

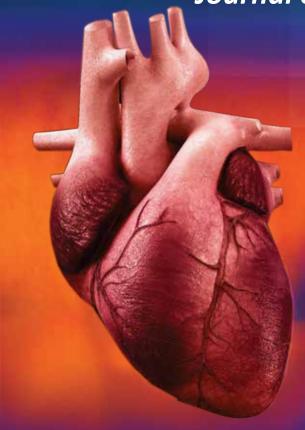
#### Časopis Udruženja kardiologa Srbije

## SRCE i krvni sudovi

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**Heart and Blood Vessels** 

Journal of the Cardiology Society of Serbia



Pozdravna reč Trećeg kongresa 34-og ogranka Američkog koledža kardiologije za Srbiju i Republiku Srpsku

Savremeno lečenje akutnog infarkta miokarda sa ST elevacijom komplikovanog srčanim zastojem na terenu

Modern treatment of acute myocardial infarction with ST-segment elevation complicated by cardiac arrest on site

Lečenje valvularnih mana u svetlu ESC/EACTS Preporuka za valvularne mane 2017 Management of the valvular heart disease in the light of 2017 ESC/EACTS Guidelines for the management of valvular heart disease

Značaj procene "vitalnosti" u lečenju aortne stenoze kod starijih Importance of frailty assessment and management in elderly with aortic stenosis

Primarna mitralna regurgitacija - ehokardiografska procena Primary mitral regurgitation - echo evaluation

Tromboza veštačke valvule tokom trudnoće Mechanical valve thrombosis during pregnancy

Oralna antikoagulantna terapija posle izolovane zamene aortne valvule Oral anticoagulation after isolated aortic valve replacement Fatalno intracerebralno krvarenje na dvojnoj antitrombocitnoj terapiji kod pacijenta sa infarktom miokarda bez ST elevacije koji je lečen urgentnom perkutanom koronarnom intervencijom

Fatal intracerebral haemorrhage on dual antiplatelet therapy in patient with myocardial infarction without ST elevation treated with urgent percutaneous coronary intervention

Antitrombocitna i antikoagulantna terapija kod bolesnika sa STEMI-jem i akutnom srčanom insuficijencijom koji je na dabigatranu zbog permanentne atrijalne fibrilacije

Antiplatelet and anticoagulation therapy in STEMI patient with acute heart failure and permanent atrial fibrillation on dabigatran

Evaluacija i lečenje pacijenata sa sinkopom: prikaz slučaja i pregled ACC/AHA/HRS preporuka iz 2017

The evaluation and management of patients with syncope: case report and overview of 2017 ACC/AHA/HRS Guidelines

Sindrom "arterial thoracic outlet" / Arterial thoracic outlet syndrome

Pacijent sa koronarnom bolešću i hipertenzijom Patient with coronary artery disease and hypertension



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# Dvostruki mehanizam protiv kardiovaskularnog kontinuuma





nebivolol

5 mg

blister, 3 x 10 tableta

Terminalna srčana insuficijencija¹

Hipertenzija<sup>1</sup>

Kongrestivna srčana insuficijencija<sup>1</sup>

Dilatacija leve komore<sup>1</sup>

Endotelna disfunkcija<sup>1</sup>

Ateroskleroza<sup>1</sup>

Remodelovanje<sup>2</sup>

Koronarna bolest<sup>1</sup>

Ožiljak miokarda<sup>1</sup>

> Infarkt miokarda<sup>1</sup>

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 Nitric oxide mechanisms of nebivolol Angelo Maffei and Giusepe Lembo; Ther Adv Cardiovasc Dis (2009) 3(4)317-327
 Effects of nebivolol in elderly heart failure patients with or witout systolic left ventricular dysfunction: results of the SENIORS echocardiographic sybstudy Stefano Ghio, Gulia Magrini, Alessandra Serio, Catherine Klersy, Alessandro Fucilli, Aleksandar Ronaszeki, Pal Karpati, Giacomo Mordenti, Angela Capriati, Philip A. Poole – Wilson, and Luigi Tavazzi Europen Heart Journal (2006) 27, 562-568 doi svako dobro HF Hemofarm

Ishemija

miokarda<sup>1</sup>



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### SRCE I KRVNI SUDOVI HEART AND BLOOD VESSELS

Volumen 37 Broj 1 2018. godina

#### Sadržaj / Content

Pozdravna reč profesora Milana Nedeljkovića organizatora Trećeg kongresa 34-og ogranka Američkog koledža kardiologije za Srbiju i Republiku Srpsku	5
Savremeno lečenje akutnog infarkta miokarda sa ST elevacijom komplikovanog srčanim zastojem na terenu <i>Modern treatment of acute myocardial infarction with ST-segment elevation complicated by cardiac arrest on sit</i> Ratko Lasica, Mina Radosavljević-Radovanović, Predrag Mitrović, Ana Ušćumlić, Igor Mrdović, Milan Nedeljković, Branislav Stefanović, Vladimir Zobenica, Milika Ašanin	
Lečenje valvularnih mana u svetlu ESC/EACTS Preporuka za valvularne mane 2017  Management of the valvular heart disease in the light of 2017 ESC/EACTS Guidelines  for the management of valvular heart disease  Biljana Obrenović-Kirćanski	9
Značaj procene "vitalnosti" u lečenju aortne stenoze kod starijih Importance of frailty assessment and management in elderly with aortic stenosis Dimitra Kalimanovska-Oštrić, Ivana Rakočević	10
Primarna mitralna regurgitacija - ehokardiografska procena / Primary mitral regurgitation - echo evaluation Anastazija Stojšić-Milosavljević, Biljana Radišić, Aleksandra Ilić, Stamanko Šušak, Ilija Srdanović, Aleksandar Redžel	<b>13</b> k
Tromboza veštačke valvule tokom trudnoće / Mechanical valve thrombosis during pregnancy Biljana Obrenović-Kirćanski	15
Oralna antikoagulantna terapija posle izolovane zamene aortne valvule  Oral anticoagulation after isolated aortic valve replacement  Ivana Burazor	18
Fatalno intracerebralno krvarenje na dvojnoj antitrombocitnoj terapiji kod pacijenta sa infarktom miokarda bez ST elevacije koji je lečen urgentnom perkutanom koronarnom intervencijom Fatal intracerebral haemorrhage on dual antiplatelet therapy in patient with myocardial infarction without ST elevation treated with urgent percutaneous coronary intervention  Marijan Spasic, Zoran Jovic, Nemanja Djenic, Boris Dzudovic, Predrag Djuric, Radoslav Romanovic, Slobodan Obradovic	<b>21</b>
Antitrombocitna i antikoagulantna terapija kod bolesnika sa STEMI-jem i akutnom srčanom insuficijencijom koji je na dabigatranu zbog permanentne atrijalne fibrilacije Antiplatelet and anticoagulation therapy in STEMI patient with acute heart failure and permanent atrial fibrillation on dabigatran Zoran Jovic, Marijan Spasic, Nemanja Djenic, Boris Dzudovic, Predrag Djuric, Radoslav Romanovic, Slobodan Obradovic	<b>24</b>
Evaluacija i lečenje pacijenata sa sinkopom: prikaz slučaja i pregled ACC/AHA/HRS preporuka iz 2017  The evaluation and management of patients with syncope: case report and overview of 2017 ACC/AHA/HRS Guidelin Kojic Dejan, Mujovic Nebojsa	28 nes
Sindrom "arterial thoracic outlet" / Arterial thoracic outlet syndrome  Dragan Vasić, Dragan Marković, Slobodan Tanasković, Lazar Davidović, Zoran Rančić	32
Pacijent sa koronarnom bolešću i hipertenzijom / Patient with coronary artery disease and hypertension  Dragan Lovic, Dragan Djordjevic, Ivan Tasic, Branko Lovic, Vesna Stojanov, Branko Jakovljevic, Milan Nedeljkovic	35
Lečenje kompleksnog bolesnika sa infarktom miokarda sa ST elevacijom – prema ESC preporukama za tretman bolesnika sa STEMI iz 2017  Complex treatment of patient with STE myocardial infarction – according to New ESC STEMI guidelines 2017.	44

Miloš Trajković, Aleksandar Davidović, Snežana Bjelić, Lućia Simona Oalđe, Branislav Crnomarković, Ilija Srdanović

#### Treći Kongres 34. ogranka Američkog koledža kardiologa za Srbiju i Republiku Srpsku

### Third Congress of the 34<sup>th</sup> American College of Cardiology Consortium Chapter of Serbia and Republic Of Srpska

Praktični aspekti i komparativna analiza ACC/AHA I ESC preporuka u Srbiji 2018 (PRACSIS 2018)

Practical aspects and comparative analysis of ACC/AHA and ESC guidelines in Serbia 2018 (PRACSIS 2018)

34 Ogranak ACC-a / 34<sup>th</sup> Chapter

Poštovane koleginice i kolege,

Veliko mi je zadovoljstvo da Vas pozdravim na početku Trećeg kongresa 34. Ogranka Američkog koledža kardiologa za Srbiju i Republiku Srpsku, koji će se održati 23-24. februara 2018. godine, u hotelu M "Best Western" u Beogradu.

