/Dobra | | Fair/Slaba | | Poor/Loša | | Good/Dobra | | Fair/Slaba | | Poor/Loša | |
| | N° | % | N° | % | N° | % | N° | % | N° | % | N° | % |
| Retention/Retencija | 12 | 50 | 7 | 29 | 5 | 21 | 13 | 36 | 13 | 36 | 10 | 28 |
| Ability to chew/Sposobnost žvakanja | 7 | 29 | 7 | 29 | 10 | 42 | 11 | 31 | 17 | 47 | 8 | 22 |
| Appearance/Izgled | 18 | 75 | 6 | 25 | 0 | 0 | 16 | 44 | 12 | 34 | 8 | 22 |
| Speech/Govor | 18 | 75 | 4 | 17 | 2 | 8 | 20 | 56 | 13 | 36 | 3 | 8 |
| Comfort/Komfor | 12 | 50 | 10 | 42 | 2 | 8 | 12 | 34 | 17 | 47 | 7 | 19 |

Table 2. Evaluation of technical denture quality and sex distribution
Tabela 2. Evaluacija tehničkog kvaliteta proteze sa polnom distribucijom

| | Male/Muškarci | | | | | | Female/Žene | | | | | | |
|---|---------------|----------------------------|------------|--------------------------------|-----------|----------------------------|-------------|--------------------------------|------------|----------------------------|-----------|--------------------------------|---|
| | Good/Dobra | | Fair/Slaba | | Poor/Loša | | Good/Dobra | | Fair/Slaba | | Poor/Loša | | |
| | N° | % | N° | % | N° | % | N° | % | N° | % | N° | % | |
| Retention and stability <i>Retencija i stabilnost</i> | 13 | 54 | 7 | 29 | 4 | 17 | 17 | 47 | 10 | 28 | 9 | 25 | |
| Occlusion/ <i>Okluzija</i> | 13 | 54 | 10 | 43 | 3 | 13 | 12 | 34 | 16 | 44 | 8 | 22 | |
| Face harmony/teeth position <i>Harmonija lica i pozicija zuba</i> | 14 | 58 | 6 | 25 | 4 | 17 | 20 | 56 | 8 | 22 | 8 | 22 | |
| Ability of mastication <i>Sposobnost žvakanja</i> | 19 | 79 | 3 | 13 | 2 | 8 | 20 | 56 | 7 | 19 | 9 | 25 | |
| | | Correct <i>Korektna</i> | % | Incorrect <i>Nekorektna</i> | % | Correct <i>Korektna</i> | % | Incorrect <i>Nekorektna</i> | % | Correct <i>Korektna</i> | % | Incorrect <i>Nekorektna</i> | % |
| Vertical dimension of occlusion <i>Vertikalna dimenzija okluzija</i> | 15 | 63 | 9 | 37 | 22 | 61 | 14 | 39 | | | | | |
| Central relation/ <i>Centralna relacija</i> | 17 | 71 | 7 | 29 | 28 | 78 | 8 | 22 | | | | | |

questionnaire, it seems that female wearers were less satisfied than male wearers.

Male wearers complained about ability to chew (42% were dissatisfied), whereas female wearers had complaints in almost every category. Their biggest issue seemed to be the appearance. In his pilot study, Ellis J et al. reported that there was a higher satisfaction among patients with improved esthetics. Esthetics has a direct impact on patient satisfaction [9].

At the bottom of the questionnaire, the patients were asked to indicate their greatest complaint, and they wrote that chewing with CDs felt strange and a lot different compared to chewing with natural

teeth. This suggests that dissatisfaction among patients is mostly caused by unrealistic expectations.

Conclusion

Patients receiving complete dentures are faced with many factors essential for adaptation, acceptance and discomfort while wearing dentures. Our study revealed that patient satisfaction was unrelated to the quality of complete dentures. The results suggest that the patient greatest dissatisfaction was with the chewing ability, also confirmed in the additional comments given at the end of the survey.

References

1. Bilhan H, Geckili O, Ergin S, Erdogan O, Ates G. Evaluation of satisfaction and complications in patients with existing complete dentures. *J Oral Sci.* 2013;55(1):29-37.
2. Zou Y, Zhan D. Patients' expectation and satisfaction with complete denture before and after the therapy. *Vojnosanit Pregl.* 2015;72(6):495-8.
3. Weinstein M, Schuchman J, Lieberman J, Rosen P. Age and denture experience as determinants in patient denture satisfaction. *J Prosthet Dent.* 1988;59(3):327-9.
4. Carlsson GE, Omar R. The future of complete dentures in oral rehabilitation. A critical review. *J Oral Rehabil.* 2010;37(2):143-56.
5. Bhat VS, Prasad KD, Malli P. A survey to assess patient satisfaction after receiving complete denture prostheses in A. B. Shetty Memorial Institute of Dental Science. *Nitte University Journal of Health Science.* 2014;4(2):81-5.
6. Knezović-Zlatarić D, Čelebić A, Valentić-Peruzović M, Jerolimov V, Čelić R, Filipović-Zore I, et al. Patients' satisfaction with partial denture therapy. *Acta Stomatol Croat.* 2000;34(4):373-8.
7. Baracat LF, Teixeira AM, Dos Santos MB, da Cunha Vde P, Marchini L. Patients' expectations before and evaluation after dental implant therapy. *Clin Implant Dent Relat Res.* 2011;13(2):141-5.
8. Marachlioglou CR, Dos Santos JF, Cunha VP, Marchini L. Expectations and final evaluation of complete dentures by patients dentist and dental technician. *J Oral Rehabil.* 2010;37(7):518-24.
9. Ellis JS, Pelekis ND, Thomson JM. Conventional rehabilitation of edentulous patients: the impact on oral health-related quality of life and patient satisfaction. *J Prosthodont.* 2007;16(1):37-42.
10. Jonkman RE, van Waas MA, van 't Hof MA, Kalk W. An analysis of satisfaction with complete immediate (over)dentures. *J Dent.* 1997;25(2):107-11.
11. van Waas MA. The influence of clinical variables on patients' satisfaction with complete dentures. *J Prosthet Dent.* 1990;63(3):307-10.
12. Marchini L. Patients' satisfaction with complete dentures: an update. *Braz Dent Sci.* 2014;17(4):5-16.

Rad je primljen 14. VI 2018.

Recenziran 25. VI 2018.

Prihvaćen za štampu 28. VI 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:247-249.

University of Novi Sad, Faculty of Medicine Novi Sad
Department of Anatomy

Professional article
Stručni članak
UDK 611.711.061
<https://doi.org/10.2298/MPNS1808250P>

MORPHOMETRIC STUDY OF THE POSTERIOR ARCH OF ATLAS VERTEBRA IN THE SERBIAN POPULATION

MORFOMETRIJSKA STUDIJA ZADNJEG LUKA ATLASA U SRPSKOJ POPULACIJI

Radmila PERIĆ, Bojana KRSTONOŠIĆ and Ivana STARČEVIĆ

Summary

Introduction. Groove for the vertebral artery and the suboccipital nerve, is located on the superior surface of the posterior arch of the first cervical vertebra (the atlas). Presence of bony variations may transform the groove into incomplete/complete canal, causing compression of its structures and consequently symptoms of vertebro-basilar insufficiency. The aim of the present study was to determine the incidence and extent of morphological variations of the posterior arch of the atlas vertebra. **Material and Methods.** The investigation was conducted on 41 atlas vertebrae, part of the Osteological Collection of the Department of Anatomy of the Faculty of Medicine in Novi Sad and the Faculty of Medicine in Niš. According to the shape of the posterior arch, the atlas vertebrae were classified into three classes. The measurements of maximum width and height diameters of the incomplete/complete canal for the vertebral artery were performed. All the measurements were done using open source software for image analysis, Image J. **Results.** The results of the study showed that in our sample of atlases the most common class was class I (78.05%), and class III the least frequent (7.32%). There was no statistically significant difference in the observed measurements of the atlas anatomical variations between the right and left side. **Conclusion.** Morphometric analysis of the superior surface of the posterior arch of the atlas vertebra has shown the existence of variations and their importance has been discussed.

Key words: Cervical Atlas; Anatomic Variations; Vertebral Artery; Image Processing, Computer-Assisted; Morphological and Microscopic Findings; Serbia

Acknowledgement

The authors wish to express their gratitude to Asst. Prof. Milena Trandafilović, Department of Anatomy, Faculty of Medicine, Niš, Serbia, for her valuable assistance in collecting material for this research.

Introduction

Atlas is the first cervical vertebra that supports the head. Due to its morphology, frequent pathology and clinical importance associated with craniovertebral junction, the posterior arch of the atlas vertebra has been extensively studied [1–11]. Behind each superior articular process is a groove which transmits the vertebral

Sažetak

Uvod. Na gornjoj strani zadnjeg luka prvog vratnog pršljena (atlas) nalazi se žleb kojim prolazi kičmena arterija na svom putu ka lobanjskoj duplji, a praćena je potpotiljačnim živcem. Prisustvom koštane varijacije, žleb može biti pretvoren u nepotpuni/potpuni kanal, što može dovesti do kompresije struktura koje njime prolaze, a tako i pojave simptoma vertebrobazilarne insuficijencije. Cilj rada bio je da se odrede učestalost i dimenzije morfoloških varijacija na zadnjem luku atlasa. **Materijal i metode.** Istraživanje je sprovedeno na 41 atlasu koji pripadaju Osteološkoj zbirci Zavoda za anatomiju Medicinskog fakulteta Univerziteta u Novom Sadu i Medicinskog fakulteta Univerziteta u Nišu. Atlasi su prema izgledu gornje strane zadnjeg luka klasifikovani u tri klase, a potom su merene maksimalna širina i visina nepotpunog/potpunog kanala kojim prolazi kičmena arterija. Merenja su vršena u javno dostupnom programu za analizu i obradu slika *ImageJ*. **Rezultati.** Najzastupljeniji su atlasi klase I, na čijem je zadnjem luku prisutan žleb kičmene arterije (78,05%), dok su najmanje zastupljeni pršljenovi klase III, sa žlebom koji je pretvoren u potpuni koštani kanal (7,32%). Ne postoji statistički značajna razlika između merenih parametara sa desne i leve strane posmatranih atlasa. **Zaključak.** Morfometrijskom analizom gornje strane zadnjeg luka atlasa pokazano je da postoje varijacije izgleda žleba kičmene arterije čiji je značaj opisan u radu.

Gljučne reči: prvi vratni pršljen; anatomske varijacije; vertebralna arterija; kompjuterska obrada slike; morfološki i mikroskopski nalazi; Srbija

artery, as well as the suboccipital nerve. In the classical literature, described as an anatomical variation, groove for the vertebral artery may sometimes be converted into an incomplete/complete foramen or canal by an ossified bridge between the back of the superior articular facet and the superolateral part of the posterior arch [12].

The prevalence of this anatomical variation has been described differently in different populations (from 6.57% in Northern Indians to 52.94% in Kenyans), in cadaveric and radiographic studies [13].

Ponticulus posticus/posterior ponticulus (PP), pons posticus/arcuate foramen, Kimmerle anomaly/variety/deformity, retroarticular ring, posterior atlantoid fo-

Abbreviations

W – width
H – height

ramen are some of the synonyms which are used to describe morphological variations of the groove for the vertebral artery [14–18]. A clear mechanism of their formation is not well understood and is still a subject of debate [19]. Because of the close relationship between the groove and the atlanto-occipital membrane, age-related ligamentous ossification may be considered as a potential cause, but the predilection in older population has not been proved [20]. As PP has been found in children as well, Schilling et al. [21] claimed that this structure should not be considered as a process of calcification, but ossification formed to protect the vertebral artery passing the area susceptible to compression or damaged as a result of craniocervical dynamics, that was later supported by other authors [22].

The importance of such anatomical variation is still controversial, from incidental finding to its involvement in causes of the upper cervical syndrome. Compression of the vertebral artery (primarily during extensive rotation of the head and neck) and consequential vertebrobasilar ischemia with symptoms such as headache, vertigo, photophobia, dizziness, head and neck pain, gives significant clinical importance to morphometric analysis of the posterior arch of the atlas vertebra [23–28].

The aim of the present study was to determine the prevalence of the morphological variations of the posterior arch of the atlas vertebra in Serbian population and to discuss the gathered results.

Material and Methods

The study was conducted in a sample of 41 undamaged, thoroughly boiled, cleaned and macerated human atlas vertebrae, of unknown sex, age and race. The analyzed vertebrae are part of the Osteological Collection of the Department of Anatomy of the Faculty of Medicine in Novi Sad (Serbia) and the Department of Anatomy of the Faculty of Medicine in Niš (Serbia). This research was approved by members of the Ethics Committees of both Faculties of Medicine. This was a two-part research study.

Part I

The first, descriptive part of study included morphological analysis of the superior surface of the posterior arch of the atlas vertebra. In accordance with Mitchell's classification [29], atlas vertebrae were classified into three classes: class I – groove for the vertebral artery; class II – vertebrae with an incomplete bony ring with a missing middle part; class III – vertebrae with a complete bony ring which encloses the vertebral artery.

During further observation of the class I vertebrae, it seemed that the groove for the vertebral artery varies in depth, which explains why we used Hasan's [30] classification for the detailed analysis.

According to the depth, a groove for the vertebral artery was described as a small impression or as a specified sulcus that transmits the vertebral artery.