Prvu ideju za osnivanje ACC Ogranka za Srbiju i Republiku Srpsku dao je Nathan Wong, kardiolog iz Irvajna (Kalifornija, SAD) tokom 62. ACC kongresa koji je održan u San Francisku 2013. godine, što je sverdno podržao William Zoghbi iz Hjustona (Teksas, SAD) koji je te godine bio predsednik Američkog koledža kardiologa. Tokom 2014. godine ispunili smo sve formalne uslove za formiranja Ogranka

(među njima je najvažniji da Ogranak broji najmanje 20 članova) i pristupni pregovori koje su sa ACC Bordom vodili Milan Nedeljković i Duško Vulić su održani na 63. ACC kongresu u Vašingtonu 2014. godine.

34. Ogranak Američkog koledža kardiologa za Srbiju i Republiku Srpsku (ACC Consortium Chapter for Serbia and Republic of Srpska) je osnovan početkom 2015. godine, a promovisan 15. marta 2015. godine u San Dijegu na 64. kongresu Američkog koledža kardiologa. Ovaj Ogranak je formiran sa ciljem unapređenja saradnje i povezivanja Američkog koledža kardiologa sa Udruženjem kardiologa Srbije i Udruženjem kardiologa Republike Srpske. Prvi vidovi ove saradnje su bili realizovani kroz organizaciju zajedničkih sesija na XX i XXI Kongresu Udruženja kardiologa Srbije održanom na Zlatiboru 2015. i 2017. godine, IV Kongresu kardiologa Republike Srpske u Banji Vrućici 2016. godine, 65. Kongresu Američkog koledža kardiologa održanom u Čikagu u martu 2016. godine, 66. Kongresu Američkog koledža kardiologa održanom u Vašingtonu u martu 2017. godine, kao i Prvom i Drugom kongresu PRACSIS 2016. i 2017.

Teme Trećeg kongresa biće prikaz i analiza 4 nova ESC vodiča (za STEMI, perifernu arterijsku bolest, bolest srčanih zalistaka i dvojnu antitrombocitnu terapiju) i 2 nova ACC/AHA vodiča (za sinkopu i arterijsku hipertenziju). Predavači i moderatori će biti najistaknutiji kardiolozi Udruženja kardiologa Srbije i Udruženja kardiologa Republike Srpske.

mon Hegepelout Prof. dr Milan A. Nedeljković

Prvi predsednik 34. Ogranka Američkog koledža kardiologa za Srbiju i Republiku Srpsku

Dear Colleagues,

It is my great pleasure to greet you at the beginning of the Third Congress of the 34th American College of Cardiology Consortium Chapter of Serbia and Republic of Srpska, which will be held on February 23-24, 2018, at Hotel M "Best Western" in Belgrade.

First idea for establishing the ACC Chapter for Serbia and Republic of Srpska was introduced by Nathan Wong, cardiologist from Irvine (California, USA), during 62nd ACC Congress held in San Francisco in 2013. This was supported by William Zoghbi form Houston (Texas, USA), who was the president of the ACC at that time. During 2014 we fulfilled all formal criteria for the formation of ACC Chapter (most important was to have at least 20 Fellows of the ACC), and negotiations with ACC Board, leaded by Milan Nedeljkovic and Dusko Vulic, took place in Washington during 63rd ACC Congress in 2014. 34th Chapter of the American College of Cardiology of Serbia and the Republic of Srpska was founded in early 2015 and was promoted on March 15, 2015 in San Diego at the 64th Congress of the American College of Cardiology. This Chapter was founded with the aim of improving cooperation and connection with the American College of Cardiology, Cardiology Society of Serbia, and Cardiology Society of the Republic of Srpska. The first steps of this cooperation were realized through the organization of joint sessions at the 20th and 21st Congress of the Cardiology Society of Serbia that was held on Zlatibor in 2015 and 2017, 4th Congress of the Republic of Srpska Society of Cardiology in Spa Vrucica 2016, 65th Congress of the American College of Cardiology held in Chicago in March 2016, 66th Congress of the American College of Cardiology held in Washington in March 2017, and during PRACSIS 2016 and 2017 meeting. The main topic of Third Congress will be the analysis of the 4 most recent ESC clinical guidelines (for STEMI, peripheral artery disease, valvular heart disease, and dual antiplatelet therapy) and 2 ACC/AHA guidelines (for syncope and arterial hypertension). Speakers and moderators will be the most prominent cardiologists of the Cardiology Society of Serbia and the Cardiology Society of Republic of Srpska.

Il wish you arsuccessful meeting.

When Hegyel South

Professor Milan A. Nedeljkovic

First president of the 34the ACC Consortium Chapter of Serbia and Republic of Srpska



# Modern Treatment of Acute Myocardial Infarction with ST-segment Elevation Complicated with Out-of-Hospital Cardiac Arrest

Ratko Lasica<sup>1</sup>, Mina Radosavljevic-Radovanovic<sup>1</sup>, Predrag Mitrovic<sup>1</sup>, Ana Uscumlic<sup>1</sup>, Igor Mrdovic<sup>1</sup>, Milan Nedeljkovic<sup>2</sup>, Branislav Stefanovic<sup>1</sup>, Vladimir Zobenica<sup>1</sup>, Milika Asanin<sup>1</sup>
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#### **Abstract**

**Background:** The most common cause of early death in acute myocardial infarction with ST elevation are malignant heart rhythm disorders, generally occurring in the first four hours of myocardial infarction. The incidence of ventricular fibrillation is greatest in the early stage of the myocardial infarction, and sudden cardiac deaths occur most often in outpatient conditions.

**Case reports:** This paper presents a patient whose first manifestation of coronary artery disease was myocardial infarction with ST elevation complicated by early ventricular fibrillation. Rapid measures of cardiopulmonal resuscitation enabled quick establishment of normal sinus rhythm. Primary percutaneous intervention was performed, with revascularization of artery responsible for acute myocardial infarction. In order to reduce ischemic brain damage, therapeutic hypothermia was applied since the patient was presented in post-reanimation coma.

**Conclusion:** Better treatment of patients with cardiac arrest in outpatient conditions and faster revascularization of the infarct artery are crucial for a reduction of mortality in acute myocardial infarction.

**Key words** 

acute myocardial infarction, cardiac arrest, modern treatment

#### **Background**

n spite of significant progress in both diagnosis and therapy, intrahospital mortality of ST segment myocardial infarction (STEMI) is still significantly high (between 4 % and 12 %), while one-year mortality in angiographic registries is 10 %.1 Ventricular fibrillation (VF) is still the most frequent cause of sudden death in patients with STEMI, occurring in 80 % of all VF in the first four hours of myocardial infarction.<sup>2</sup> Since this arrhythmia early ocurrs most commonly in the course of myocardial infarction, sudden deaths usually happen out of hospital. Fast defibrillation is the main determinant of survival in patients with VF and urgent coronary angiography with primary percutaneous intervention (pPCI) is the treatment of choice in patients with cardiac arrest in the course of STEMI.3 If there are no contraindications, therapeutic hypothermia is indicated in early phase after resuscitation in patients in postreanimation coma.4-6

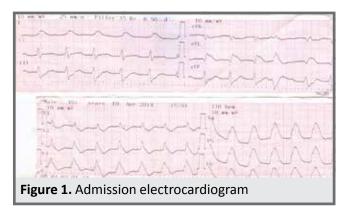
#### Case report

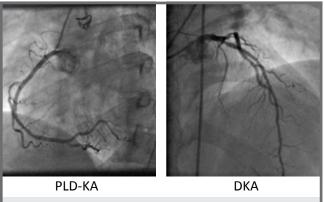
We present a male patient aged 37 who experienced the out-of-hospital syncopa on the day of admission to

the Emergency Hospital of the Clinical Center of Serbia. He was not injured since his was held by his wife standing by his side. Patient's wife started external cardiac massage and since Emergency Medical Service arrived and did not register pulsees on big body arteries, cardiopulmonal resuscitation was continued. Electrocardiogram had shown VF which was terminated with an asynchrone DC shock. After the cardiac rhythm was established, electrocardiogram showed anterolateral STEMI and the patient was referred to Emergency Hospital and then admitted to the Urgent Cardiology Department of the Clinical Center of Serbia.

On admission, the patient was unconscious, intubated, insufficiently breathing, afebrile, acyanotic. He was in sinus rhythm, tachycardia was observed, with gallop rhythm and third heart sound. Normal breathing sound was registered. He was hypertensive (160/100 mmHg) and tachycardic (Heart rate: 110/min). Admission electrocardiogram had shown wider QRS complexes with right brunch block and ST segment elevation in anterolateral lead series. (Figure 1.)

Shortly after admission a nasogastric probe was placed and loading doses of Acetylsalycilic acid (300mg) and Ticagrelor (180mg) were administered. Since the patient was in cardiac arrest and resuscitated, his bleed-





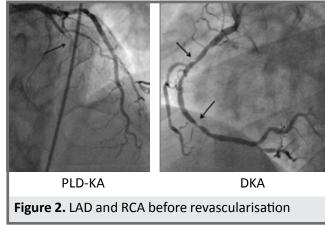
ing risk was high and Pantoprasol was administered through nasogastric probe. Due to agitation and insufficient breathing, sedation with Propofol and Midasolam was administered and assisted mechanical ventila-

Figure 3. LAD and RCA after revascularization

tion was performed. The patient was urgently transfered to the catheterisation laboratory for coronary angiography and pPCI.