Part II

All the atlas vertebrae were numbered. They were photographed (Sony W830 Compact camera, 10x

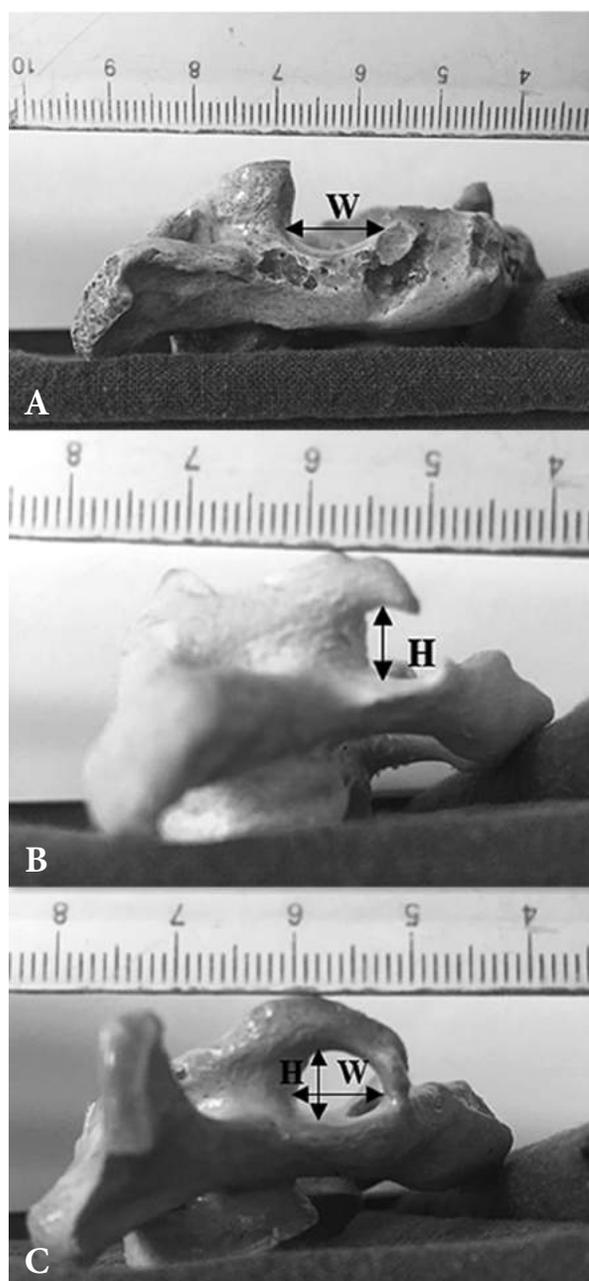


Figure 1. Morphometric analysis of the atlas vertebrae by measuring width and height of the anatomical variations of the groove for the vertebral artery: A - atlas class I; B - atlas class II; C- the atlas class III

Slika 1. Morfometrijska analiza atlasa merenjem širine (W) i visine (H) anatomske varijacije žleba kičmene arterije: A – atlas klase I; B – atlas klase II; C – atlas klase III

optical zoom) from the lateral view, placed in the same position on the osteometric table and at the same distance from the camera eyepiece. The digital images were loaded into open source software for image reconstruction and analysis – Image J (National Institute of Health, Bethesda, MD; <http://rsbweb.nih.gov/ij>). All the measurements were made using the ‘Ruler’ tool. Morphology of the groove for the vertebral artery was evaluated quantitatively using two parameters: width (W) and height (H) of the incomplete/complete anatomical variation of PP. Measurements were taken as maximum dimensions of the groove/foramen in both, antero-posterior (width) and superio-inferior (height) planes (**Figure 1**). The exception was made for the atlas vertebrae class I in which only W was measured.

The obtained results were evaluated by Student’s T-test and presented comparing the side of orientation.

Results

Part I - results

The results of the qualitative analysis of the examined vertebrae are shown in **Table 1**. Forty-one

human atlas vertebrae were examined. Out of these, in six cases (7.32%) complete bony bridge was found over the superior surface of the atlas vertebra posterior arch, bilaterally in one case. Class II atlas vertebrae with incomplete bony ring were found in 12 cases (14.63%), bilaterally in three vertebrae. The most common was the class I atlas vertebrae, found in 64 cases (78.05%), bilateral in 28 vertebrae. The latter one was an expected result, since the superior surface of the atlas posterior arch is most commonly converted into a groove for vertebral artery, as described in classic anatomical literature.

Descriptive analysis showed that class I vertebrae may be divided into two subclasses according to the depth of the groove for the vertebral artery (**Table 2**).

Part II - results

Table 3 shows statistical morphometric analysis of the atlas vertebral artery groove class I with minimum and maximum values of measured parameters, mean values and standard deviations. It can be seen that there is no statistically significant difference between the W of the groove for the ver-

Table 1. Prevalence of various classes of the atlas vertebrae in the examined sample ($n = 41$)

Tabela 1. Prevalencija različitih klasa atlasa u ispitivanom uzorku ($n = 41$)

| Atlas vertebrae/Atlas | Unilateral/Jednostrano | | Bilateral/Obostrano |
|-----------------------|-------------------------|-----------------------|---------------------|
| | Right side/Desna strana | Left side/Leva strana | |
| Class I/Klasa I | 35 (85.36%) | 29 (70.73%) | 28 (68.29%) |
| Class II/Klasa II | 4 (9.75%) | 8 (19.51%) | 3 (7.37%) |
| Class III/Klasa III | 2 (4.87%) | 4 (9.75) | 1 (2.43%) |

Table 2. Morphological analysis of the atlas vertebrae class I based on the description of the depth of the groove for the vertebral artery

Tabela 2. Morfološka analiza atlasa klase I zasnovana na opisu dubine žleba kičmene arterije

| Atlas vertebrae class I/Atlas klase I | Right side/Desna strana | Left side/Leva strana |
|---|-------------------------|-----------------------|
| Shallower groove for vertebral artery/Plići žleb kičmene arterije | 25 (60.97%) | 11 (26.39%) |
| Deeper groove for vertebral artery/Dublji žleb kičmene arterije | 10 (24.39%) | 18 (43.90%) |

Table 3. Morphometric analysis of the class I atlas vertebrae posterior arch (All the measures are given in cm)

Tabela 3. Morfometrijska analiza zadnjeg luka atlasa klase I. Sve mere su date u cm

| Parameter Parametar | Right side/Desna strana | | | Left side/Leva strana | | | p |
|------------------------|-------------------------|---------------------|------------|-----------------------|---------------------|-----------|------|
| | Minimum Minimum | Maximum Maksimum | X ± SD | Minimum Minimum | Maximum Maksimum | X ± SD | |
| Width (W)/Širina | 0.46 | 0.867 | 0.634±0.11 | 0.446 | 0.932 | 0.63±0.06 | 0.43 |

Table 4. Morphometric analysis of the class II atlas vertebrae posterior arch (All the measures are given in cm)

Tabela 4. Morfometrijska analiza zadnjeg luka atlasa klase II. Sve mere su date u cm

| Parameters Parametri | Right side/Desna strana | | | Left side/Leva strana | | | p |
|-------------------------|-------------------------|---------------------|-----------|-----------------------|---------------------|-----------|------|
| | Minimum Minimum | Maximum Maksimum | X ± SD | Minimum Minimum | Maximum Maksimum | X ± SD | |
| Width (W)/Širina | 0.41 | 0.72 | 0.57±0.12 | 0.43 | 0.69 | 0.56±0.1 | 0.42 |
| Height (H)/Visina | 0.43 | 0.51 | 0.47±0.04 | 0.34 | 0.56 | 0.44±0.08 | 0.27 |

Table 5. Morphometric analysis of the class III atlas vertebrae posterior arch (All the measures are given in cm)
Tabela 5. Morfometrijska analiza zadnjeg luka atlasa klase III. Sve mere su date u cm.

| Parameters <i>Parametri</i> | Right side/ <i>Desna strana</i> | | | Left side/ <i>Leva strana</i> | | | p |
|--------------------------------|---------------------------------|----------------------------|-----------|-------------------------------|----------------------------|-----------|------|
| | Minimum <i>Minimum</i> | Maximum <i>Maksimum</i> | X ± SD | Minimum <i>Minimum</i> | Maximum <i>Maksimum</i> | X ± SD | |
| Width (W)/ <i>Širina</i> | 0.43 | 0.573 | 0.5±0.1 | 0.44 | 0.67 | 0.57±0.09 | 0.23 |
| Height (H)/ <i>Visina</i> | 0.385 | 0.45 | 0.42±0.04 | 0.42 | 0.5 | 0.44±0.03 | 0.24 |

tebral artery on the right and left sides of the examined vertebrae.

Table 4 and **Table 5** show that there is no statistically significant difference between results obtained by morphometric analysis on the posterior arch of the atlas vertebrae class II and III.

Discussion

The existence of bony bridges (ponticles) may reduce the area through which the vertebral artery passes, compromising its blood flow and causing vertebrobasilar insufficiency. Having that in mind, knowledge of the anatomical variations of the posterior arch of the atlas vertebra should be considered during diagnostic, surgical and other therapeutic manipulations of the cervical spine [24]. The morphometric analysis of the posterior arch of the atlas vertebra is done in order to investigate the association between their anatomy and certain clinical symptoms, as well as to improve diagnostic and surgical procedures by indicating possible complications and contraindications.

During phylogeny, the cervical and the upper thoracic part of the vertebral column are the most susceptible to changes, which may lead to certain morphological variations [2]. Among all cervical vertebrae, the atlas vertebra shows the highest variability [28]. After 1869, when Macalister [3] first described the PP, many anatomists started studying the morphology of the atlas vertebrae. The bony bridges of the atlas vertebrae are found in humans as well as in non-human primates [29]. The origin of the bridges is a matter of much debate and numerous theories have been explained in the available literature [4–6, 14, 19, 31]. It could be a congenital phenomenon due to the persistence of the superior oblique process [5], or it could be developed from the pro-atlas as a part of the occipital vertebra [6, 31]. Saunders and Popović [7] conducted family studies and noted a significant correlation of the atlas bony bridges among parents and children, as well as among siblings [8]. While a group of authors stated that such anatomical variations could be due to the ossification of the posterior atlanto-occipital membrane or acquired ossification of the oblique ligament (lateral border of the posterior atlanto-occipital membrane which forms the aperture for the vertebral artery and the suboccipital nerve) as a consequence of the vertebral artery pulsation [3, 9], others claimed that the PP might be related to erect posture and bipedalism [14, 17]. There

was a belief that development of the bony bridges could be caused by external stimuli and that a study on Bedouin women would be of interest to determine whether carrying heavy objects may contribute in formation of such variations [14, 25].

Studies of the first cervical vertebrae were performed on dry bones and radiographic images (computed tomography and X-ray images) of cervical part of vertebral column. It was noted that radiographic researches give less detailed data [22]. Examination performed on dry bones and three-dimensional images of computed tomography have an advantage over X-ray images because they provide better insight and transparency of the observed region [23].

Part I

In the present research, the overall prevalence of PP was 21.95% (14.63% cases of incomplete and 7.32% cases of complete bony bridges). The prevalence of this anatomical variation has been reported differently by different authors. The incomplete PP is found in 9.8 - 25.9% of the general population [2, 4, 14, 29]. Taitz and Nathan [25] found incomplete PP in 25.9% and complete PP in 7.9% of the population. This coincides with the results of the present study. Patel et al. [28] found a prevalence of complete PP of 13% in the Gujarat region, while Ckmak et al. [26] found a prevalence of complete PP of 11.6% in the sample of 60 atlas vertebrae in the Turkish population.

The data in **Table 1** show that in the sample of atlas vertebrae found in the territory of Serbia, unilateral complete, as well as incomplete, bony bridges are more frequent than bilateral, which is in accordance with the findings of other authors [11, 14, 22]. The reason why such variations are more often found on the left side may be explained by right handedness and consequently larger and stronger sternocleidomastoid muscle on the same side which tilts the head to the opposite side [32]. Dhall et al. also reported higher prevalence of left-sided PP [11] as well as Hasan et al. [30], which also correlated with the larger superior articular facets on the left side.

Apart from Mitchell's classification, Hasan et al. [30] described six classes of atlas vertebrae bridges. In order to describe the posterior arch of atlas vertebra extensively, we used Hasan's protocol and divided the class I vertebra into two subclasses – with deeper and with shallower groove for the vertebral artery. As the bony bridges are more likely present on the left side of the atlas posterior arch, deeper

grooves for the vertebral artery are common on the same side, but this is inconsistent with the results from the sample of Northern Punjabi population [17].

Part II

In the present research, the morphometric analysis of class II atlas vertebrae (**Table 4**) shows that the mean W of the PP is 0.57 ± 0.12 cm on the right side, vs. 0.56 ± 0.1 cm on the left side, while the mean H of the PP is 0.47 ± 0.04 cm on the right side, vs. 0.44 ± 0.08 cm on the left side. **Table 5** presents the same data for class III atlas vertebrae – the mean W of the PP (0.5 ± 0.1 cm on the right vs. 0.57 ± 0.09 cm on the left side) and the mean H of the PP (0.42 ± 0.04 cm on the right vs. 0.44 ± 0.03 cm on the left side). Krishnamurthy et al. [18] noted that the mean vertical H of the complete PP was 6.52 mm on the right side and 6.57 mm on the left side in bilateral samples, while it was 5.38 mm and 4.91 mm, respectively in the unilateral samples of the atlas vertebrae, which is higher than findings in the present study. Unur et al. [1] studied dimensions of the complete PP on radiographic images and found that the mean H was higher than in the present research (5.7 mm), which can be explained by using a different material.

The presence of anatomical variations on the posterior arch of the atlas vertebra is a common cause of vertebro-basilar insufficiency. Any abnormal course of the vertebral artery can lead to deficiency in vascular supply of the brainstem and the

cerebellum [27]. The importance of this anatomical variation is underestimated in practice and clinicians must be alert about its possible presence in patients complaining of dizziness, vertigo, higher headache ratio, temporal pain, photophobia, pain in the arm and shoulder [16, 20]. Cervical spine radiography is a very useful technique to detect PP [26].

Study limitations

The limitation of this study is the small sample size, as well as that it attempted to explore the characteristics of the superior surface of the posterior arch on dry atlas vertebrae of unknown sex and age.

Our idea is to expand the research by using magnetic resonance images of patients with symptoms of vertebro-basilar insufficiency.