Coronary angiography revealed a two-vessel coronary artery disease. An occlusive lesion in the medial segment of left descendent coronary artery (LAD) spreading to the first diagonal brunch was observed along with two significant stenoses in medial and distal segments of the right coronary artery (RCA) (Figure 2). Revascularisation of LAD with implantation of two drug eluting stents in LAD was performed (drug-eluting stent-DES). Tranzienr hypotension was registered in cath lab, so revascularisarion of RCA was performed with implantation of two DES (Figure 3.). Electrocardiogram after revascularization had shown a resolution of ST segment elevation in anterolateral lead series, with loss of right brunch block. (Figure 4).

Upon arrival from catheterization laboratory the patient was still unconscious, on assisted mechanical ventilation, normotensive (110/70 mmHg). Laboratory analysis showed increased values of markers of cardiac necrosis (CK 1017 IU/L; Tn I 0.9 ng/ml), increased values of total cholesterol and disturbed fraction of cholesterols (Holesterol - 6.34; HDL holesterol 0.94, LDL holesterol 4.68 mmol/L). Echocardiogram had shown the left ventricle normal in size and shape (EDD/ESD- 52/37 mm). The analysis of regional kinetics revealed hypokinesis of left ventricle apex and ejection fraction measured according to Simpson was approximately 50 %.



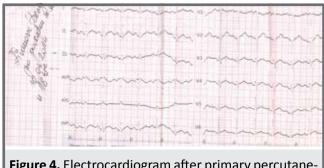


Figure 4. Electrocardiogram after primary percutaneous intervention

Neurologic examination was performed along with endocranial CT, and after exclusion of contrainidications therapeutic hypothermia was initiated and continued during next 24 hours followed by constant hemodynamic and laboratory monitoring. After 24 hours of therapeutic hypothermia gradual rewarming was initiated, intravenous sedation (started before hypothermia) was stopped; then the patient became conscious. He was extubated and stable throughout hospitalization. He was discharged to outpatient treatment with double antiplatelet therapy (Acetyl salicylic acid 100 mg and Ticagrelor 2x90 mg), beta blocker, ACE inhibitor and Rosuvastatin.

On follow-up, the patient was asymptomatic, with high tolerance for physical efforts. A new echocardiogram showed no disturbances in regional kinetics.

#### **Discussion**

Considering that STEMI in our patient was complicated with out-of-hospital cardiac arrest it is clear that improvement of pre-hospital care of STEMI patients is crucial for their better survival. According to the latest recommendations for STEMI published in 2017, it is evident that all medical professionals should be trained and familiar with the use of defibrillators and be able to maintain vital functions, which was the case with our patient. Fast defibrillation is the main determinant of survival in patients with VF. If cardiopulmonary resuscitation measures are applied in patients with VF and DC shock is applied in the first four minutes, the survival rate is up to 30%, while in patients in whom cardiopulmonary resuscitation and DC shock were applied in the course of 10 minutes the survival rate is up to 2 %.6 Prehospital care for patients with STEMI should be improved by better regional network development in order to ensure rapid reperfusion therapy and pPCI available to as many patients as possible. According to modern recommendations, patients in whom pPCI is to be performed should receive dual antiplatelet therapy (Acetyl salicylic acid and P2Y12 inhibitor), so our patient in addition to Aspirin was loaded with a dose of 180 mg Ticagrelor (non-thienopyridine antithrombotic drug with dual mechanism of action). Clopidogrel is indicated only if Ticagrelor or Prasugrel are unavailable or contraindicated.7 It has been shown earlier that patients after prolonged resuscitation can suffer more frequently from bleeding complications and in accordance with this experience, our patient was protected with Pantoprazole through a nasogastric probe. According to 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with STEMI, for those presenting with out of hospital cardiac arrest in the course of STEMI, emergency coronary angiogram and pPCI is a therapeutic treatment of choice, and our patient was treated this way. Revascularization of the infarction artery with implantation of drug-releasing stents has an advantage over bare metal stents, especially when there is possibility of stent thrombosis.8 According to Guidelines, drug eluting stents were used in our patient. Results of the study by Belliard SA et al. clearly suggest that application of therapeutic hypothermia to haemodynamically stable patients with STEMI in the postresuscitated coma for not more then six hours from cardiac arrest can reduce brain ischemic damage.4 Based on current recommendations for managing STE-MI patients and previous experiences, and after consulting a neurologist and performing endocranium CT (in order to exclude intracranial haemorrhage), therapeutic hypothermia was initiated in our patient. He did not have the following contraindications for implementation of therapeutic hypothermia: recent major surgical intervention, systemic infection-sepsis, coma of other etiology (drug poisoning, coma before resuscitation), current bleeding, isolated respiratory arrest preceded by coma. Recommended time for therapeutic hypothermia is 24 hours (from the cooling onset) and it was performed in our patient since he did not have any indication for premature interruption of hypothermia (signs of bleeding, severe bradycardia, arrhythmias, occurrence of Osborne waves in the ECG). Fast timely cardiopulmonary reanimation with application of therapeutic hypothermia significantly contributed to successful and complete recovery of our patient.

**Conclusion:** Fast and adequate measures of cardio-pulmonal resuscitation in patients with STEMI complicated with out-of-hospital cardiac arrest are most important for their full recovery. pPCI is a treatment of choice for revascularization of infarction artery (especially in the first 120 minutes from chest pain). Prevention and better treatment of out-of-hospital cardiac arrest is of crucial importance for mortality reduction caused by coronary ischemic disease.

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#### Sažetak

#### Savremeno lečenje akutnog infarkta miokarda sa ST elevacijom komplikovanog srčanim zastojem na terenu

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**Uvod:** Najčešći uzrok mortaliteta u akutnom infarktu miokarda sa ST elevacijom su maligni poremećaji srčanog ritma koji se uglavnom javljaju u prva četiri časa infarkta miokarda. Incidenca ventrikularne fibrilacije je najveća u ranoj fazi infarkta pa se naprasne srčane smrti najčešće dešavaju u vanbolničkim uslovima.

Prikaz bolesnika: U radu je prikazan bolesnik kod koga je prva manifestacija koronarne bolesti bio infarkt miokarda sa ST elevacijom komplikovan ranom ventrikularnom fibrilacijom. Brzim merama kardiopulmonalne reanimacije uspostavljena je srčana radnja. Bolesniku je učinjena primarna perkutana intervencija u toku koje je revaskularizovana infarktna arterija. Zbog održavanja postreanimacione kome bolesniku su primenjene mere terapijske hipotermije u cilju redukcije ishemijskog oštećenja mozga.

**Zaključak:** Bolje lečenje srčanog zastoja u vanbolničkim uslovima i brža revaskularizacija infarktne arterije su od ključnog značaja za redukciju mortaliteta u akutnom infarktu miokarda.

Ključne reči: akutni infarkt miokarda, srčani zastoj, savremeno lečenje



# Management of the valvular heart disease in the light of 2017 ESC/EACTS Guidelines for the management of valvular heart disease

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uring Third Congress of the 34<sup>th</sup> American College of cardiology consortium chapter of Serbia and Republic of Srpska, **PR**actical aspects and comparative analysis of **ACC/AHA** and **ESC** guidelines **In S**erbia 2018 (**PRACSIS 2018**) in Belgrade February 23-24 will be held.

At the turn of this century valvular heart disease is coming in the focus of cardiologist with the first catheter-based valve implantation, soon followed by the first-in-man transarterial aortic valve implantation or TAVI in man. In the period from 2012, when the previous guidelines of valvular heart disease were published, new data in diagnosing and management od valvular heart disease have accumulated requiring new guidelines. New updated Guidelines made by The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) were presented in August 2017 at the ESC Congress in Barcelona.

#### Key messages from these 2017 ESC/EACTS Guidelines<sup>1</sup>

- 1. Heart valve centres are needed for high-quality care of patients with valvular heart diseases. These centers include highly specialized multidisciplinary teams, comprehensive equipment, and sufficient volume of procedures.
- **2. Echocardiography** is the key technique for diagnosis of valvular heart diseases. Other investigations include stress testing, CMR, CT, fluoroscopy, biomarkers and coronary angiography (in situations where non-invasive evaluation is inconclusive).
- 3. In patient with **aortic stenosis** the strongest indication for intervention are symptoms (spontaneous or on exercise testing).

- 4. In **asymptomatic patients** the presence of predictors of rapid symptom development can justify early surgery.
- 5. The decision between **TAVI** and **SAVI** (surgical aortic valve implantation) should be made by the Heart Team after careful and comprehensive individual patient evaluation weighing risk and benefit.
- 6. Mitral valve repair is the preferred method in **primary mitral regurgitation**.
- 7. In **secondary mitral regurgitation**, mitral surgery is recommended concomitantly in patients with an indication for coronary bypass grafting. Surgery may be considered when revascularization is not indicated but patients are symptomatic, despite optimal medical therapy.
- 8. In patients at high-surgical risk **percutaneous edge-to-edge repair** may be considered, avoiding futility.
- 9. Wish of the informed patient should be taken into account in deciding between **mechanical prosthesis** and a **bioprosthesis**, but the choice between a mechanical prosthesis and a bioprosthesis should not overstress the role of age of the patient.
- 10. In patients with atrial fibrillation and aortic stenosis, aortic regurgitation, mitral regurgitation, or aortic bioprostheses beyond 3 months after implantation **new oral anticoagulants** may be used. New oral anticoagulants are contraindicated in patients with atrial fibrillation and mitral stenosis and mechanical valves. **INR selfmanagement** is recommended provided appropriate training and quality control are performed.