Conclusion

A thorough knowledge of the anatomy of the first cervical vertebra is of great importance not only for anatomists and anthropologists, but also for neurologists, neurosurgeons and vascular surgeons. This research showed that the most common are atlas vertebrae that, according to Mitchell's classification, belong to the class I (78.05%) and the least common are class III atlas vertebrae (7.32%). There is no statistically significant difference in the dimensions of the anatomical variations of all three classes of atlas vertebrae between the right and the left side.

References

- Unur E, Erdoğan N, Ülger H, Ekinci N, Ozturk O. Radiographic incidence of complete arcuate foramen in Turkish population. *Erciyes Medical Journal*. 2004;26(2):50–4.
- Wysocki J, Bubrowski M, Reymond J, Kwiatkowski J. Anatomical variants of the cervical vertebrae and the first thoracic vertebra in man. *Folia Morphol (Warsz)*. 2003;62(4):357–63.
- Macalister A. Homologies and comparative anatomy of the atlas and axis. *J Anat Physiol*. 1869;3(Pt 1):54–64.
- Manjunath KY. Posterior bridging of the atlas vertebra in south Indians. *Indian J Med Sci*. 2001;55(9):488–90.
- Allen W. The varieties of atlas in the human subject and the homologies of its transverse processes. *J Anat Physiol*. 1879;14(Pt 1):18–27.
- Von Torklus D, Gele W. The upper cervical spine. New York: Grunne and Stratton; 1972. p. 28–30.
- Saunders SR, Popovich F. A family study of two skeletal variants: atlas bridging and clinoid bridging. *Am J Phys Anthropol*. 1978;49(2):193–203.
- Peçala PA, Henry BM, Peçala JR, Hsieh WC, Vikse J, Sanna B, et al. Prevalence of foramen arcuale and its clinical significance: a meta-analysis of 55,985 subjects. *J Neurosurg Spine*. 2017;27(3):276–90.
- Le Double AF. *Traite des variations de la colonne vertebrale de l'homme; et de leur signification au point de vue de l'anthropologie zoologique*. Paris: Vigot; 1912.
- Young JP, Young PH, Ackermann MJ, Anderson PA, Riew KD. The ponticulus posticus: implications for screw insertion into the first cervical lateral mass. *J Bone Joint Surg Am*. 2005;87(11):2495–8.
- Dhall U, Chhabra S, Dhall JC. Bilateral asymmetry in bridges and superior articular facets of atlas vertebra. *J Anat Soc India*. 1993;42(1):23–7.
- Gibelli D, Cappella A, Cerutti E, Spagnoli L, Dolci C, Sforza C. Prevalence of ponticulus posticus in a Northern Italian population: a lateral cephalometric study. *Surg Radiol Anat*. 2016;38(3):309–12.
- Tassoker M, Kok H, Ozcan S. Investigation of the relationship between “sella turcica bridge” and “ponticulus posticus”: a lateral cephalometric study. *Int J Morphol*. 2017;35(1):337–44.
- Paraskevas G, Papaziogas B, Tsonidis C, Kapetanios G. Gross morphology of the bridges over the vertebral artery groove on the atlas. *Surg Radiol Anat*. 2005;27(2):129–36.
- Kuhta P, Hart J, Greene-Orndorff L, McDowell-Reizer B, Rush P. The prevalence of posticus ponticus: retrospective analysis of radiographs from a chiropractic health center. *J Chiropr Med*. 2010;9(4):162–5.
- Akhtar MJ, Fatima N, Ritu, Kumar V. A morphological study of ponticuli of the human atlas vertebrae and its clinical significance. *Int J Anat Res*. 2015;3(4):1597–602.
- Lalit M, Piplani S, Arora AK, Kullar JS, Sharma T. Incidence of atlas bridges and tunnels—their phylogeny, ontogeny and clinical implications. *Revista Argentina de Anatomía Clínica*. 2014;6(1):26–34.
- Krishnamurthy A, Nayak SR, Khan S, Prabhu LV, Ramanathan LA, Ganesh Kumar C, et al. Arcuate foramen of atlas: incidence, phylogenetic and clinical significance. *Rom J Morphol Embryol*. 2007;48(3):263–6.

19. Tubbs RS, Johnson PC, Shoja MM, Loukas M, Oakes WJ. Foramen arcuale: anatomical study and review of the literature. *J Neurosurg Spine*. 2007;6(1):31-4.
20. Wight S, Osborne N, Breen AC. Incidence of ponticulus posterior of the atlas in migraine and cervicogenic headache. *J Manipulative Physiol Ther*. 1999;22(1):15-20.
21. Schilling J, Schilling A, Galdames IS. Ponticulus posticus on the posterior arch of atlas, prevalence analysis in asymptomatic patients. *Int J Morphol*. 2010;28(1):317-22.
22. Lamberty BG, Zivanović S. The retro-articular vertebral artery ring of the atlas and its significance. *Acta Anat (Basel)*. 1973;85(1):113-22.
23. Kim KH, Park KW, Manh TH, Yeom JS, Chang BS, Lee CK. Prevalence and morphologic features of ponticulus posticus in Koreans: analysis of 312 radiographs and 225 three-dimensional CT scans. *Asian Spine J*. 2007;1(1):27-31.
24. Patel NP, Gupta DS, Parmar ND. Incidence of ponticles in human atlas vertebrae – a study from South Gujarat population. *Indian J Clin Anat Physiol*. 2015;2(3):135-9.
25. Taitz C, Nathan H. Some observations on the posterior and lateral bridge of the atlas. *Acta Anat (Basel)*. 1986;127(3):212-7.
- Rad je primljen 30. VI 2018.
- Recenziran 12. VII 2018.
- Prihvaćen za štampu 12. VII 2018.
- BIBLID.0025-8105:(2018):LXXI:7-8:250-255.
26. Cakmak O, Gurdal E, Ekinci G, Yildiz E, Cavdar S. Arcuate foramen and its clinical significance. *Saudi Med J*. 2005;26(9):1409-13.
27. Kwiatkowska B, Szczurowski J, Nowakowski D. Variation in foramina transversaria of human cervical vertebrae in the medieval population from Sypniewo (Poland). *Anthropological Review*. 2014;77(2):175-88.
28. Patel Z, Zalawadia A, Pensi CA. Study of arcuate foramen in atlas vertebrae in Gujarat region. *Natl J Integr Res Med*. 2012;3(2):73-5.
29. Mitchell J. The incidence and dimensions of the retro-articular canal of the atlas vertebra. *Acta Anat (Basel)*. 1998;163(2):113-20.
30. Hasan M, Shukla S, Siddiqui MS, Singh D. Posterolateral tunnels and ponticuli in human atlas vertebrae. *J Anat*. 2001;199(Pt 3):339-43.
31. Von Torklus D, Gele W. The upper cervical spine. New York: Grunne and Stratton; 1972. p. 28-30. SAME AS REF 6
32. Pande BS, Singh I. One-sided dominance in the upper limbs of human fetuses as evidenced by asymmetry in muscle and bone weight. *J Anat*. 1971;109(Pt 3):457-9.

CASE REPORTS

PRIKAZI SLUČAJEVA

Clinical Center of Serbia, Clinic of Urology, Belgrade¹University Medical Center "Zvezdara", Department of Urology, Belgrade²Clinical Center of Vojvodina, Clinic for gynecology and obstetrics, Novi Sad³University of Novi Sad, Faculty of Medicine⁴Serbian Academy of Sciences and Arts, Belgrade⁵

Case report

Prikaz slučaja

UDK 616.62-006.6-06/-08

<https://doi.org/10.2298/MPNS1808257P>SPONTANEOUS URINOMA DIAGNOSED BEFORE RADICAL CYSTECTOMY
– A CASE REPORT

SPONTANI URINOM DIJAGNOSTIKOVAN PRE RADIKALNE CISTEKTOMIJE – PRIKAZ SLUČAJA

Tomislav PEJČIĆ¹, Vladimir VASIĆ², Vladan DIMITRIJEVIĆ¹, Milomir TUFEGDŽIĆ²,
Tihomir VEJNOVIĆ^{3,4} and Jovan HADŽIĐOKIĆ⁵

Summary

Introduction. Rupture of the urinary collecting system, associated with perirenal or retroperitoneal extravasation of the urine, is a rare condition usually associated with the obstruction of the urinary system. A urinoma is a localized collection of urine in the retroperitoneum, outside the urinary tract, and occurs after injury to the wall of the urinary system. Ureteral obstruction caused by a bladder tumor is a rare cause of urinoma. **Case Report.** We report a case of a 62-year-old patient who was admitted to the Clinic of Urology of the Clinical Center of Serbia, due to an invasive bladder cancer. A computerized tomography scan of the abdomen and pelvis revealed a massive bladder tumor dominant on the left side, invading the vagina, uterus and significantly obstructing both kidneys. Intraoperatively, a mass of 18 cm in diameter was identified in the right retroperitoneal space and it was dissected from the peritoneum. Two liters of clear fluid were aspirated from the mass, and the walls of urinoma were resected. The site of perforation was not identified. The patient underwent anterior pelvic exenteration. The pathohistological analysis revealed a high grade transitional cell carcinoma of the bladder. The treatment is individual and involves surgical and interventional radiology treatment. **Conclusion.** A spontaneous retroperitoneal urinoma is a very rare condition. In this case report it appeared most likely due to right ureteral obstruction and perforation. The growth of urinoma was slow, due to the absence of acute symptoms and the thickness of the urinoma wall.

Key words: Urinoma; Retroperitoneal Space; Urinary Bladder Neoplasms; Ureteral Obstruction; Diagnosis; Treatment Outcome; Cystectomy

Introduction

Rupture of the urinary tract, associated with urine extravasation into the perirenal or retroperitoneal spaces is a rare condition, usually associated with the obstruction of the urinary system. The perforation can

Sažetak

Uvod. Ruptura mokraćnih puteva, udružena sa perirenalnom ili retroperitonealnom ekstrasvacijom urina je retko stanje, najčešće povezano sa opstrukcijom urinarnog trakta. Urinom predstavlja lokalizovanu kolekciju urina u retroperitoneumu, izvan urinarnog sistema koja nastaje nakon povrede urotela. Opstrukcija uretera izazvana tumorom mokraćne bešike je redak uzrok nastanka urinoma. **Prikaz slučaja.** Prikazujemo slučaj pacijentkinje stare 62 godine, koja je primljena na Klinku za urologiju, Kliničkog centra Srbije, zbog invazivnog tumora mokraćne bešike. Kompjuterizovanom tomografijom abdomena i male karlice uočeno je prisustvo masivnog tumora mokraćne bešike sa zahvatanjem vagine i uterusa uz značajnu opstrukciju oba bubrega, dominantno sa leve strane. Intraoperativno, identifikovana je masa, promera 18 cm u desnom retroperitonealnom prostoru. Aspirirano je dva litra bistre tečnosti iz mase, a zidovi urinoma su resecirani. Mesto perforacije nije identifikovano. Kod bolesnice je učinjena prednja egzenteracija karlice. Patohistološki pregled je potvrdio da je karcinom prelaznog epitela mokraćne bešike visokog gradusa, sa infiltracijom prednjeg zida vagine i uterusa; zid urinoma je bio sačinjen od peritoneuma. **Zaključak.** Spontani retroperitonealni urinom nastaje veoma retko. U prikazanom slučaju, spontani urinom je nastao najverovatnije zbog opstrukcije i perforacije desnog uretera. Usled odsustva akutnih simptoma i na osnovu debljine zida urinoma, urinom se verovatno formirao veoma sporo.

Ključne reči: urinom; retroperitonealni prostor; karcinomi mokraćne bešike; ureterana opstrukcija; dijagnoza; ishod lečenja; cistektomija

occur from the renal pelvis to the bladder; however, it is most frequent at the level of renal fornix and upper segment of the ureter [1]. The urinary system obstruction is followed by an increase of intraluminal pressure, which can cause rupture of the urinary tract, urinary extravasation and development of urinoma. A urinoma

Abbreviations

CT – computerized tomography

is a localized collection of urine in the retroperitoneum, outside of the urinary tract that occurs after an injury of the urinary system wall [2]. Congenital anomalies, calculus formation and malignancies of the urinary tract can also cause perforation. Furthermore, degenerative renal diseases, endoscopic manipulations, retroperitoneal fibrosis, tumors of the abdomen and pelvis and post radiation strictures may also lead to this condition [3]. Ureteral obstruction caused by a bladder tumor is a rare cause of urinoma [2]. Extravasation of urine can be asymptomatic, but the most common symptoms are abdominal pain, vomiting, fever, oliguria and ileus. The treatment is individual; in some cases, endoscopic insertion of ureteral Double-J stent, or percutaneous nephrostomy are sufficient [4], while some cases require surgical treatment [5].

Case Report

The presented patient was a 62-year-old woman admitted to the Clinic of Urology, Clinical Center of Serbia, due to invasive bladder cancer. The patient was examined by a gynecologist and a colorectal surgeon and vaginal involvement was confirmed. Computerized tomography (CT) scan revealed a massive bladder tumor, invading the vagina and uterus and significantly obstructing both kidneys, mostly on the left side (**Figures 1 and 2**). The patient was scheduled for anterior pelvic exenteration and ileal conduit urinary diversion. The abdominal mass was noted on the operating table, after administration of general anesthesia (**Figure 3**). A portable ultrasound was used in the operating theatre and it revealed a massive, anechoic abdominal lesion. The mass was absent on the CT scan performed a few weeks before. After the surgery, the patient said that she had noticed



Figure 2. Dilated renal collecting system
Slika 2. Dilatiran kolektorni sistem bubrega



Figure 3. Abdominal mass in the right hemiabdomen
Slika 3. Abdominalna masa u desnom hemiabdomenu

a mass at the right side of the abdomen, but she had not reported it to the medical staff.



Figure 1. Infiltrating tumor in the left bladder wall
Slika 1. Infiltrativni tumor levog bočnog zida mokraćne bešike

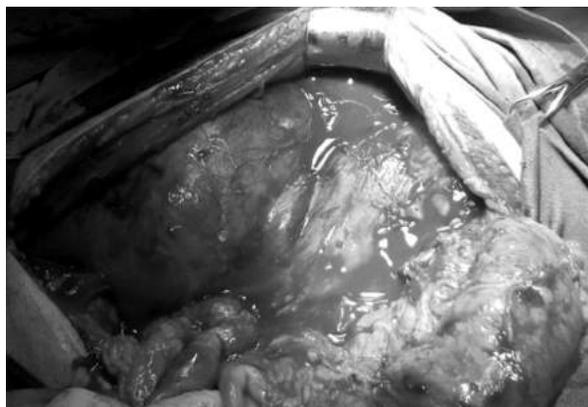


Figure 4. Oval mass in the right retroperitoneal space, after the release of increased right colon and peritoneum
Slika 4. Ovalna masa u desnom retroperitoneumu nakon oslobađanja ushodnog kolona i peritoneuma

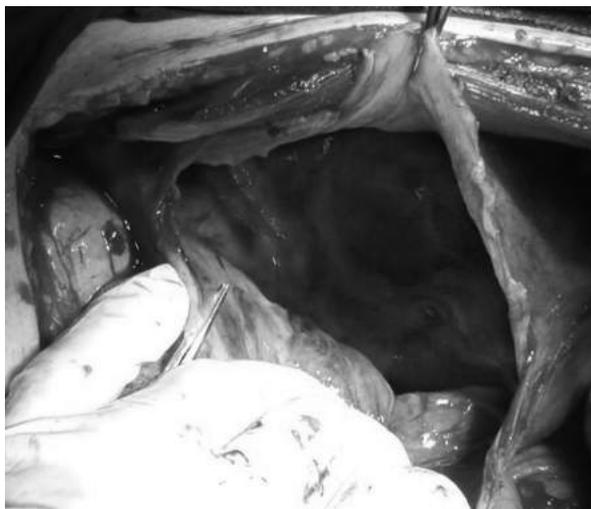


Figure 5. Walls of the urinoma
Slika 5. Zidovi urinoma

A lesion, 18 cm in diameter, was identified intraoperatively in the right retroperitoneal space and it was dissected from the peritoneum (**Figure 4**). Two liters of clear fluid were aspirated from the mass, and it was completely resected (**Figure 5**). The site of perforation was not identified. The pathological analysis confirmed that walls of the retroperitoneal mass originated from the peritoneum. In addition, the examination revealed a high grade transitional cell cancer of the bladder, with the invasion of the anterior vaginal wall and the uterus.

Discussion

Spontaneous urinoma is defined as urine extravasation through the perforation of the urinary tract caused by high hydrostatic pressure due to urinary obstruction. The most common causes of spontaneous urinoma are urinary stones [6], while bladder tumors are rare [1, 2, 7]. Other causes are congenital anomalies, tumors of the abdomen and pelvis, retroperitoneal fibrosis, iatrogenic and post radiation strictures and connective tissue disorders [5]. Few cases of fornical rupture in pregnancy were described in the literature [8].

Acute spontaneous urinoma is usually the consequence of acute urinary obstruction. In such cases, a rupture at the level of calyceal fornix provides decompression and protects the kidney from a high-pressure injury. Acute urinoma is associated with ipsilateral abdominal pain, nausea, and vomiting, symptoms reminding on diverticulitis, cholecystitis, or appendicitis [7]. On the other hand, chronic spontaneous uri-

noma grows slowly, due to gradual urinary obstruction, sometimes without specific symptoms [9]. It is the mechanism often seen in malignant tumors of the pelvis. Rarely, urinoma is associated with unusual symptoms, as spontaneous drainage through the scrotal wall [10]. The diagnosis of urinoma is based on ultrasound, which usually reveals liquid collection and hydronephrosis. However, CT scans are more precise and determine the level of obstruction, localization of rupture, dimensions of the collection and its relationship with other structures [11, 12].

The incidence of spontaneous urinoma in patients with bladder cancer is very low, even in cases of bladder cancer associated with marked hydronephrosis. On the other hand, the incidence of hydronephrosis in patients with bladder cancer is relatively high, accounting for 13.7% of cases in large series [9] Bilateral hydronephrosis is a common sign of bladder cancer local invasion in more than 90% of cases [13].

Cooke and Bartucz [14] described 14 cases of spontaneous urinoma. The most common causes of urinoma was ureteral calculus. Koga et al. [15] reported 11 cases of spontaneous urinoma. The most common cause was also an ureteral stone, while sigmoid and ureteral cancer was the cause in the remaining two patients. Rectal cancer was the cause of spontaneous urinoma in the case report published by Garg [3]. Other pelvic malignancies, like cervical and ovarian cancer were also found as causes of urinoma [2, 3, 14]. Very rare causes of spontaneous urinoma include B-cell lymphoma of the omentum [16], neurogenic bladder [5] and dermatomyositis [17]. In children, urinoma may be the consequence of congenital anomalies, like posterior urethral valves or uretero-pelvic junction obstruction [18].

In the case presented herein, spontaneous urinoma appeared due to advanced invasive bladder cancer and ureteral obstruction. The evolution of urinoma was slow, so the patient did not complain of any pain. A few days before surgery, the woman noticed an abdominal mass in the right half of the abdomen, but she did not report it to the medical staff. The mass was discovered on the operating table, under general anesthesia and muscle relaxation. The therapy included surgical exploration, complete resection of the urinoma and anterior pelvic exenteration.

Conclusion

Spontaneous retroperitoneal urinoma is a very rare condition. In this case report, the spontaneous urinoma appeared most likely due to right ureteral obstruction and perforation. The absence of acute symptoms and the thickness of the urinoma wall pointed to a slow-growing urinoma.

References

1. Pampana E, Altobelli S, Morini M, Ricci A, D'Onofrio S, Simonetti G. Spontaneous ureteral rupture, diagnosis and treatment. *Case Rep Radiol.* 2013;2013:851859.

2. Jou YC, Shen CH, Cheng MC, Lin CT, Chen PC. Bilateral ureteral complete obstruction with huge spontaneous urinoma formation in a patient with advanced bladder cancer. *J Chin Med Assoc.* 2012;75(2):84-6.

3. Garg PK, Mohanty D, Rathi V, Jain BK. Spontaneous rupture of the renal pelvis presenting as an urinoma in locally advanced rectal cancer. *World J Clin Cases*. 2014;2(4):108-10.
4. Akpınar H, Kural AR, Turek I, Obek C, Demirkesen O, Solok V, et al. Spontaneous ureteral rupture: is immediate surgical intervention always necessary? Presentation of four cases and review of the literature. *J Endourol*. 2002;16(3):179-83.
5. Fujita K, Sugao H, Tsujikawa K. Perinephric urinoma secondary to neurogenic bladder with vesicoureteral reflux: report of an adult case. *Int J Urol*. 2004;11(1):53-5.
6. Gershman B, Kulkarni N, Sahani DV, Eisner BH. Causes of renal fornical rupture. *BJU Int*. 2011;108(11):1909-11.
7. Diaz ES, Buenrostro FG. Renal pelvis spontaneous rupture secondary to ureteral lithiasis. Case report and bibliographic review. *Arch Esp Urol*. 2011;64(7):640-2.
8. Upputalla R, Moore RM, Jim B. Spontaneous fornical rupture in pregnancy. *Case Rep Nephrol*. 2015;2015:379061.
9. Haleblan GE, Skinner EC, Dickinson MG, Lieskovsky G, Boyd SD, Skinner DG. Hydronephrosis as a prognostic indicator in bladder cancer patients. *J Urol*. 1998;160(6 Pt 1):2011-4.
10. Ataus S, Yaycioglu O, Onder AU, Onal B, Solok V. Giant spontaneous urinoma draining from the scrotal wall. *J Urol*. 2000;163(6):1874-5.
11. Titton RL, Gervais DA, Hahn PF, Harisinghani MG, Arellano RS, Mueller PR. Urine leaks and urinomas: diagnosis and imaging-guided intervention. *Radiographics*. 2003;23(5):1133-47.
12. Stravodimos K, Adamakis I, Koutalellis G, Kortsiadis G, Grigoriou I, Srepetis K, et al. Spontaneous perforation of the ureter: clinical presentation and endourologic management. *J Endourol*. 2008;22(3):479-84.
13. Leibovitch I, Ben-Chaim J, Ramon J, Madjar I, Engelberg IS, Goldwasser B. The significance of ureteral obstruction in invasive transitional cell carcinoma of the urinary bladder. *J Surg Oncol*. 1993;52(1):31-5.
14. Cooke GM, Bartucz JP. Spontaneous extravasation of contrast medium during intravenous urography: report of fourteen cases and a review of the literature. *Clin Radiol*. 1974;25(1):87-93.
15. Koga S, Arakaki Y, Matsuoka M, Ohyama C. Spontaneous peripelvic extravasation of urine. *Int Urol Nephrol*. 1992;24(5):465-9.
16. Yoshii T, Horiguchi A, Shirotake S, Tobe M, Hayakawa M, Sumitomo M, et al. Spontaneous rupture of the ureter as the primary symptom of malignant lymphoma. *Hinyokika Kyo*. 2010;56(11):639-43.
17. Huang KH, Hsieh SC, Huang CY, Chen SC, Chen J. Dermatomyositis associated with bilateral ureteral spontaneous rupture. *J Formos Med Assoc*. 2007;106(3):251-4.
18. Tseng PC, Liu TY, Pan SJ, Sung DS. Spontaneous perirenal urinoma associated with ureteropelvic junction obstruction in a child: a case report. *Pediatr Neonatol*. 2009;50(3):121-4.

Rad je primljen 18. IV 2018.

Recenziran 8. VII 2018.

Prihvaćen za štampu 9. VII 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:257-260.

University Clinical Center "Zemun", Belgrade¹
 Institute of Rheumatology, University of Belgrade²
 Clinical Hospital Center "Dragiša Mišović", Belgrade³
 Military Medical Academy, Clinic for Lung Disease⁴
 Clinic for Lung Diseases, Clinical Center of Serbia, Belgrade⁵
 School of Medicine, University of Belgrade⁶

Case report
Prikaz slučaja
 UDK 616.25-003.219-02
<https://doi.org/10.2298/MPNS1808261L>

SPONTANEOUS PNEUMOTHORAX INDUCED BY HIGH ALTITUDE – A CASE REPORT

SPONTANI PNEUMOTORAKS INDUKOVAN VELIKOM NADMORSKOM VISINOM – PRIKAZ SLUČAJA

Biljana LAZOVIĆ^{1,6}, Ivana BLAŽIĆ¹, Mirjana ZLATKOVIĆ SVENDA^{2,6}, Vesna ĐURIĆ³,
 Rade MILIĆ⁴ and Vladimir ŽUGIĆ^{5,6}

Summary

Introduction. Primary spontaneous pneumothorax is an infrequent condition which requires emergency medical treatment. Nowadays, due to hiking and tourism, many people reach high altitudes in a hypobaric hypoxia environment. These hypoxic conditions can be tolerated if one is exposed to low oxygen pressure, leading to a sequence of physiological responses. Occasionally, hypoxia causes maladaptive responses which leads to different forms of high altitude diseases. **Case Report.** We report a case of a 49-year-old man, a former professional athlete, passionate about hiking and still physically active. He was admitted to our Emergency Department with short breath and a chest X-ray revealed a large right sided pneumothorax which was successfully treated with tube drainage.

Conclusion. Although primary spontaneous pneumothorax is a rare condition, it should be suspected during physical examination. Therefore, physicians should be prepared to recognize it, especially paying attention to all hikers and high-altitude travelers in order to avoid possible risks for high-altitude sickness.

Key words: Pneumothorax; Altitude; Atmospheric Pressure; Altitude Sickness; Travel; Mountaineering; Chest Tubes; Hypoxia; Radiography; Signs and Symptoms

Introduction

Spontaneous pneumothorax (SP) refers to the presence of air or gas in the space between the chest and the lungs, in other words a "collapse" of the lungs which prevents complete inflation [1]. More than a half of pneumothorax cases are traumatic, either iatrogenic or accidental; the remaining are referred to as SP. There are two types of SP - primary and secondary. Primary spontaneous pneumothorax (PSP) is an idiopathic disease which appears in otherwise healthy person. Secondary spontaneous pneumothorax (SSP) is an underlying condition which appears in patients with various pul-

Sažetak

Uvod. Primarni spontani pneumotoraks je retko stanje koje zahteva neodložni medicinski tretman. Danas, sa razvojem civilizacije, putovanja, raznih ekstremnih sportova, planinarenja, mnogi ljudi dosegnu do visokih nadmorskih visina koje su u hipobaričnom hipoksičnom okruženju. Hipoksični uslovi se mogu tolerisati kada je osoba izložena niskom pritisku kiseonika, što stimuliše odgovarajući fiziološki odgovor. Povremeno hipoksija može dovesti do različitih reakcija i bolesti usled neadaptacije na visoku nadmorsku visinu. **Prikaz slučaja.** Prezentujemo slučaj osobe stare 49 godina, fizički aktivne, bivšeg profesionalnog sportiste, strastvenog planinara. On dolazi u hitan internistički prijem zbog tegoba u vidu plitkog daha; na radiogramu grudnog koša vizualizovan je veliki desni pneumotoraks, koji je uspešno tertiran drenažom. **Zaključak.** Iako je primarni spontani pneumotoraks redak entitet, izuzetno je važno posumnjati na njega tokom fizikalnog pregleda. Zbog toga, uloga lekara treba da bude značajnija u planiranju dugih, ekstremnih putovanja i sportova kako bi se izbegao mogući rizik od nepredviđenih bolesti.