Further in the text below we present parts of this Guidelines with presentation of our cases and comments from the expert.

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 Baumgartner H, Falk V, Bax JJ et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017; 38: 2739–2786.



### Importance of frailty assessment and management in elderly with aortic stenosis

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#### **Abstract**

In developed countries aortic stenosis (AS) is the most common acquired valvular heart disease in elder population.

A 75 years old patient has been admitted to our institution due to symptomatic severe AS. Preoperative transthoracic echocardiography confirmed severe, calcified AS with a gradients of 95/49 mmHg, AVA 0.5 cm2 and moderate aortic regurgitation. Left ventricular ejection fraction was preserved. Preoperative coronary angiography and Duplex scan of carotid arteries excluded significant stenosis. Surgical risk assessed with EuroScore II was increased 5.9%. In the presence of restricted mobility, significant frailty and other circumstances that may affect the rehabilitation, TAVI as an intervention mode would have been more suitable. Since this was not available, our patient underwent successful surgical aortic valve replacement. The first postoperative echocardiogram revealed normal function of the bileaflet mechanical valve 29/14mmHg with mild transvalvular regurgitation. Without any prior psychiatric disorders, patient after the operation experienced complete lack of energy and willingness to cooperate or to perform any daily activity so she remained immobile. The antidepressives were ineffective. The rehabilitation process was complicated with decubitus and Acinetobacter and Proteus mirrabilis in wound culture. After antibiotic treatment we had the appearance of diarrhea, severe hypoalbuminaemia and the global edemas progressed to anasarca This three monthslong and costly struggle of all cardiovascular practitioners and family unfortunately was unsuccessful. This case is one more confirmation that we need objective frailty assessment, as one of major risk factors in elderly with AS, before making definitive decision of interventional, either surgical or transcatheter treatment.

**Key words** 

Aortic stenosis, elderly, frailty, surgical aortic valve replacement

#### Introduction

ortic stenosis (AS) is the most common acquired valvular heart disease (VHD) in well developed countries and is becoming more prevalent in populations over the age of 65. It is commonly expressed in old-age as degenerative, calcific aortic valve disease. The only effective treatment is valve replacement since untreated, severe AS leads to diastolic and systolic left ventricular dysfunction and ultimately heart failure with life-threatening complications <sup>1-3</sup> The outcomes in elders with AS can be improved by optimal treatment of comorbidities and/or frailty as an overall marker of impaired functional, cognitive and nutritional status associated with increased risk for adverse effects after surgical or transcatheter interventions.

#### **Case report**

We report the case of a 75-year-old female patient, who was referred to our department for evaluation of

chest pain, dyspnea and palpitations associated with an increase in troponin level (hs Tn 482 ng/L). Three years earlier, the patient was diagnosed with severe aortic valve stenosis. Indicated surgery was postponed 3 times since she had multiple co-morbidities including hypertension, type 2 diabetes, bronchial asthma, chronic kidney disease, anaemia, and a history of paroxysmal atrial fibrillation and cerebral infarction. She was obese and poorly mobile.

Physical examination at admission revealed a 4/6 systolic murmur over the aortic area that radiated to the carotid arteries. There were no pathologic findings on lung auscultation. Blood pressure was 150/80 mmHg.

Laboratory results showed elevated glucose and creatinine levels of 14.3 mmol/L and 243 umol/L respectively, as well as lower hemoglobin level of 100 g/L.

Electrocardiography initially showed sinus rhythm and voltage criteria for left ventricular hypertrophy. Onset of permanent atrial fibrillation occured a week later.

Preoperative transthoracic echocardiography (TTE) confirmed severe, calcified aortic stenosis with a peak

transvalvular pressure gradient of 95 mmHg (mean 49 mmHg) and a calculated aortic valve area of 0.5 cm² with moderate aortic regurgitation. Ascending aorta was dilated (4.3 mm). Left ventricular ejection fraction was preserved with normal left ventricular diametres (5.1x2.8 cm). Left atrium was enlarged (5.3x7.6x8.4 cm) with moderate mitral regurgitation. Preoperative coronary angiography revealed completely normal coronary arteries. Duplex scan excluded significant stenoses of the carotid arteries. Spirometry confirmed obstructive pulmonary disease - FEV1 85 % of the predicted value.

Nephrologist and pulmonologist consulted in the preoperative work-up excluded absolute contraindications for the planned surgical procedure following adequate rehidration and a 3-day preventive therapy with 20mg pronison in addition to the rest preoperative therapy with Enoxaparin, Cardiopirin, Bisoprolol, Amiodaron, Fosinopril, Furosemid, Rosuvastatin, Aminophyline, Seretide inhaler, Insulin.

The latest ESC/EACTS guidelines for the management of valvular heart disease state that Intervention is indicated in symptomatic patients with severe, high-gradient aortic stenosis (mean gradient ≥40 mmHg or peak velocity ≥4.0 m/s)( Class I level B)

In patients who are at increased surgical risk (STS or EuroSCORE II > 4 % or logistic EuroSCORE I > 10 % or other risk factors not included in these scores such as frailty, porcelain aorta, sequelae of chest radiation), the decision between SAVR and TAVI should be made by the Heart Team according to the individual patient characteristics, with TAVI being favored in elderly patients suitable for transfemoral access. (Class I, level B) .

Our 75 years old patient had symptomatic severe aortic stenosis. Surgical risk assessed with EuroScore II was increased, calculated 5.9 %. In the presence of restricted mobility and other conditions that may affect the rehabilitation process and significant frailty, TAVI as an intervention mode would have been more suitable. Since this alternative was not available, our patient underwent surgical aortic valve replacement as decided consilliary with our cardiac surgeons and anaesthesiologists (Heart team equivalent in our Institution).

The severely calcified stenotic aortic valve was excised and replaced with St Jude No 21 mechanical valve prosthesis. Early postoperative recovery was free of significant complications. She was extubated the first day after the procedure, with sufficient diuresis. There was no need for hemodialysis thereafter. The first postoperative echocardiogram revealed normal function of the bileaflet mechanical valve (PG 29 mmHg, MPG 14 mmHg) with mild transvalvular regurgitation. Diameters and ejection fraction of the hypertrophic left ventricle were normal (EF 70 %) with calcified mitral annulus and moderate mitral regurgitation in the dilated left atrium (5.1x7.2x7.1 cm) . The right ventricle was normal-sized with moderate tricuspid regurgitation and indirectly assessed RVSP of 39mmHg. There was no pericardial effusion even though a small right-side pleural effusion was detected.

Without prior remarkable psychiatric disorders, following the operation we witnessed complete lack of

energy and willingness of our patient to cooperate. The patient was refusing to perform any daily activity and remained immobile in bed. The inclusion of antidepressive therapy for dysthymia suggested by a psychiatric was ineffective. The rehabilitation process was further complicated with a grade IV decubitus in the sacral area with isolated Acinetobacter and Proteus mirrabilis in wound culture. In order to prevent prosthetic endocarditis, we started high dosage antibiotic treatment in accordance to the antimicrobial susceptibilities. The appearance of diarrhoea was reason for adding metronidazole besides preventive fluconazole. Despite continuous diuretic therapy, in the setting of still preserved left ventricle ejection fraction, our patient started developing generalized edema. We associated them to marked hypoalbuminaemia that persisted even after intravenous application of at least 20 doses of albumins and a protein rich diet. In the absence of significant proteinuria, this was explained as a consequence of protein loss due to large decubitus ulcer and lymphorrhoea as the global edemas progressed to anasarca preventing even regular blood sampling and intravenous therapy. Furthermore, restricted mobility led to worsening of COPD. requiering intermittent corticosteroid and oxygen therapy. This three months-long and costly struggle of all cardiovascular practitioners, nurses, physiotherapeutics, numerous consulted organ-specific subspecialists and her family unfortunately seems useless.

#### Discussion

Aortic stenosis (AS) in elderly often exists with comorbid conditions, disability, polypharmacy, risk of falling and other changes in the body with aging which have complex and predominantly negative impact on morbidity and mortality. Frailty is defined as a syndrome of decreased physiologic reserve that a person has to tolerate stress associated with aging, disease and even therapy<sup>3</sup>. The prevalence of frailty ranges from 10% to 60% in older patients. It contributes to reported 3-fold increase in post-operative mortality or major morbidity after valvular surgery<sup>4.5</sup>.

The assessment of frailty should not be subjective, but rather rely on a combination of objective markers. The most frequently used has been the Fried frailty scale based on evaluation of slowness, weakness, low physical activity, exhaustion, and shrinking (unintentional weight loss)<sup>4</sup>. Diagnosis of frailty is based on the presence of ≥3 of 5 criteria. In contrast to other time-consuming frailty scales, 5-m gait speed can be used as a single and simple measure of frailty.