KLjučne reči: pneumotoraks; visina; atmosferski pritisak; visinska bolest; putovanja; planinarenje; torakalna drenaža; hipoksija; radiografija; znaci i simptomi

monary disorders such as chronic obstructive pulmonary disease (COPD), cystic fibrosis, acquired immune deficiency syndrome and tuberculosis [2]. It mostly affects the elderly population and if it is not treated immediately, the condition can get worse and cause death. Chest pain and sometimes mild breathlessness are the most common symptoms in PSP. Some patients may wait for a few days before they seek medical help, although there are many cases when PSP is life threatening [1, 2]. The course of SP remains unpredictable with a recurrence rate ranging from 25 – 54%. An important risk factor for PSP is smoking. Also, patients with PSP tend to be taller than controls. Furthermore, PSP often oc-

Abbreviations

| | |
|------------------|---|
| SP | – spontaneous pneumothorax |
| PSP | – primary spontaneous pneumothorax |
| SSP | – secondary spontaneous pneumothorax |
| COPD | – chronic obstructive pulmonary disease |
| CK | – creatine kinase |
| PaO ₂ | – partial pressure of oxygen |
| HVR | – hypoxic ventilatory response |

curs among young adults [3]. The rise of negative pleural pressure increases from the lung base to the apex, so that alveoli at the lung apex in tall persons are subject to remarkably greater distending pressure than those at the base of the lung, and the vectors in theory, predispose to the development of apical subpleural blebs [2]. Surprisingly, SP may occur even during sedentary activity, despite recognized association between the onset of pneumothorax and physical activity [3].

Case Report

A 49-year-old man (190 cm tall, 90 kg weight, body mass index 24.93 kg/m²) was admitted to our Emergency Department with a high level of suspicion for acute coronary syndrome. He was sweating, pale, with shortness of breath and chest pain that spread to the arms and back with no response to nitroglycerin. The patient felt a severe chest pain an hour before admittance after a short rapid run to catch the bus to work. In his youth, he was an active professional footballer and after retirement he continued playing football three times a week and occasionally went hiking. At his previous medical check-up, he reported that he climbed Mount Everest 3 days before. After returning home, he had a dry cough followed by mild dyspnea without any treatment. He used some secretolytic bang drag to eliminate the symptoms, but without any improvement. There was no relevant personal, traumatic or psychiatric history or any basic lung disease. He was not a smoker and no allergies were reported. He had general medical examinations annually, and in his opinion he was in perfect condition without illness. On admittance, his blood pressure was 110/80 mmHg, pulse rate 106/min, respiratory rate 26/min, body temperature 36.7°C, oxygen saturation 88% in room air and 96% with an oxygen mask at a flow of 8 L/min. On examination, he had breathing difficulties, with reduced breath sound on the right side. The physical examination showed no other abnormalities. Cardio sensitive enzymes (troponin, creatine kinase (CK), CK-MB) were within normal limits as well as complete blood count and biochemistry results. A 12-lead electrocardiogram showed sinus tachycardia with 110 beats/min and no ST-T changes or ischemic changes. Chest X-ray revealed a unilateral right sided pneumothorax with no mediastinal change (**Figure 1**). Based on radiographic findings, two emergency surgeons concurrently performed one-sided catheter drainage. Thereafter, his dyspnea and chest pain im-



Figure 1. Chest X-ray showing a large unilateral pneumothorax on the right side

Slika 1. Radiogram grudnog koša sa velikim unilateralnim pneumotoraksom sa desne strane

proved. The patient was hospitalized after consultation with the chest surgeon. Two days later, no blebs were found on chest computed tomography, which also showed that the right lung was fully expanded. On the third day after admission, after X-ray confirmation of pneumothorax absence, the catheter was removed. The patient was discharged from the hospital on the 7th day after admission without any complications. The six-month and annual follow-ups showed no recurrence. A written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Discussion

The pathophysiology of PSP still remains unknown [4, 5]. There are several theories explaining the etiology of PSP. The first is that subpleural blebs and bullae that are found at the lung apices at thoracoscopy and on computed tomography scan in up to 90% of cases of PSP are considered to play a role [6]. The second theory asserts that pulmonary blebs are small subpleural thin walled spaces with presence of air, not larger than 1 – 2 cm in diameter; it is thought that bleb rupture permits the air to enter into pleural space causing pneumothorax. The third theory states that blebs are also observed in cell apoptosis which is a cells self-execution plan to guided rupture. There is a theory that the pleural lining cells are performing apoptosis leading to SP [6]. However, the location of unique or diffuse sites of air leakage in PSP is generally unknown [7, 8]. Interestingly, literature data show that 40% of SP cases are found in the left lung [9, 10], like in our patient. The potential contributing factors for PSP

are climate changes and cold temperatures with decreased atmospheric pressure [11]. Nowadays, more and more people are looking for adventure travels, so they hike to high altitudes, over 2000 meters with hypobaric hypoxia environment [12]. Whether or not they have an underlying lung disease, acute exposure to hypoxia causes several critical changes in respiratory physiology that affects persons hiking at high altitudes. After the rise to high elevation, the low partial pressure of oxygen (PaO₂) takes to an increase in minute ventilation, known as hypoxic ventilatory response (HVR). Mediated by the carotid bodies, the HVR varies among persons and tends to increase PaO₂ [12]. The HVR also causes a decrease in the partial pressure of carbon dioxide (PaCO₂); the resulting respiratory alkalosis causes a leftward shift of the oxyhemoglobin dissociation curve, which improves alveolar oxygen uptake and, to a lesser degree, reduces oxygen delivery to the tissues. This shift on left side is balanced by increased production of 2,3-diphosphoglycerate by red blood cells after prominent increase elevation; in vivo P50 stays approximately the same as at the sea level, and the mechanism in turn produces a compensatory rightward shift in the curve [13, 14]. Theoretically, there is a concern that in patients with COPD, bullous emphysema may expand or/and rupture during exposure to lower atmospheric pressure, but these patients belong to a group at risk and they should avoid sudden changes in atmospheric pressure, until proven otherwise. Statistics suggest that this concern is not warranted, because it is found in limited available literature. In a research of nine non-COPD patients fast decompressed to a simulated altitude of 13.100 m, bleb and cyst size increased in

just one patient without development of pneumothorax [15]. These discoveries were supported by other COPD patient-based studies: persons quickly decompressed to lower atmospheric pressure showed no pneumothorax nor clinical or radiographic evidence of bullae expansion, but it should be taken with reserve, because there is a limited number of studies analyzing this issue, only some case reports or studies including a small sample of respondents that focus on narrow end-points [16, 17].

It is difficult to draw concrete conclusions on understanding the pathophysiology of SPP from the previous studies and how it interacts with the high-altitude environment. However, it is possible to conclude what kind of patients should undergo medical examination before hiking and going to high-altitudes.

Given that increasing numbers of people are traveling to high altitudes for pleasure or work, and certain health conditions are frequent in the whole population, there is a high probability that many high altitude travelers have underlying medical diseases. While other organ systems, such as kidneys, heart and hematological system undergo important adaptations, we have to emphasize that lungs play a primary role in the early and late responses to high altitudes [18].

Conclusion

We suggest that patients with any pulmonary disorders who go hiking or travel to high altitudes should be examined before these activities. The evaluation of pre-travel health check-ups, in order to accurately predict the risk of high altitude travel, should be the aim of future research.

References

- Zarogoulidis P, Kioumis I, Pitsiou G, Porpodis K, Lampaki S, Papaiwannou A, et al. Pneumothorax from definition to diagnosis and treatment. *J Thorac Dis.* 2014;6(Suppl 4):S372–6.
- Sudduth CL, Shinnick JK, Geng Z, McCracken CE, Clifton MS, Raval MV. Optimal surgical technique in spontaneous pneumothorax: a systematic review and meta-analysis. *J Surg Res.* 2017;210:32–46.
- Bense L, Wiman LG, Hedenstierna G. Onset of symptoms in spontaneous pneumothorax: correlations to physical activity. *Eur J Respir Dis.* 1987;71(3):181–6.
- Luh SP. Diagnosis and treatment of primary spontaneous pneumothorax. *J Zhejiang Univ Sci B.* 2010;11(10):735–44.
- Donahue DM, Wright CD, Viale G, Mathisen DJ. Resection of pulmonary blebs and pleurodesis for spontaneous pneumothorax. *Chest.* 1993;104(6):1767–9.
- Mills JC, Stone NL, Erhardt J, Pittman RN. Apoptotic membrane blebbing is regulated by myosin light chain phosphorylation. *J Cell Biol.* 1998;140(3):627–36.
- Stern EJ, Frank MS. CT of the lung in patients with pulmonary emphysema: diagnosis, quantification, and correlation with pathologic and physiologic findings. *AJR Am J Roentgenol.* 1994;162(4):791–8.
- Kelly AM, Weldon D, Tsang AY, Graham CA. Comparison between two methods for estimating pneumothorax size from chest X-rays. *Respir Med.* 2006;100(8):1356–9.
- Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson LJ. *Harrison's principles of internal medicine.* 15th ed. New York: McGraw-Hill; 2001.
- Noppen M. Spontaneous pneumothorax: epidemiology, pathophysiology and cause. *Eur Respir Rev.* 2010;19(117):217–9.
- Haga T, Kurihara M, Kataoka H, Ebana H. Influence of weather conditions on the onset of primary spontaneous pneumothorax: positive association with decreased atmospheric pressure. *Ann Thorac Cardiovasc Surg.* 2013;19(3):212–5.
- Wagner PD, Sutton JR, Reeves JT, Cymerman A, Groves BM, Malconian MK. Operation Everest II: pulmonary gas exchange during a simulated ascent of Mt. Everest. *J Appl Physiol.* 1987;63(6):2348–59.
- Wagner PD, Wagner HE, Groves BM, Cymerman A, Houston CS. Hemoglobin P(50) during a simulated ascent of Mt. Everest, Operation Everest II. *High Alt Med Biol.* 2007;8(1):32–42.
- Lazovic B, Zlatkovic Svenda M, Durmic T, Stajic Z, Duric V, Zugic V. The regulation role of carotid body peripheral chemoreceptors in physiological and pathophysiological conditions. *Med Pregl.* 2016;69(11-12):385–90.

15. Parker GW, Stonehill RB. Further considerations of the roentgenologic evaluation of flying personnel at simulated altitude. *Aerosp Med.* 1961;32:501–4.

16. Yanda RL, Herschensohn HL. Changes in lung volumes of emphysema patients upon short exposures to simulated altitude of 18,000 feet. *Aerosp Med.* 1964;35:1201–3.

Rad je primljen 28. V 2018.

Recenziran 26. VI 2018.

Prihvaćen za štampu 28. VI 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:261-264.

17. Tomashefski JF, Feeley DR, Shillito FH. Effects of altitude on emphysematous blebs and bullae. *Aerosp Med.* 1966;37(11):1158–62.

18. Leon-Velarde F, Reeves JT. International consensus group on chronic mountain sickness. *Adv Exp Med Biol.* 1999;474:351–3.

SEMINAR FOR PHYSICIANS *SEMINAR ZA LEKARE U PRAKSI*

Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica
Clinic of Cardiology¹
University of Novi Sad, Faculty of Medicine Novi Sad²

Seminar for physicians
Seminar za lekare u praksi
UDK 616.127-005.8-073.97
<https://doi.org/10.2298/MPNS1808265I>

ST ELEVATION MYOCARDIAL INFARCTION EQUIVALENT - DE WINTER T-WAVE ELECTROCARDIOGRAPHY PATTERN

*EKVIVALENT INFARKTA MIOKARDA SA ELEVACIJOM ST SEGMENTA
- ELEKTROKARDIOGRAM DE VINTEROVOG T-TALASA*

Igor IVANOV^{1,2}, Anastazija STOJŠIĆ MILOSAVLJEVIĆ^{1,2}, Vladimir IVANOVIĆ^{1,2},
Miloš TRAJKOVIĆ¹, Aleksandra VULIN^{1,2} and Milenko ČANKOVIĆ^{1,2}

Summary

Introduction. Rapid diagnosis of acute myocardial infarction is essential for proper treatment and reduction of patient mortality. Electrocardiography plays an important role in its diagnosis. Acute myocardial infarction with ST segment elevation requires urgent reperfusion therapy, that is, primary percutaneous coronary revascularization. A small number of patients with acute myocardial infarction have ST segment depression in one or more leads, whereas ST segment elevation in augmented vector right the electrocardiogram is characteristic for a myocardial infarction without ST elevation, but the clinical course and the severity of disease correspond to the anterior myocardial infarction with ST segment elevation. **De Winter T-wave electrocardiography.** One of these forms is known as de Winter T-wave pattern, characterized by ST segment depression at the J-point (> 1 mm) in the precordial leads, the absence of ST segment elevation in the precordial leads, high peaked and symmetrical T-waves in the precordial leads and, in most cases, mild ST segment elevation (0.5 mm to 1 mm) in the augmented vector right. These patients have occlusion of the left main coronary artery, occlusion of the proximal segment of the anterior descending artery, or a severe multivessel coronary disease. Patients with this electrocardiographic pattern, which is equivalent to acute myocardial infarction with ST segment elevation, require consideration of emergency reperfusion therapy due to high mortality, compared to other patients with acute myocardial infarction without ST elevation. Primary percutaneous intervention is recommended, or if there is no catheterization laboratory nearby, fibrinolytic therapy may be considered. Because of the lack of clear recommendations, treatment decisions are made individually, from case to case. **Conclusion.** We need large prospective studies with this specific electrocardiographic pattern to provide quick recognition and proper treatment of the anterior myocardial infarction with ST elevation.

Key words: Electrocardiography; ST Elevation Myocardial Infarction; Non-ST Elevated Myocardial Infarction; Early Diagnosis; Reperfusion; Percutaneous Coronary Intervention

Sažetak

Uvod. Brza dijagnostika akutnog infarkta miokarda je neophodna zbog pravilnog lečenja i smanjenja mortaliteta bolesnika. Važna uloga u dijagnostici pripada elektrokardiogramu. Akutni infarkt miokarda sa ST elevacijom zahteva urgentnu reperfuziju, prvenstveno primarnu perkutanu angioplastiku. Postoji mala grupa bolesnika koja ima akutni infarkt miokarda sa denivelacijom ST segmenta u više odvoda i elevacijom ST segmenta u aVR; elektrokardiografski se prikazuje kao infarkt miokarda bez ST elevacije, ali klinički tok i težina bolesti odgovaraju anteriornom infarktu miokarda sa ST elevacijom. **Elektrokardiogram de Vinterovog T-talasa.** Jedan od tih oblika je poznat kao De Winterov T-talasa. Karakteriše ga depresija ST segmenta i J tačke (> 1 mm) u prekordijalnim odvodima, odsustvo elevacije ST segmenta u prekordijalnim odvodima, visok, šiljat i simetričan T-talasa u prekordijalnim odvodima i, u većini slučajeva, blaga elevacija ST segmenta (0,5 mm do 1 mm) u aVR. Ovi bolesnici imaju okluziju glavnog stabla leve koronarne arterije, okluzije proksimalnog segmenta prednje silazne arterije ili tešku višesudovnu koronarnu bolest. Bolesnici sa pomenutim elektrokardiogramom, koji predstavlja ekvivalent akutnog infarkta miokarda sa elevacijom ST segmenta, zahtevaju razmatranje urgentne reperfuzione terapije jer imaju veći mortalitet u poređenju sa drugim bolesnicima sa akutnim infarktom miokarda bez ST elevacije. Preporučuje se primarna perkutana intervencija, ali u slučaju da u blizini ne postoji referentni centar, može se razmotriti i fibrinolitička terapija. Za sada, s obzirom da ne postoje jasne smernice, odlučivanje o načinu lečenja je individualno, od slučaja do slučaja. **Zaključak.** Neophodne su velike prospektivne studije da bi se ovaj ekvivalent akutnog infarkta miokarda sa ST elevacijom ekvivalent brzo prepoznao i adekvatno lečio kao prednji ST elevirani infarkt miokarda.

Ključne reči: elektrokardiografija; STEMI; NSTEMI; rana dijagnoza; znaci i simptomi; reperfuzija; perkutana koronarna intervencija

Abbreviations

| | |
|--------|---|
| STEMI | – ST-elevation myocardial infarction |
| MI | – myocardial infarction |
| AMI | – acute myocardial infarction |
| ECG | – electrocardiogram |
| NSTEMI | – non-ST-elevation myocardial infarction |
| LAD | – left anterior descending coronary artery |
| ATP | – adenosine triphosphate |
| KATP | – adenosine triphosphate-sensitive potassium channels |
| pPCI | – primary percutaneous coronary intervention |

Introduction

Acute myocardial infarction (AMI) is a clinical manifestation of coronary disease resulting from coronary artery occlusion that leads to irreversible myocardial ischemia and progresses to myocardial necrosis. In contrast to stable and unstable angina pectoris, where ischemia is transient and myocardial changes are reversible, AMI is characterized by a permanent damage, loss of cardiac tissue, and impairment of left ventricular function [1].

The term AMI is used for myocardial necrosis with evidence of myocardial ischemia, specific electrocardiogram (ECG) findings, elevated biomarkers of myocardial necrosis, by imaging, or may be defined by pathology. The terminology and diagnostic criteria for the diagnosis of myocardial infarction (MI) have changed over the time [2].

For the sake of immediate reperfusion treatment, it is usual practice to differentiate MI with ST elevation in two contiguous leads, as ST elevation myocardial infarction (STEMI), and MI without ST elevation, usually designated as non-ST elevation myocardial infarction (NSTEMI). ECG manifestations of acute myocardial ischemia with ST segment elevation are at the J-point in at least two contiguous leads with the cut-points: ≥ 2.5 mm in men < 40 years, ≥ 2 mm in men ≥ 40 years, or ≥ 1.5 mm in women in leads V2 – V3 and/or ≥ 1 mm in other leads (in the absence of left ventricular hypertrophy or left bundle branch block). Likewise, ST segment depression in leads V1 – V3 suggests myocardial ischemia, especially when the terminal T-wave is positive (ST segment elevation equivalent), and confirmation by concomitant ST segment elevation ≥ 0.5 mm recorded in leads V7 – V9 should be considered as a means to identify posterior MI.

Rapid detection of these two types of MI is done by implementation of the guidelines for the management of acute coronary syndromes in patients presenting with ST segment elevation or without persistent ST segment elevation, having a have different approach to invasive treatment strategy [4, 5].

It should be emphasized that nonspecific ECG changes, such as complete left bundle branch block and changes in avR lead, make the diagnosis of MI more difficult [6, 7]. A great diagnostic problem are some ECG patterns called ST elevation myocardial infarction equivalents. They are: ST segment elevation in avR lead indicating left main coronary artery stenosis, the left main coronary artery stenosis, the

left bundle branch block in myocardial infarction, and posterior myocardial infarction [6–8]. In some cases, chest pain along with the signs of ischemia on ECG and cardiac enzymes may be caused by conditions other than coronary, like in myopericarditis [9].

The European Society of Cardiology (ESC) Guidelines for the management of AMI in patients with ST segment elevation [4] recognized atypical electrocardiographic presentations that should prompt a primary percutaneous coronary intervention strategy in patients with ongoing symptoms consistent with myocardial ischemia: bundle branch block, ventricular paced rhythm, isolated posterior MI (ST segment depression ≥ 0.5 mm in leads V1 – V3, and elevation in V7 – V9 ≥ 0.5), and ischemia due to left main coronary artery occlusion with ST depression ≥ 1 mm in eight or more surface leads (inferolateral ST depression), associated with ST segment elevation in avR and/or V1. These patients are easily overlooked and they may potentially benefit from emergent reperfusion therapy, because they present with higher mortality, compared to other patients with AMI without ST elevation [10, 11].

Thus, precise identification of the dynamics of the QRS complex, T wave and ST segment associated with acute proximal occlusion of major epicardial coronary artery is essential in predicting the size of the affected myocardium and determining the need for urgent reperfusion therapy [12, 13].

Electrocardiographic and clinical characteristics of de Winter pattern

In 2008, Robert J, de Winter RJ, and Wellens HJ, published a study and for the first time pointed out the importance of recognizing the equivalent of AMI with ST segment elevation and the need for emergency myocardial reperfusion. The analyzed data obtained from the percutaneous coronary intervention database, electrocardiographic examinations in the first contact with the patient, electrocardiographic review before the intervention, the findings of coronary angiography, helped them to describe a new electrocardiographic pattern without ST segment elevation that signified an occlusion of the anterior descending coronary artery. Instead of ST elevation, ST segment showed a 1 to 3 mm upsloping ST segment depression at the J-point in leads V1 to V6 that continued into tall, positive symmetrical T waves of the same leads. The QRS complexes were usually of normal width or slightly wider, sometimes with reduced R wave in the same leads. In most patients there was a ST elevation of 1 to 2 mm in the avR lead, persisting from the first ECG until the preprocedural ECG was performed and angiographic evidence of an occluded left anterior descending coronary artery (LAD) was obtained. Of 1.532 patients with acute AMI, this electrocardiographic pattern was found in 30 (2%), and it was termed by the author - de Winter T pattern [14]. Some call it de Winter syndrome [15], some de Winter T-wave [16, 17].

De Winter ECG pattern is a specific anterior STEMI equivalent, but presents like a NSTEMI [15]. Diagnostic criteria for de Winter pattern include:

1. Tall, prominent, symmetric T-waves in the precordial leads,
2. Upsloping ST segment depression >1 mm at the J-point in the precordial leads,
3. Absence of ST elevation in the precordial leads,
4. ST segment elevation (0.5 mm – 1 mm) in aVR, and
5. Normal STEMI morphology may precede or follow the de Winter pattern.

The de Winter pattern may be confused with hyperacute T waves which occur within minutes of coronary artery occlusion and progress rapidly to classical STEMI pattern [16] (**Figure 1**).

Verouden et al. [16] confirmed the results of de Winter and Wellens in their research conducted a year later. They established de Winter T-wave in 35 of 1.890 patients who needed percutaneous coronary intervention in the LAD artery (about 2% of subjects). Patients with de Winter T-wave were younger, more often male, with a greater incidence of hypercholesterolemia compared with patients with classi-

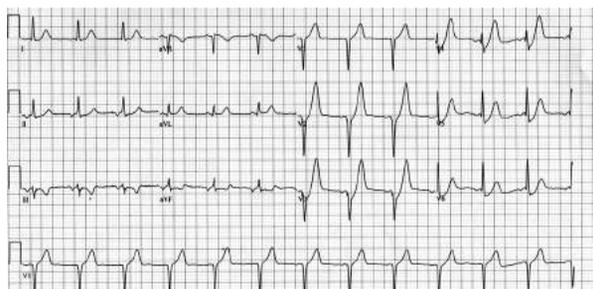


Figure 1. The electrocardiogram revealed upsloping ST segment depression at the J-point in leads V3 – V6, with prominent T-waves and slight ST segment elevation evident in the aVR lead

Slika 1. Elektrokardiogram (EKG) pokazuje ushodnu depresiju ST segmenta sa depresijom J tačke u odvodima V3-V6, sa visokim T-talasima i blagom ST elevacijom u odvodu desnog proširenog vektora

cal MI with ST segment elevation and LAD artery occlusion.

Another large retrospective study monitored ECG changes and coronary angiography findings in patients with NSTEMI infarction. ST segment depression ≥ 0.05 mV in more than two contiguous leads was recorded and classified as upsloping or non-upsloping. Of 330 patients, 109 (33%) had ST segment depression; only six had an upsloping depression, and all had a culprit lesion and underwent urgent revascularization: three had a culprit lesion of the LAD artery, two of circumflex artery, and one patient had a serious three-vessel disease. At the same time, all had higher troponin levels and lower systolic left ventricular function than patients

with non-upsloping ST segment depression did. Two patients had lesions of the dominant circumflex artery within the posterior MI, which has been described in the literature [18].

De Winter et al. proposed that an anatomical variant of Purkinje fibers with an endocardial conduction delay may be responsible for the ECG changes. They also hypothesized that the absence of ST elevation could be related to the lack of activation of sarcolemmal adenosine triphosphate (ATP) - sensitive potassium channels (KATP) by ischemic ATP depletion as shown in KATP knock-out animal models of acute ischemia [19]. Verouden et al. hypothesized that patients with such pattern have a very extensive transmural ischemic area of infarction that generates only little current which is not sufficient to travel toward the precordial leads but can go toward the aVR lead [16]. The exact mechanism of evolution of this pattern is still a matter of debate [20]. The de Winter ECG pattern had positive predictive values of 95.2% (95% confidence interval: 76.2 – 99.9%), 100% (69.2 – 100.0%) and 100% (51.7 – 100%) in three diagnostic studies, respectively. The available data suggest that the pattern had high positive predictive value for acute occlusion [21].

Information about electrographic changes related to de Winter syndrome is limited, usually from sporadic case reports.

Goktas et al. [15] reported a case of a 34-year-old woman with extended chest pain whose first ECG showed STEMI equivalent phenomenon associated with acute occlusion of the LAD artery (ST-segment depression > 1 mm at the J-point in leads V3 – V6, with tall, positively symmetrical T-waves, ST segment elevation of 0.5 mm in aVR lead). She had a history of heavy smoking and hypercholesterolemia. Urgent primary percutaneous coronary intervention (pPCI) was performed, opening the middle of the left descending artery total occlusion. After a successful intervention, the ECG returned to normal. Actually, American Guide recommended pPCI in the first two hours of first medical contact in patients with STEMI-equivalents ECG patterns [22]. Most patients with this ECG pattern had risk factors. The most common were hypertension and hyperlipoproteinemia. Authors presented cases of men who came to the emergency department with long-term chest pain, but their first troponin values were normal. Based on the ECG showing de Winter phenomenon, urgent coronary angiography was done revealing proximal occlusion of the LAD coronary artery in these patient. They were successfully treated via mechanical reperfusion therapy and stent placement [20, 23].

Qayyum et al. presented a case of an older woman with anginal pain and ECG with ST segment elevation in the inferolateral leads. During the evaluation in the Emergency Department, dynamics in ECG changed to the de Winter ECG pattern. It was the reason for emergency coronary angiography and primary PCI of the culprit lesion of the LAD artery. Once again the importance of monitoring and iden-

tification of ECG patterns was emphasized, particularly in the case of STEMI equivalents that are the hallmark of acute coronary occlusion [24].

De Winter RW et al. reported another three cases with typical symptoms of AMI accompanied by ECG patterns lacking ST segment elevation and exhibiting slight J-point ST wave depression combined with high symmetrical T-waves. Urgent coronary angiography revealed complete occlusion of the LAD coronary artery and PCI was successfully performed [25].

Timely reperfusion therapy, primary PCI, was the preferred treatment for patients with ST elevation MI, and early recognition of STEMI equivalents give a chance to patients with AMI induced by occlusion of an epicardial coronary artery to obtain reperfusion and a greater chance of survival. The great dilemma was how to treat patients with de Winter pattern in hospitals without interventional cardiology. There are no clear recommendations for fibrinolysis in such cases, apart from conservative treatment. The proposal of Indonesian authors for these patients in rural areas was to con-

sider fibrinolysis, especially in young people with strong chest pain and acute coronary lesion in the period up to 3 hours from the start of symptoms and de Winter T-wave ECG pattern [17].

Conclusion

It is of great importance for physicians in emergency departments to recognize the de Winter syndrome, a condition associated with typical chest pain and a characteristic electrocardiogram pattern without ST segment elevation, which usually suggests acute total occlusion of the proximal left anterior descending coronary artery. Rapid recognition may provide early treatment, and many patients may benefit from urgent invasive revascularization instead of conservative strategy. The de Winter T-wave electrocardiogram pattern is yet to be included in European Society of Cardiology and American College of Cardiology/American Heart Association guidelines for management of acute coronary syndromes in both persistent and non-persistent ST elevation.