In the PARTNER trial, frailty was assessed using a composite of four markers (serum albumin, dominant hand grip strength, gait speed, and Katz activity of daily living (ADLs) survey), which were combined into a frailty score². Outcomes measures were the time to death from any cause over 1 year of follow up and poor outcome at one year. Poor outcome was defined as: (1) death, (2) Kansas City Cardiomyopathy Questionnaire – Overall Summary score (KCCQ-OS) <60, or (3) decrease of ≥10 points in the KCCQ-OS score from baseline to 1

year. At 1 year, the Kaplan-Meier estimated all-cause mortality rate was 32.7% in the frail group and 15.9% in the non-frail group (log-rank p=0.004). At 1 year, poor outcome occurred in 50.0% of the frail group and 31.5% of the non-frail group (p=0.02). In conclusion, frailty was associated with increased mortality and a higher rate of poor outcome 1 year after TAVR. Considered as a safer alternative for patients at high risk of complications with open heart surgery, TAVR is not risk-free.

Frailty should not be viewed as a reason to withhold contemporary treatment and care but rather as an argument for delivering it in a more patient-centered fashion<sup>6</sup>. Multidisciplinary approach including specialists for geriatric problems is of great importance when weighing the risks and benefits of interventional versus conservative treatment. Adverse outcomes in elders would be reduced by optimal treatment of the presenting VHD, comorbidities and frailty. Interventions to reduce frailty include cardiac rehabilitation (resistance and aerobic exercise), dietary counseling (caloric and protein support), and vitamin D supplementation advocated by experts in nutrition, physical function, cognition, psychogeriatrics and social support.

We report this case as an argument for objective

frailty assessment as a major risk factor in elderly with AS that should be considered by the Heart team before reaching decision for interventional, either surgical or transcatheter treatment<sup>3-6</sup>. Equally important is to take into account patient's life expectancy, expected quality of life, patient preference as well as local resources.<sup>1</sup>.

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#### Sažetak

#### Primarna mitralna regurgitacija - ehokardiografska procena

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U razvijenim zemljama Aortna stenoza (AS) je najčešće stečeno valvularno obolenje starije populacije. Bolesnica u starosnoj dobi od 75 godina je primljena u našu bolnicu zbog simptomatske, teške AS. Preoperativna transtora-kalna ehokardiografija je potvrdila tešku, kalcifikantnu AS sa gradijentom 95/49 mmHg, AVA 0.5 cm2 i umerenom aortnom regurgitacijom. Globalna kontraktilna funkcija leve komore je bila očuvana. Preoperativna koronarografija i Doppler krvnih sudova vrata su bili uredni.

Rizik od hirurgije procenjen sa EuroScore II je bio povišen 5.9%. Obzirom, na ograničenu pokretljivost, značajnu slabost i druge otežavajuće okolnosti za sprovođenje rehabilitacije, TAVI bi bio najadekvatnija terapijska procedura. Obzirom da nismo bili u mogućnosti sprovesti TAVI, kod bolesnika je učinjena hiruška zamena aortne valvule. Prvi postoperativni ehokardiogram je ukazao na urednu funkciju dvolisne mehaničke proteze sa 29/19 mmHg gradijentima i lakom transvalvularnom regurgitacijom

lako bez preoperativnih psihijatrijskih poremećaja postoperativno kod bolesnice dolazi do potpunog gubitka energije, volje za sprovođenjem svakodnevnih aktivnosti, te je praktično celo vreme nepokretna. Antidepresivna terapija je bila u potpnosti neefikasna. Tokom rehabilitacije dolazi do razvoja decubitusa sa komplikacijama u vidu infekcije rane sa Acinetobacter i Proteus mirrabilis. Nakon uvođenja antibiotske terapije dolazi do pojave diareje, teške hipoalbuminemie, generalizovanih edema, a potom i anasarke. Ova teška tromesečna borba svih lekara i porodice je na kraju bila ne uspešna.

Ovaj prikaz slučaja ukazuje na neophodnu,objektivnu procenu stepena slabosti starijih pacijenata, kao jednog od glavnih rizik faktora za stariju populaciju sa AS, pre donošenja definitivne odluke o primeni načina lečenja bilo putem valvularne hirurgije ili TAVI procedure.

Ključne reči: Aortna stenoza, starije osobe, osetljiv pacijent, hiruška zamena aortnog zaliska



#### Primary mitral regurgitation - echo evaluation

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**Abstract** 

A 57 year old woman referred to our clinic for the evaluation of the mitral regurgitation. She was a candidate for potential valvular intervention. Transthoracic echo showed a flail leaflet in the region of the prolapsing P2 scallop of the posterior leaflet and the mitral regurgitant jet was directed toward the interatrial septum. The left ventricle systolic function was preserved. The patient underwent three-dimensional transoephageal echocardiography to investigate the precise anatomy of the mitral valve complex. The anatomical analysis was done by post-processing prior the reconstruction. During surgery, a rigid ring was implanted and Gerbode plastic of the large P3 segment was performed-which turned out to be the prolapsing scallop with "flail". Echocardiography is important in assessing mitral valve disease.

**Kew words** 

mitral valve regurgitation, mitral valve repair, echocardiography

ur patient is a 57 year old woman referred to our clinic for the evaluation of the mitral regurgitation (MR). Since her childhood she was told that she has a murmur, but she was never send to an echo exam. Several months ago she noted dyspnea on exertion. On the physical exam holosystolic murmur was noted at the apex. She was in sinus rhythm. Laboratory values were within normal values.

Transthoracic echocardiogram (TTE) showed normal left ventricle (LV) systolic function. The ejection fraction of the LV was 65%, with no regional wall motion abnormalities, and enlarged left atrium. With 2D TTE a flail leaflet in the region of the prolapsing posterior mitral cusp in the region of the P2 scallop and severe MR was registered. The MR color Doppler jet was excentric toward the interatrial septum. The grading of the MR and mitral valve (MV) disease involved qualitative, semi-quantitative and quantitative parameters - as recommended by the Guidelines¹ indicating sever MR.

TTE and the 3D reconstruction of the LV and right (RV) were done with postprocessing on EchoPAC version 201 GE. TEE is recommended in most cases before cardiac surgery, which enables a precise anatomical analysis of the lesion prior the reconstruction which was also performed. The MV parameter analysis was obtained with postprocessing for 4D Mitral valve assessment, so mitral annular, leaflet parameters and the feasibility of the repair were obtained.

Coronary angiography showed no significant coronary artery disease. All the TTE and TEE parameters were analyzed and referred to the Heart team, who indicated surgery after using operative risk stratification.

#### **Discussion**

Our patient has an evidence of flail mitral leaflet and severe consequent MR. According the Carpentier classification the MR was type II. This patient represents one of the most common form of primary MR. "Mitral regurgitation is the second-most frequent indication for valve surgery in Europe."<sup>2</sup>

"MV surgery is recommended for symptomatic patients with chronic severe primary MR and LVEF greater than 30 %", what remains current from the previous recommendation.<sup>3</sup>

Reconstruction surgery was an option in this case. Intraoperative 3D TEE usually impacts the outcome of the repaire, and provides additional information for the repair strategy. According to the surgeon who performed the reconstruction of the flail leaflet, large P3 was identified-which occupied the majority of the posterior mitral annulus circumferention, and not the P2 scallop as it was previously reported according to the comprehensive echo finding. The flail leaflet corresponded on TTE and TEE with the position of P2, but instead of it, the enlarged P3 scallop was the diseased part of the MV. Annuloplasty of the MV with rigid ring was implanted and Gerbode plastic of the P3 segment was performed. In patients with flail leaflet, an LVESD of 40-44 mm has been reported to predict a worse outcome compared with LVESD <40 mm.4

Before dissmission, TTE revealed no residual MR. "Patients with a predictably complex repair should undergo surgery in experienced repair centers with high repair rates, low operative mortality and a record of durable results".<sup>1</sup>

Today, there are transcatheter MV interventions widely accepted to correct primary MR. The indications for MV surgery are to be dicussed by the heart team before the intervention.

Lessons from the guidelines: "Echocardiography is essential to assess the etiology of MR, as well as valve anatomy and function. An integrative approach is needed to assess the severity of mitral regurgitation. Indication for intervention in primary MR is guided by symptoms and risk stratification that includes the assessment of ventricular function and size, atrial fibrillation, systolic pulmonary pressure and left atrial size. Mitral valve repair is the preferred method, but mitral valve replacement should be considered in patients with unfavorable morphological characteristics." 1,5

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#### Sažetak

#### Savremeno lečenje akutnog infarkta miokarda sa ST elevacijom komplikovanog srčanim zastojem na terenu

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Bolesnica stara 57 godina, upućena je radi evaluacije mitralne regurgitacije na našu kliniku. Razmatrana je mogućnost intervencije na mitralnoj valvuli. Transtorakalna ehokardiografija je ukazivala na "flail" u predelu prolabirajućeg P2 skalopa zadnjeg mitralnog kuspisa, a mlaz mitralne regurgitacije je bio usmeren ka interatrijalnom septumu. Globalna sistolna funkcija leve komore je bila očuvana. Urađena je I trodimenzionalna transezofagealna ehokardiografija radi precizne evaluacije mitralno-valvularnog kompleksa. Pre operacije, postprocesuiranjem je rekonstruisana mitralna valvula. Tokom operacije je implantiran rigidni ring uz Gerbode plastiku velikog P3 skalopa sa "flailom", koji se ispostavilo se bio prolabirajući. Ehokardiografija je bitna u proceni mitralno-valvularnih holesti

Ključne reči: regurgitacija mitralnog zaliska, hirurgija mitralnog zaliska, ehokardiografija



#### Mechanical valve thrombosis during pregnancy

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**Abstract** 

**Introduction:** In pregnant women with mechanical prosthetic heart valves one of the most important changes is the increased risk for thromboembolic events.