References

1. Vasiljević Z. Acute coronary syndrome. In: Ostojić M, Kanjuh V, Beleslin B, editors. *Cardiology*. Beograd: Zavod za udžbenike; 2011. p. 423-64.
2. Kovačević B, Štajnić M, Čemerlić Adjić N, Dejanović J. Terminologija i dijagnostički kriterijumi non-Q-infarakta miokarda. *Med Pregl*. 2002;55(1-2):28-33.
3. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. *Eur Heart J*. 2012;33:2551-67.
4. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39(2):119-77.
5. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016;37(3):267-315.
6. Ivanov I, Bugarski S, Dejanović J, Stojšić-Milosavljević A, Radišić-Bosić J, Vujan B. Electrocardiographic signs of acute myocardial infarction in left bundle branch block. *Med Pregl*. 2013;66(11-12):503-6.
7. Ivanov I, Dejanović J, Čurić I, Ivanov M, Čikoš J, Radišić B, et al. Right ventricular infarction. *Medicina danas*. 2003;2(3-4):239-49.
8. Ivanov I, Jaraković M, Dejanović J, Petrović M, Srdanović I, Obradović D. Diagnostic and prognostic utility of aVR lead in electrocardiogram. *Medicinski časopis*. 2014;48(2):104-7.
9. Ivanov I, Dejanović J, Ivanov O, Petrović M, Jung R, Panić G. Miopericarditis - diagnostic dilemmas in relation to acute myocardial infarction. *Med Pregl*. 2013;66(9-10):396-400.
10. Hennings JR, Fesmire FM. A new electrocardiographic criteria for emergent reperfusion therapy. *Am J Emerg Med*. 2012;30(6):994-1000.
11. Ivanov I, Lovrenski A, Dejanović J, Petrović M, Jung R, Raffay V. Double heart rupture after acute myocardial infarction: a case report. *Vojnosanit Pregl*. 2014;71(12):1151-4.
12. Engelen DJ, Gorgels AP, Cheriex EC, De Muinck ED, Ophuis AJ, Dassen WR, et al. Value of the electrocardiogram in localizing the occlusion site in the left anterior descending coronary artery in acute anterior myocardial infarction. *J Am Coll Cardiol*. 1999;34(2):389-95.
13. Wang K, Asinger RW, Marriott HJ. ST-segment elevation in conditions other than acute myocardial infarction. *N Engl J Med*. 2003;349(22):2128-35.
14. de Winter RJ, Verouden NJ, Wellens HJ, Wilde AA; Interventional Cardiology Group of the Academic Medical Center. A new ECG sign of proximal LAD occlusion. *N Engl J Med*. 2008;359(19):2071-3.
15. Goktas MU, Sogut O, Yigit M, Kaplan O. A novel electrocardiographic sign of an ST-segment elevation myocardial infarction-equivalent: De Winter. *Cardiol Res*. 2017;8(4):165-8.
16. Verouden NJ, Koch KT, Peters RJ, Henriques JP, Baan J, van der Schaaf RJ, et al. Persistent precordial "hyperacute" T-waves signify proximal left anterior descending artery occlusion. *Heart*. 2009;95(20):1701-6.
17. Pranata R, Huang I, Damay V. Should de Winter T-wave electrocardiography pattern be treated as ST-segment elevation myocardial infarction equivalent with consequent reperfusion? A dilemmatic experience in rural area of Indonesia. *Case Rep Cardiol*. 2018;2018:6868204.
18. Misumida N, Kobayashi A, Schweitzer P, Kanei Y. Prevalence and clinical significance of up-sloping ST-segment depression in patients with non-ST-segment elevation myocardial infarction. *Cardiol Res*. 2015;6(4-5):306-10.

19. Li RA, Leppo M, Miki T, Seino S, Marban E. Molecular basis of electrocardiographic ST-segment elevation. *Circ Res.* 2000;87(10):837-9.

20. Goebel M, Bledsoe J, Orford JL, Mattu A, Brady WJ. A new ST-segment elevation myocardial infarction equivalent pattern? Prominent T wave and J-point depression in the precordial leads associated with ST-segment elevation in lead aVr. *Am J Emerg Med.* 2014;32(3):287.e5-8.

21. Morris NP, Body R. The De Winter ECG pattern: morphology and accuracy for diagnosing acute coronary occlusion systematic review. *Eur J Emerg Med.* 2017;24(4):236-42.

22. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report

of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013;127(4):e362-425.

23. Zhao YT, Huang YS. ECG pattern associated with left anterior descending coronary artery occlusion. *N Engl J Med.* 2018;378(16):e22.

24. Qayyum H, Hemaya S, Squires J, Adam Z. Recognising the de Winter ECG pattern – a time critical electrocardiographic diagnosis in the Emergency Department. *J Electrocardiol.* 2018;51(3):392-5.

25. de Winter RW, Adams R, Verouden NJ, de Winter RJ. Precordial junctional ST-segment depression with tall symmetric T-waves signifying proximal LAD occlusion, case reports of STEMI equivalence. *J Electrocardiol.* 2016;49(1):76-80.

Rad je primljen 3. VII 2018.

Recenziran 6. VII 2018.

Prihvaćen za štampu 9. VII 2018.

BIBLID.0025-8105:(2018):LXXI:7-8:265-269.

UPUTSTVO ZA AUTORE

Časopis *Medicinski pregled* objavljuje radove koji prethodno nisu objavljeni niti poslani u drugi časopis. U Časopisu mogu biti objavljeni radovi iz različitih oblasti biomedicine, koji su namenjeni lekarima različitih specijalnosti.

Od 1. januara 2013. godine *Medicinski pregled* je počeo da koristi usluge *e-Ur* – Elektronskog uređivanja časopisa. Svi korisnici sistema – autori, recenzenti i urednici, moraju biti registrovani korisnici sa jednom elektronskom adresom.

Korisnici časopisa treba da se registruju na adresi:

<http://aseestant.ceon.rs/index.php/medpreg/user/register>

Prijava rada treba da se učini na adresi:

<http://aseestant.ceon.rs/index.php/medpreg/>

U postupku prijave neophodno je da se pošalje saglasnost i izjava autora i svih koautora da rad nije delimično ili u celini objavljen ili prihvaćen za štampu u drugom časopisu.

Elektronsko uređivanje časopisa obezbeđuje korišćenje sistema *CrossCheck*, koji prijavljene radove automatski proverava na plagijarizam i autoplagijarizam. Autori ne bi smeli da pošalju isti rad u više časopisa istovremeno. Ukoliko se to desi, glavni urednik časopisa *Medicinski pregled* ima pravo da rad vrati autorima bez prethodnog slanja rada na recenziju; da odbije štampanje rada; da se obrati urednicima drugih časopisa u koje je rad poslat ili da se obrati direktoru ustanove u kojoj su autori rada zaposleni.

Primaju se samo radovi koji su napisani na engleskom jeziku, uz sažetak rada i naslov rada koji treba da budu napisani na engleskom i srpskom jeziku.

Radove koji su pristigli u časopis *Medicinski pregled* pregleda jedan ili više članova Uređivačkog odbora Časopisa. Oni radovi koji su napisani prema pravilima Časopisa šalju se na anonimnu recenziju kod najmanje dva recenzenta, stručnjaka iz odgovarajuće oblasti biomedicine. Načinjene recenzije radova pregleda glavni urednik ili članovi Uređivačkog odbora i one nisu garancija da će rad biti prihvaćen za štampu. Materijal koji je pristigao u časopis ostaje poverljiv dok se rad nalazi na recenziji, a identitet autora i recenzentata su zaštićeni, osim u slučaju ako oni odluče drugačije.

U časopisu *Medicinski pregled* objavljuju se: uvodnici, originalni članci, prethodna ili kratka saopštenja, pregledni članci, stručni članci, prikazi slučajeva, članci iz istorije medicine i drugi članci.

1. Uvodnici – do 5 strana. Sadrže mišljenja ili diskusiju o posebno značajnoj temi za Časopis, kao i o podacima koji su štampani u ovom ili nekom drugom časopisu. Obično ih piše jedan autor po pozivu.

2. Originalni članci – do 12 strana. Predstavljaju rezultate istraživanja autora rada i njihovo tumačenje. Istraživanje treba da bude obrađeno i izloženo na način da se može ponoviti, a analiza rezultata i zaključci jasni da bi se mogli proveriti.

3. Pregledni članci – do 10 strana. Predstavljaju sistematsko, sveobuhvatno i kritičko izlaganje problema na osnovu analiziranih i diskutovanih podataka iz literature, a koji oslikavaju postojeću situaciju u određenom području istraživanja. Literatura koja se koristi u radu mora da sadrži najmanje 5 radova autora članka iz uže naučne oblasti koja je opisana u radu.

4. Prethodna ili kratka saopštenja – do 4 strane. Sadrže izuzetno važne naučne rezultate koje bi trebalo objaviti u što kraćem vremenu. Ne moraju da sadrže detaljan opis metodologije rada i rezultata, ali moraju da imaju sva poglavlja kao originalni članci u sažetoj formi.

5. Stručni članci – do 10 strana. Odnose se na proveru ili prikaz prethodnog istraživanja i predstavljaju koristan izvor za širenje znanja i prilagođavanja originalnog istraživanja potrebama postojeće nauke i prakse.

6. Prikazi slučajeva – do 6 strana. Opisuju retke slučajeve iz prakse. Slični su stručnim člancima. U ovim radovima pri-

kazuju se neobičajeni oblici i tokovi oboljenja, neočekivane reakcije na primenjenu terapiju, primene novih dijagnostičkih procedura ili retke i nove bolesti.

7. Članci iz istorije medicine – do 10 strana. Ovi članci opisuju događaje iz prošlosti sa ciljem da omoguće očuvanje medicinske i zdravstvene kulture. Imaju karakter stručnih članaka.

8. Ostali članci – U časopisu *Medicinski pregled* objavljuju se feljtoni, prikazi knjiga, izvodi iz strane literature, izveštaji sa kongresa i stručnih sastanaka, saopštenja o radu pojedinih zdravstvenih organizacija, podružnica i sekcija, saopštenja Uredništva, pisma Uredništvu, novosti u medicini, pitanja i odgovori, stručne i staleške vesti i članci napisani u znak sećanja (*In memoriam*).

Priprema rukopisa

Kompletan rukopis, uključujući tekst rada, sve priloge i propratno pismo, treba poslati na elektronsku adresu koja je prethodno navedena.

Propratno pismo:

– mora da sadrži izjavu svih autora da se radi o originalnom radu koji prethodno nije objavljen niti prihvaćen za štampu u drugim časopisima;

– autori svojim potpisom preuzimaju odgovornost da rad ispunjava sve postavljene uslove i da ne postoji sukob interesa i

– autor mora navesti kategoriju članka (originalni rad, pregledni rad, prethodno saopštenje, stručni rad, prikaz slučaja, rad iz istorije medicine, itd.).

Rukopis

Opšta uputstva

Tekst rada treba da bude napisan u programu *Microsoft Word* za *Windows*, na A4 formatu stranice (sve četiri margine 2,5 cm), proreda 1,5 (isto važi i za tabele), fontom *Times New Roman*, veličinom slova 12 pt. Neophodno je koristiti međunarodni sistem mernih jedinica (*SI*), uz izuzetak temperature ($^{\circ}C$) i krvnog pritiska (*mmHg*).

Rukopis treba da sadrži sledeće elemente:

1. Naslovna strana

Naslovna strana treba da sadrži: kratak i sažet naslov rada, bez skraćenica, skraćeni naslov rada (do 40 karaktera), imena i prezimena autora (ne više od 6) i afilijacije svih autora. Na dnu strane treba da piše ime, prezime i titula autora zaduženog za korespondenciju, njena/njegova adresa, elektronska adresa, broj telefona i faksa.

2. Sažetak

Sažetak ne može da sadrži više od 250 reči niti skraćenice. Treba da bude strukturisan, kratak i sažet, sa jasnim pregledom problema istraživanja, ciljevima, metodama, značajnim rezultatima i zaključcima.

Sažetak originalnih i stručnih članaka treba da sadrži uvod (sa ciljevima istraživanja), materijale i metode, rezultate i zaključak.

Sažetak prikaza slučaja treba da sadrži uvod, prikaz slučaja i zaključak.

Sažetak preglednih članaka treba da sadrži Uvod, podnaslove koji odgovaraju istima u tekstu i Zaključak.

Navesti do 10 ključnih reči ispod sažetka. One su pomoć prilikom indeksiranja, ali autorove ključne reči mogu biti izmenjene u skladu sa odgovarajućim deskriptorima, odnosno terminima iz *Medical Subject Headings, MeSH*.

Sažetak treba da bude napisan na srpskom i engleskom jeziku. Sažetak na srpskom jeziku trebalo bi da predstavlja prevod sažetka na engleskom, što podrazumeva da sadrži jednake delove.

3. Tekst članka

Originalni rad treba da sadrži sledeća poglavlja: Uvod (sa jasno definisanim ciljevima istraživanja), Materijal i metode, Rezultati, Diskusija, Zaključak, spisak skraćenica (ukoliko su

korišćene u tekstu). Nije neophodno da se u posebnom poglavlju rada napiše zahvalnica onima koji su pomogli da se istraživanje uradi, kao i da se rad napiše.

Prikaz slučaja treba da sadrži sledeća poglavlja: Uvod (sa jasno definisanim ciljevima), Prikaz slučaja, Diskusija i Zaključak.

Uvod

U poglavlju Uvod potrebno je jasno definisati predmet istraživanja (prirodu i značaj istraživanja), navesti značajne navode literature i jasno definisati ciljeve istraživanja i hipoteze.

Materijal i metode

Materijal i metode rada treba da sadrže podatke o vrsti studije (prospektivna/retrospektivna, uslove za uključivanje i ograničenja studije, trajanje istraživanja, demografske podatke, period praćenja). Detaljno treba opisati statističke metode da bi čitaoci rada mogli da provere iznesene rezultate.

Rezultati

Rezultati predstavljaju detaljan prikaz podataka koji su dobijeni istraživanjem. Sve tabele, grafikoni, sheme i slike moraju biti citirani u tekstu rada i označeni brojevima po redosledu njihovog navođenja.