**Case report:** We report a case of nonobstructive aortic prosthetic valve thrombosis in early pregnancy. The patient was successfully treated with unfractioned heparin.

**Conclusion:** Our case is an example of the successful use of unfractionated heparin in a pregnant women with nonobstructive mechanical valve thrombosis. With this case we review the treatment of prosthetic valve thrombosis during pregnancy, and prevention (with oral and parentheral anticoagulant therapy) according to 2017 ESC/EACTS guidelines for the management of valvular heart disease.

**Kew words** 

mechanical valve, thrombosis, pregnancy

#### Introduction

regnancy causes changes in cardiovascular system (increase in blood volume and cardiac output, reduction in systemic vascular resistance and blood pressure and increased risk of thrombothic events (hypercoagulability due to increased concentration of coagulation factors and diminished fibrinolysis).

Hemodynamic chances during pregnancy, witch are normal in all pregnant women, may exacerbate underlying cardiac disease. Physiological changes in pharmacokinetics of drugs make adjustments of anticoagulant drugs doses very important. In order to prevent these complications adequate anticoagulation is very important.

In pregnant women with mechanical prosthetic heart valves one of the most important changes is the increased risk for thromboembolic events.<sup>1</sup>

We present a case of a pregnant women with aortic valve thrombosis at 10 weeks of gestation who was successfully treated with parenteral anticoagulant therapy.

#### **Case report**

A 35-year-old female with a history of bicuspid aortic valve stenosis is presented. A surgical aortic valvulotomy was performed at the age od 6, repeated at the age od 12 due to restenosis. At the age od 28, due to severe symptomatic aortic stenosis (NYHA II, pressure gradient across the aortic valve 104 mmHg (peak)/ 64mmHg (mean) (PG/MPG) aortic regurgitation (AR) 1-2+, mitral prolaps with regurgitation (MR) 1-2+, prostetic mechanical aortic valve (St. Jude No 19) was implanted with patch plastica of aortic ostium ascendant aorta. Postoperative echo showed good functioning prosthetic valve with PG/MPG 30/18 mmHg.

The patient became pregnant at 35 year of age in October 2014. In the second month od pregnancy she began to feel fatigue on effort and during climbing the stairs. Echo exam showed nearly the same findings. Complaints progressed. At that time she was receiving low molecular weight heparin (LMWH) instead of oral anticoagulant (OAC) therapy acenocumarol. Repeated echo exam in December showed elevated gradient across arteficial valve (PG/MPG 85/50 mmHg, AVA 0.9 cm²). She was admitted to Obstetrics and gynecology clinic for control. Pregnancy was without other complications. Due to thrombosis of prosthetic aortic valve (repeated echo – PG/MPG 102/64 mmHg) she was transferred to Cardiology clinic.

At admission she was in NYHA class II, without signs of heart failure. Heart sounds were rhythmic, the prosthetic heart sounds were not decreased and 2-3/6 systolic murmor was heard at aortic area, blood pressure was 120/70 mmHg, pulse rate was 112 beats/min, normal body temperature (36.4° C). The electrocardiogram showed sinus tachycardia. Blood tests showed mild hypochromic anemia.

All signs indicated nonobstructive aortic valve thrombosis. Prosthetic heart valve thrombosis (PVHT) still remains one of the most serious and potentially lethal complications of implanted mechanical heart valves despite improvements of valve design and materials. It is especially serious in pregnant women when is potentially lethal for both mother and fetus. Our version of heart team (cardiologist, cardiac surgeon, gynecologist) after detailed analysis decided to treat patient with continuous infusion of unfractionated heparin (UFH) and to monitor aPTT close. Several days later, gradient over valve began to fall, the patient was feeling better. Serial echo exams showed smaller (still elevated for this type of valve) gradients. These find-

ings were confirmed on transoesophageal echocardiography. Fetal echocardiography showed normal gestation, as gynecological controls. At the middle of March when she was switched to OAC therapy with acenocumarol and when, the lowest gradient was 54/29 mmHg she was discharged. At the begining of the IX month of pregnancy, in June 2015. she was addmitted to Obstetrics and gynecology clinic, for switching to UFH. After that she underwent an elective cesarean section and delivered a healthy baby. After delivery OAC was started. Both mother and baby were discharged from hospital in a good clinical condition. Control echocardiogram in November 2017. showed pressure gradient across the aortic valve 57/39 mmHg (PG/MPG), AR 1+, MR 1-2+ and normal dimension of heart structures. In the follow up period of 2.5 years she is well, on OAC therapy, INR is in therapeutic range.

#### **Discussion**

Pregnancy in women with prosthetic valves is associated with increased maternal risk and the risk for the baby. In women with a mechanical heart valve it might be associated with a high risk for maternal and foetal complications: mother mortality in 1-4 % and other complications in up to 40 % cases.<sup>2</sup> That is the reason why women with the family, before planning pregnancy, should be informed in detail. Women also, before planing pregnancy, if prosthetic valve in unavoidable because of valve disease, according to the 2017 ESC/EACTS guidelines, may chose biological valve. For this type of valve three months after the operation OAC therapy is not necesery, but they carry risk of the rapid occurrence of structural valve deterioration. I.d. a bioprosthesis is recommended according to the desire of the informed patient (Class I, level C).

Haemodynamically, women with well-functioning mechanical prostheses tolerate pregnancy well, but the need for anticoagulation raises risk of valve thrombosis, of haemorrhagic complications, and of offspring complications. <sup>4,5,6,7</sup> OACs cross the placenta. Their use in the first trimester can result in embryopathy in 0.6–10% of cases. <sup>5,8,9</sup> UFH and LMWH do not cross the placenta and do not have these complications. The risk depends on the anticoagulation regimen used during pregnancy and the quality of anticoagulation control.

When the diagnosis of pregnancy is made in women with mechanical prosthetic valve, the change of anticoagulation regimen should be implemented in hospital. According to guidelines³,¹0,¹1,¹1² continuation of OACs should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is <5 mg/day (or acenocoumarol <2 mg/day), after patient information and consent. In patients with a warfarin dose required of >5 mg/day (or acenocoumarol >2mg/day) OAC should be discontinuated between weeks 6 and 12 and replaced by adjusted-dose UFH (a PTT ≥2× control; in high risk patients applied as intravenous infusion) or LMWH twice a day (with dose adjustment according to weight and target anti-Xa level 4–6 hours post-dose 0.8–1.2 U/mL, assessed weekly).¹³,¹⁴,¹⁵

Guidelines recomend OACS during the second and third trimesters until the 36<sup>th</sup> week. Then OAC should be discontinued and dose-adjusted UFH (a PTT ≥2× control) or adjusted-dose LMWH (target anti-Xa level 4–6 hours post-dose 0.8-1.2 U/mL) started at the 36th week of gestation. If delivery starts while on OACs, caesarean delivery is indicated.<sup>3</sup>

The same regimen for the first several weeks of pregnancy was used in our patient but without strict control od anti Xa which resulted in non obstructive valve thrombosis. According to guidelines for non-obstructive mechanical prosthetic valve thrombosis without previous adequate anticoagulant therapy<sup>3</sup> we optimized anticoagulant therapy with UFH. This resulted in decreasing pressure gradient accros the prosthetic valve, pregnancy was well terminated and healthy baby was born by caesarean delivery. In the follow up period of 2.5 years both mother and the baby are well.

In our case a course of OAC therapy with UFH was effective without complications. Our case is a good example of the successful use of UFH in a pregnant women with nonobstructive mechanical valve thrombosis.

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#### Sažetak

#### Tromboza veštačke valvule tokom trudnoće

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**Uvod:** Jedna od najvažnijih promena kod trudnica sa mehaničkim veštačkim srčanim valvulama je povećani rizik od tromboembolijskih događaja.

**Prikaz slučaja:** Prikazujemo slučaj neopstruktivne tromboze veštačke mehaničke aortne valvule u ranoj trunoći. Pacijentkinja je uspešno lečena nefrakcioniranim heparinom.

**Zaključak:** Ovaj slučaj je prikaz uspešne primene nefrakcioniranog heparina kod trudnice sa neopstruktivnom trombozom mehaničke veštačke aortne valvule. Uz prikaz slučaja izložen je i pregled lečenja tromboze veštačkih srčanih zalistaka u trudnoći i prevencija (oralnom i parenteralnom antikoagulantnom terapijom) prema 2017 ESC/EACTS vodiču za lečenje valvularnih bolesti srca.

Ključne reči: mahanička valvula, tromboza, trudnoća



### Oral anticoagulation after isolated aortic valve replacement

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#### **Abstract**

Aortic stenosis is the most common primary valve disease leading to surgery or catheter intervention in Europe and North America, with a growing prevalence due to the ageing population. In this case report we present case of a patient who was referred to our cardiology department for in-patient exercise based cardiac rehabilitation after isolated aortic valve replacement and who was treated successfully with special emphases on anticoagulant therapy choice and patient education. Novel oral anticoagulant was replaced with VKA according to guidelines.

Regarding oral anticoagulants, guidelines from both sides of the Atlantic ocean remain the same. Oral anticoagulation using a VKA is recommended lifelong for all patients with mechanical prosthesis! INR self-management is recommended. Target INR after mechanical prosthesis according the 2017 Guidelines will depend on prosthesis trombogenicity and patient related risk factors (mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation, mitral stenosis any degree, LVEF <35 %).

**Key words** 

Oral anticoagulants, aortic valve replacement, cardiac rehabilitation

#### Introduction

urrent guidelines from the European Society of Cardiology recommend exercise-based cardiac rehabilitation for patients after heart valve surgery, based on reviews of observational studies, and clinical expertise. After surgery, people are often immobilized due to hospitalization, possible post-surgery complications, and restrictions designed to assist healing of the sternum. Consequently, their physical capacity is at risk of additional decline. As open heart surgery can be an extraordinary and stressful life event (1), quality of life may be affected (2), with mental problems such as depressive symptoms and anxiety.

European guidelines for people after heart valve surgery recommend rehabilitation that includes exercise training, anticoagulant therapy, and medical and echocardiographic follow-up, but do not mention that psycho-educational interventions should be part of the rehabilitation programs (3). In contrast, American guidelines do not currently include any recommendations or information about cardiac rehabilitation after heart valve surgery, either exercise-based or including psychoeducation.

In this case report we present the case of a patients who was referred to our cardiology department for inpatient exercise based cardiac rehabilitation after aortic valve replacement and who was treated successfully with special emphases on anticoagulant therapy choice and patient education.

#### Case presentation

A 69-year-old woman was referred to our Cardiology department for in-patient three weeks cardiac rehabilitation program after isolated aortic valve replacement with mechanical prosthesis St Jude No 19.

Patient assessment

History of present illness and previous heart investigations

- In 2010 patient was diagnosed aortic valve stenosis and was followed up.
- In 2017 because of disease and symptoms progression, aortic stenosis was characterized echocardiographically and subsequently required mechanical aortic valve replacement according to guidelines (both ACC and ESC 2017).
- Coronary angiography showed no coronary artery stenosis.
- The patient was scheduled for operative mechanical AV replacement through sternotomy.
- Postoperative TTE confirmed the adequate functioning of the extra-anatomically placed aortic prosthesis with the mean transvalvular gradient of 12 mmHg. Postoperative paroxysmal atrial fibrillation occurred on day 5 and was converted to sinus rhythm by using medications.

Past medical history:

- Hypertension
- Obesity
- Postoperative AF, medical conversion to sinus rhythm

Social history: married, two children, non-smoker, Physical activity level: poor, sedentary lifestyle, indoor activities, lives on 3<sup>rd</sup> floor, no elevator

Home medication:

- 1. Dabigatran 150 mg BID given by Private Practice MD (reason: warfarin replaced due to poor INR control)
- 2. Amiodarone 1x200 mg (weekend break) OD given by Private Practice MD (Bisoprolol was replaced)
  - 3. Lercandipine 10 mg OD
  - 4. Rosuvastatin 5 mg OD

Vital signs on admission:

BP 170/100 mmHg • Pulse 82/min • Temp 36,6 °C • Resp 20 • Ht (1.65 m) • Wt 72 • BMI 27 kg/m² • SpO2 99 %

Labs: • WBC 7.0 • RBC 4.68; Hb 133; Ht Na 141; K 4.3 Chol 7.02, HDL 1.28, LDL 4.83, TG 2.0 • Glucose 5.97

Physical examination: no signs of heart failure, poor blood pressure regulation,

ECG: sin. rhythm, heart rate 82/min, R/S V2, micro q D3

Exercise capacity on day 1st: estimated by 6 minute walking test (due to poor prior physical activity) walking distance 320 m, max BP 170/100 mmHg, heart rate 100/min

Three weeks in house cardiac rehabilitation program was created individually according to patient's age, past habits, co-morbidities, preferences and goals, with aim to:

- 1. Improve exercise capacity 30 min moderate intensity aerobic activity 6 days a week
- 2. Perform additional heart test 24 h ECG monitoring, BP monitoring, echocardiography
  - 3. Optimize medical therapy:
    - a. oral anticoagulation: dabigatran replaced with warfarin
    - b. better blood pressure control: doses optimized and ramipril added
    - c. better lipid levels control: increase the dose
    - d. heart rate and rhythm control: amiodaron replaced with bisoprolol
- 4. Educate the patient: about anticoagulation including drug interactions and self-management, in depth knowledge on endocarditis prophylaxis, diet intake

Medication during in hospital staying:

- 1. Warfarin to reach target INR once daily (OD); INR results as follows 1.16...2.14...3.04
  - 2. Bisoprolol 5 mg OD
  - 3. Lercandipine 20 mg OD
  - 4. Rosuvastatin 20 mg OD
  - 5. Ramipril 5 mg OD to achive target BP

Additional heart test were performed. The results were as follows:

- 1. During 24 hours of ECG recording the mean heart rate was 61/min, minimal heart was 49/min at 2.00am, maximal 88/min at 1.pm. No episodes of atrial fibrillation were recorded; there were 25 SVES and 2 VES.
- 2. Echocardiography exam: left ventricle was normal in diameter with preserved ejection fraction, mechani-

cal valve on aortic position good in function, with gradient 22/12mmHg. No signs of pericardial effusion.

Exercise capacity on day 21<sup>st</sup> (estimated by 6 minute walking test): walking distance 420 m, max BP 150/80 mmHg, heart rate 89/min

#### **Discussion**

Aortic stenosis is the most common primary valve disease leading to surgery or catheter intervention in Europe and North America, with a growing prevalence due to the ageing population. In 2017 new guidelines were published by ESC and AHA/ACC<sup>4,5</sup>. Guidelines summarize and evaluate available evidence with the aim of assisting health professionals in selecting the best management strategies for an individual patient with a given condition. Guidelines and their recommendations should facilitate decision making of health professionals in their daily practice. However, the final decisions concerning an individual patient must be made by the responsible health professional(s) in consultation with the patient and caregiver as appropriate.

We aim to present the case that illustrate management after valve intervention, potential misunderstandings and correct new guidelines interpretation. General management should address effective control of modifiable risk factors. All patients require lifelong follow up by cardiologist after valve surgery.

Cardiac rehabilitation is indicated and performed by cardiologist in Western and Central Europe but not strongly in US. Cardiac rehabilitation (CR) programs should be available for all patients undergoing coronary artery surgery and valve surgery. CR should be according to individual risk profile, physical, psychological and social status assessed as part of preoperative medical history and examination. Furthermore, it should be appreciated that the clinical condition and concerns of surgical patients often relate to the surgical procedure itself (wound healing, co morbidities, complications and disabilities)<sup>6</sup>.

Our patient had postoperative atrial fibrillation (POAF) after isolated aortic valve replacement that may cause a concern. Recent studies indicated that POAF occures in 40% of operated patients, but according to data POAF is a risk factor for short-term morbidity and it is not associated with a higher rate of early or late mortality after isolated AVR<sup>7</sup>. Amiodaron in this case is not indicated in the long term therapy in patients with sinus rhythm. Bisoprolol was indicated instead. The 24 hours ECG monitoring showed good heart rate and rhythm control.

Exercise training was created according to clinical condition (poor BP control of patient at the beginning of the program), baseline exercise capacity (poor; estimated by 6MWT -healthy adults range from 400 to 700 m). After valve surgery exercise tolerance will take a significant time to recover compared to coronary artery surgery (after mitral valve replacement exercise tolerance is much lower than that after aortic valve replacement, particularly if there is residual pulmonary hypertension). Upper body training was indicated since chest was stabile (i.e. usually after 6 weeks or as advise by cardiosurgeon). Moderate intensity aerobic physical

training composed of bicycling, walking and crossing over Nyllin steps, 6 times per week during 21 days. Exercise capacity of our patient was improved on discharged.

Regarding oral anticoagulants, guidelines from both sides of the world<sup>4,5</sup> remain the same. Oral anticoagulation using a VKA is recommended lifelong for all patients with mechanical prosthesis! INR self-management is recommended to provide appropriate training and quality control. Target INR after mechanical prosthesis according the 2017 Guidelines will depend on prosthesis trombogenicity and patient related risk factors (mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation, mitral stenosis any degrees, LVEF <35 %). In our patient case (for St Jude prosthesis without risk factors) target INR is 3.0. During in patient CR program patient was educated in this term. Novel oral anticoagulants are not indicated in this patient population.