Diskusija

Diskusija treba da bude koncizna, jasna i da predstavlja tumačenje i poređenje rezultata studije sa relevantnim studijama koje su objavljene u domaćoj i međunarodnoj literaturi. U poglavlju Diskusija potrebno je naglasiti da li su postavljene hipoteze potvrđene ili nisu, kao i istaknuti značaj i nedostatke istraživanja.

Zaključak

Zaključci moraju proisteći isključivo iz rezultata istraživanja rada; treba izbegavati uopštene i nepotrebne zaključke. Zaključci koji su navedeni u tekstu rada moraju biti u saglasnosti sa zaključcima iz Sažetka.

4. Literatura

Potrebno je da se literatura numeriče arapskim brojevima redosledom kojim je u tekstu navedena u parentezama; izbegavati nepotrebno velik broj navoda literature. Časopise bi trebalo navoditi u skraćenom obliku koji se koristi u *Index Medicus* (<http://www.nlm.nih.gov/tsd/serials/lji.html>). Pri citiranju literature koristiti Vankuverski sistem. Potrebno je da se navedu svi autori rada, osim ukoliko je broj autora veći od šest. U tom slučaju napisati imena prvih šest autora praćeno sa *et al.*

Primeri pravilnog navođenja literature nalaze se u nastavku.

Radovi u časopisima

* Standardni rad

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. *J Thromb Haemost* 2003;1:1435-42.

* Organizacija kao autor

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002;40(5):679-86.

* Bez autora

21st century heart solution may have a sting in the tail. *BMJ*. 2002;325(7357):184.

* Volumen sa suplementom

Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxis. *Pharmacol Res Commun* 1988;20 Suppl 5:75-8.

* Sveska sa suplementom

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. *J Clin Psychopharmacol* 1988;8(4 Suppl):31S-37S.

* Sažetak u časopisu

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by *Toxoplasma gondi* [abstract]. *Clin Res* 1987;35:475A.

Knjige i druge monografije

* Jedan ili više autora

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical microbiology*. 4th ed. St. Louis: Mosby; 2002.

* Urednik (urednici) kao autor (autori)

Danset J, Colombani J, eds. *Histocompatibility testing* 1972. Copenhagen: Munksgaard, 1973:12-8.

* Poglavlje u knjizi

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: Saunders; 1974. p. 457-72.

* Zbornik radova sa kongresa

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.

* Disertacija

Borkowski MM. *Infant sleep and feeding: a telephone survey of Hispanic Americans* [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

Elektronski materijal

* Članak iz časopisa u elektronskom formatu

Aboud S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

* Monografija u elektronskom formatu

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

* Kompjuterska datoteka

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

5. Prilozi (tabele, grafikoni, sheme i slike)

BROJ PRILOGA NE SME BITI VEĆI OD ŠEST!

Tabele, grafikoni, sheme i slike se postavljaju kao posebni dokumenti.

– Tabele i grafikone bi trebalo pripremiti u formatu koji je kompatibilan programu u kojem je napisan tekst rada. Slike bi trebalo poslati u jednom od sledećih oblika: *JPG, GIF, TIFF, EPS*.

– Svaki prilog mora biti obeležen arapskim brojem prema redosledu po kojem se navodi u tekstu rada.

– Naslovi, tekst u tabelama, grafikonima, shemama i legende slika bi trebalo da budu napisani na srpskom i engleskom jeziku.

– Nestandardne priloge označiti u fusnoti uz korišćenje sledećih simbola: *, †, ‡, §, ||, ¶, **, † †, ‡ ‡.

– U legendi slika trebalo bi napisati korišćeno uveličanje okulara i objektivna mikroskopa. Svaka fotografija treba da ima vidljivu skalu.

– Ako su tabele, grafikoni, sheme ili slike već objavljene, navesti originalni izvor i priložiti pisano odobrenje autora za njihovo korišćenje.

– Svi prilozi će biti štampani kao crno-bele slike. Ukoliko autori žele da se prilozi štampaju u boji, obavezno treba da plate dodatne troškove.

6. Dodatne obaveze

AUTORI I SVI KOAUTORI RADA OBAVEZNO TREBA DA PLATE GODIŠNJU PRETPLATU ZA ČASOPIS *MEDICINSKI PREGLED*. U PROTIVNOM, RAD NEĆE BITI ŠTAMPAN U ČASOPISU.

INFORMATION FOR AUTHORS

Medical Review publishes papers (previously neither published in nor submitted to any other journals) from various fields of biomedicine intended for broad circles of doctors.

Since January 1st, 2013 the Medical Review has been using the service e-Ur: Electronic Journal Editing. All users of the Registration system, i.e. authors, reviewers, and editors have to be registered users with only one e-mail address. Registration should be made on the web address:

<http://aseestant.ceon.rs/index.php/medpreg/user/register>.

Manuscript submission should be made on the web address:

<http://aseestant.ceon.rs/index.php/medpreg/>

A SUPPLEMENTARY FILE, WITH THE STATEMENT THAT THE PAPER HAS NOT BEEN SUBMITTED OR ACCEPTED FOR PUBLICATION ELSEWHERE AND A CONSENT SIGNED BY ALL AUTHORS, HAVE TO BE ENCLOSED WITH THE MANUSCRIPT.

Authors may not send the same manuscript to more than one journal concurrently. If this occurs, the Editor may return the paper without reviewing it, reject the paper, contact the Editor of the other journal(s) in question and/or contact the author's employers.

Papers should be written in English language, with an abstract and title page in English, as well as in Serbian language.

All papers submitted to **Medical Review** are seen by one or more members of the Editorial Board. Suitable articles are sent to at least two experts to be reviewed, their reports are returned to the assigned member of the Editorial Board and the Editor. Revision of an article gives no guarantee of acceptance and in some cases revised articles are rejected if the improvements are not sufficient or new issues have arisen. Material submitted to *the Journal* remains confidential while being reviewed and peer-reviewers' identities are protected unless they elect to lose anonymity.

Medical Review publishes the following types of articles: editorials, original studies, preliminary reports, review articles, professional articles, case reports, articles from history of medicine and other types of publications.

1. Editorials – up to 5 pages – convey opinions or discussions on a subject relevant for the Journal. Editorials are commonly written by one author by invitation.

2. Original studies – up to 12 pages – present the authors' own investigations and their interpretations. They should contain data which could be the basis to check the obtained results and reproduce the investigative procedure.

3. Review articles – up to 10 pages – provide a condensed, comprehensive and critical review of a problem on the basis of the published material being analyzed and discussed, reflecting the current situation in one area of research. Papers of this type will be accepted for publication provided that the authors confirm their expertise in the relevant area by citing at least 5 self-citations.

4. Preliminary reports – up to 4 pages – contain scientific results of significant importance requiring urgent publishing; however, it need not provide detailed description for repeating the obtained results. It presents new scientific data without a detailed explanation of methods and results. It contains all parts of an original study in an abridged form.

5. Professional articles – up to 10 pages – examine or reproduce previous investigation and represent a valuable source of knowledge and adaption of original investigations for the needs of current science and practice.

6. Case reports – up to 6 pages – deal with rare casuistry from practice important for doctors in direct charge of patients and are similar to professional articles. They emphasize unusual characteristics and course of a disease, unexpected reactions to a therapy, application of new diagnostic procedures and describe a rare or new disease.

7. History of medicine – up to 10 pages – deals with history with the aim of providing continuity of medical and health care culture. They have the character of professional articles.

8. Other types of publications – The journal also publishes feuilletons, book reviews, extracts from foreign literature, reports from congresses and professional meetings, communications on activities of certain medical institutions, branches and sections, announcements of the Editorial Board, letters to the Editorial Board, novelties in medicine, questions and answers, professional and vocational news and In memoriam.

Preparation of the manuscript

The complete manuscript, including the text, all supplementary material and covering letter, is to be sent to the web address above.

The covering letter:

– It must contain the proof given by the author that the paper represents an original work that it has neither been previously published in other journals nor is under consideration to be published in other journals.

– It must confirm that all the authors meet criteria set for the authorship of the paper, that they agree completely with the text and that there is no conflict of interest.

– It must state the type of the paper submitted (an original study, a review article, a preliminary report, a professional article, a case report, history of medicine).

The manuscript:

General instructions.

Use Microsoft Word for Windows to type the text. The text must be typed in font *Times New Roman*, page format A4, space 1.5 (for tables as well), margins set to 2.5 cm and font size 12pt. All measurements should be reported in the metric system of the International System of Units – SI. Temperature should be expressed in Celsius degrees (°C) and pressure in mmHg.

The manuscript should contain the following elements:

1. The title page.

The title page should contain a concise and clear title of the paper, without abbreviations, then a short title (up to 40 characters), full names and surnames of the authors (not more than 6) indexed by numbers corresponding to those given in the heading along with the full name and place of the institutions they work for. Contact information including the academic degree(s), full address, e-mail and number of phone or fax of the corresponding author (the author responsible for correspondence) are to be given at the bottom of this page.

2. Summary.

The summary should contain up to 250 words, without abbreviations, with the precise review of problems, objectives, methods, important results and conclusions. It should be structured into the paragraphs as follows:

– Original and professional papers should have the introduction (with the objective of the paper), materials and methods, results and conclusion

– Case reports should have the introduction, case report and conclusion

– Review papers should have the introduction, subtitles corresponding to those in the paper and conclusion.

The authors should provide up to 10 keywords below the summary. These keywords will assist indexers in cross-indexing the article and will be published with the summary, but the authors' keywords could be changed in accordance with the list of Medical Subject Headings, MeSH of the American National Medical Library.

The summary should be written in both languages, English as well as Serbian. The summary in Serbian language should be the translation of the summary in English; therefore, it has to contain the same paragraphs.

3. The text of the paper.

The text of original studies must contain the following: introduction (with the clearly defined objective of the study), materials and methods, results, discussion, conclusion, list of abbreviations (if used in the text) and not necessarily, the acknowledgment mentioning those who have helped in the investigation and preparation of the paper.

The text of a case report should contain the following: introduction (with clearly defined objective of the study), case report, discussion and conclusion.

Introduction contains clearly defined problem dealt with in the study (its nature and importance), with the relevant references and clearly defined objective of the investigation and hypothesis.

Materials and methods should contain data on design of the study (prospective/retrospective, eligibility and exclusion criteria, duration, demographic data, follow-up period). Statistical methods applied should be clear and described in details.

Results give a detailed review of data obtained during the study. All tables, graphs, schemes and figures must be cited in the text and numbered consecutively in the order of their first citation in the text.

Discussion should be concise and clear, interpreting the basic findings of the study in comparison with the results of relevant studies published in international and national literature. It should be stated whether the hypothesis has been confirmed or denied. Merits and demerits of the study should be mentioned.

Conclusion must deny or confirm the attitude towards the Obased solely on the author's own results, corroborating them. Avoid generalized and unnecessary conclusions. Conclusions in the text must be in accordance with those given in the summary.

4. References are to be given in the text under Arabic numerals in parentheses consecutively in the order of their first citation. Avoid a large number of citations in the text. The title of journals should be abbreviated according to the style used in Index Medicus (<http://www.nlm.nih.gov/tsd/serials/lji.html>). Apply Vancouver Group's Criteria, which define the order of data and punctuation marks separating them. Examples of correct forms of references are given below. List all authors, but if the number exceeds six, give the names of six authors followed by 'et al'.

Articles in journals

** A standard article*

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. *J Thromb Haemost* 2003;1:1435-42.

** An organization as the author*

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002;40(5):679-86.

** No author given*

21st century heart solution may have a sting in the tail. *BMJ*. 2002;325(7357):184.

** A volume with supplement*

Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxis. *Pharmacol Res Commun* 1988;20 Suppl 5:75-8.

** An issue with supplement*

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. *J Clin Psychopharmacol* 1988;8(4 Suppl):31S-37S.

** A summary in a journal*

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by *Toxoplasma gondii* [abstract]. *Clin Res* 1987;35:475A.

Books and other monographs

** One or more authors*

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical microbiology*. 4th ed. St. Louis: Mosby; 2002.

** Editor(s) as author(s)*

Danet J, Colombani J, eds. *Histocompatibility testing 1972*. Copenhagen: Munksgaard, 1973:12-8.

** A chapter in a book*

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: Saunders; 1974. p. 457-72.

** A conference paper*

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.

** A dissertation and theses*

Borkowski MM. *Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]*. Mount Pleasant (MI): Central Michigan University; 2002.

Electronic material

** A journal article in electronic format*

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. *Am J Nurs* [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: <http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle>

** Monographs in electronic format*

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

** A computer file*

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

5. Attachments (tables, graphs, schemes and photographs).

THE MAXIMUM NUMBER OF ATTACHMENTS ALLOWED IS SIX!

– Tables, graphs, schemes and photographs are to be submitted as separate documents, on separate pages.

– Tables and graphs are to be prepared in the format compatible with Microsoft Word for Windows programme. Photographs are to be prepared in JPG, GIF, TIFF, EPS or similar format.

– Each attachment must be numbered by Arabic numerals consecutively in the order of their appearance in the text

– The title, text in tables, graphs, schemes and legends must be given in both Serbian and English languages.

– Explain all non-standard abbreviations in footnotes using the following symbols *, †, ‡, §, ||, ¶, **, † †, ‡ ‡.

– State the type of color used and microscope magnification in the legends of photomicrographs. Photomicrographs should have internal scale markers.

– If a table, graph, scheme or figure has been previously published, acknowledge the original source and submit written permission from the copyright holder to reproduce it.

– All attachments will be printed in black and white. If the authors wish to have the attachments in color, they will have to pay additional cost.

6. Additional requirements

SHOULD THE AUTHOR AND ALL CO-AUTHORS FAIL TO PAY THE SUBSCRIPTION FOR MEDICAL REVIEW, THEIR PAPER WILL NOT BE PUBLISHED.