#### Conclusion

2017 ESC/EACTS Guidelines for the management of valvular heart diseases and 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease in patients with mechanical valve remains the same indicating that anticoagulation with a VKA and INR monitoring is rec-

ommended in patients with a mechanical prosthetic valve

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#### Sažetak

#### Oralna antikoagulantna terapija posle izolovane zamene aortne valvule

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Aorte stenoza je najčešća bolest valvula koja zahteva zamenu bilo operativnim lečenjem bilo transkateter intervencijom i to kako u Evropi tako i u Severnoj Americi, sa rastućom rasprostranjenošću zbog starenja stanovništva. Prikazali smo bolesnicu koja je upućena u naše kardiološko odelenje na tronedeljni program kardiološke rehabilitacije nakon izolovane zamene aortne valvule mehaničkom protezom. Kardiološka rehabilitacija ima za cilj da poboljša funkcionalni kapacitet aerobnim fizičkim treningom i optimizira terapiju sa posebnim osvrtom na upotrebu oralnih antikoagulanasa. Bolesnica je uspešno završila program, unapredila funkcionalni kapacitet i dostigla ciljne vrednosti INRa.

Izbor oralne antikoagulantne terapije nakon zamene zalistaka mehaničkim protezama prema preporukama i evropskog i američkog udruženja kardiologa je VKA, sa ciljnim INRom koji je definisan u odnosu na trombogenost mehaničkih proteza i prisustvo faktora rizika (mitralni ili trikuspidni veštački zalistak, prethodne tromboembolijske komplikacije, atrijalna fibrilacija, EF 35%, mitralna stenoza).

Ključne reči: aortna stenoza, oralni antikoagulansi, kardiološka rehabilitacija



# Fatal intracerebral haemorrhage on dual antiplatelet therapy in patient with myocardial infarction without ST elevation treated with urgent percutaneous coronary intervention— case report

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**Abstract** 

According to valid guidelines for the use of dual antiplatelet therapy in patients with myocardial infarction without ST elevation (NSTEMI), the use of dual antiplatelet therapy -ASA and ticagrelor is recommended (class I level of evidence B). We report a case of a successful early percutaneous coronary intervention (early PCI) in a patient with a myocardial infarction without ST elevation which received a loding dose ticagrelor after coronary angiography. We found the subtotal stenosis of the right coronary artery and stent implantation is performed. Our case showed implementation of 2015. ESC guidelines on dual antiplatelet therapy in patient with NSTEMI. The procedure was successful without periprocedural complication.but at 22 hours next day patient was intracranial hemorrhage and 48 after patient died.

**Key words** 

myocardial infarction without ST elevation, dual antiplatelet therapy; percutaneous coronary intervention; intracranial haemorrhage

#### Introduction:

ccording to current guidelines for the use of dual antiplatelet therapy (DAPT) in patients with myocardial infarction without ST elevation (NSTEMI), the use of dual antiplatelet therapy -ASA and ticagrelor is recommended (class I level of evidence B). We report a case of a successful emergency percutaneous coronary intervention (PCI) in a patient with a myocardial infarction without ST elevation who received a loading dose of ticagrelor after coronary angiography and decision to perform PCI.<sup>1</sup>

#### **Case Report**

84-year old male patient, with chest pain was admitted to coronary unit in Military Medical Academy (MMA) several hours after the last onset of repeated chest pain. In his disease history he suffered from hypertension and diabetes mellitus type 2. Angina started five days ago and the patient had chest discomfort on minimal effort. His physical finding on admission was unremarkable and blood pressure was 140/90 mmHg. ECG showed ST-segment depression in leads for inferior and lateral wall (Figure 1). In laboratory findings: CK and CK-MB was normal but troponin I was high 0.79 µg/L. Prehospital, patient received aspirin 300 mg.

NSTEMI was diagnosed and the patient was transferred to the Cath lab at 21.00 hours. Coronary angiography was showed left main and circumflex artery without significant stenosis (Figure 2) left anterior descending artery without stenosis (Figure 3) but subtotal stenosis in middle part right coronary artery (Figure 4). Than patient received loading doses ticagrelor 180 mg, and parenteral administration of unfractionated heparin 60U per kilogram of body weight. Procedure was continued was made with implantation of one stent, (bare metal stent) (Figure 5). We continued with next therapy: ticagrelor 90 mg twice a day, aspirin 100 mg once a day, ramipril and rosuvastatin. At 22.00 hours next day patient was complained to headache, vomiting and became comatose soon after complaints arose. Emergency cranial tomography showed massive intracranial hemorrhage (Figure 6) and 48 hours after patient died.

#### Discussion

In the our case DAPT received after coronary angiography and was showed one vessel coronary disease with subtotal stenosis in right coronary artery.PCI was successful in 84-year old male patient. However, 48 hours after PCI patient died from massive intracranial hemorrhage. Should we consider in people older than

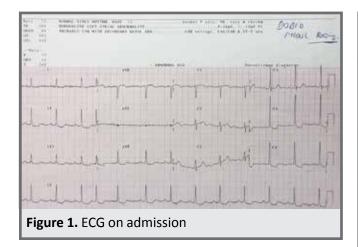




Figure 3. Left anterior descending artery. Guliistilin



Figure 5. Right coronary artery after the PCI



Figure 2. Coronary angiography –left main and circumflex artery

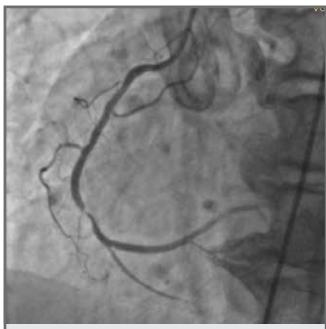
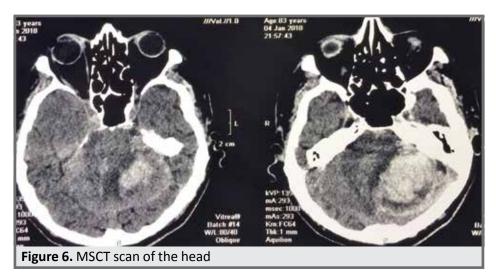


Figure 4. Subtotal stenosis in middle part of right coronary artery

80 years of age using less potent P2Y12 receptor blockers in premedication and continuation of treatment, for example, the basis of calculating the PRECISE-DAPT score on implementation of 2017 ESC guidelines on dual antiplatelet therapy in coronary artery disease.2

#### **Conclusion**

Our case showed example of implementation of 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. The procedure was successful but patient had massive, fatal intracranial hemorrhage on DAPT.



Commentary on the case according to DAPT guidelines. Current DAPT guidelines recommend more potent P2Y12 receptor antagonist before clopidogrel for the treatment of patients undergoing PCI for ACS. However, non-CABG major bleeding was higher for ticagrelor and prasugrel in randomized trials which introduced these drugs. Intracranial bleeding was non-significantly higher on ticagrelor compare to clopidogrel (26 vs 14, p=0.06) and fatal intracranial bleeding was significantly higher on ticagrelor (11 vs 1, p=0.02). However, the benefit of ticagrelor regarding to reduction of major ischemic events was very pronounced and overcome this excess of intracranial bleeding. There were only 15% of patients on ticagrelor in PLATO older than 74 years and there were no signs of excess of major bleeding in this group of patients, but with a wide confidence interval for hazard ratio. We do not know how many patients was older than 80 years in PLATO and according to data we must be very careful to treat patients with ACS older than 80 years especially with the history of hypertension with more potent antiplatelet drug ticagrelor.

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#### Sažetak

### Fatalno intracerebralno krvarenje na dvojnoj antitrombocitnoj terapiji kod pacijenta sa infarktom miokarda bez ST elevacije koji je lečen urgentnom perkutanom koronarnom intervencijom

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Po važećim smernicama za upotrebu dvojne antiagregacione terapije u pacijenata sa infarktom miokarda bez ST elevacije (NSTEMI) primena dvojne antiagregacione terapije-ASA i ticagrelora se preporučuje (klasa I nivo dokaza B). Prikazujemo slučaj uspešne urgentne perkutane koronarne intervencije ( hitna PCI) kod pacijenta sa infarktom miokarda bez ST elevacije , koji je dobio udarnu dozu ticagrelora nakon učinjene koronarografije. Verifikovana je subtotalna stenoza desne koronarne arterije i učinjena implantacija stenta. Naš slučaj je pokazao primenu 2015. ESC smernica za primenu dvojne antiagregacione terapije u pacijenata sa NSTEMI. Procedura je bila uspešna, bez periproceduralnih komplikacija ali je oko 22 sata sledećeg dana došlo do fatalnog intrakranijalnog krvarenja a 48 sati od intervencije i do letalnog ishoda.

**Ključne reči:** infarkt miokarda bez ST elevacije; dvojna antiagregaciona terapija, perkutana koronarna intervencija, intracerebralna hemoragija



# Antiplatelet and anticoagulation therapy in STEMI patient with acute heart failure and permanent atrial fibrillation on dabigatran

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#### **Abstract**

Dual antiplatelet therapy (DAPT) present therapy consisting of aspirin and P2Y12, receptor for adenosine 5'-diphosphate (ADP), medicines which protect patients from stent thrombosis and major adverse cardiovascular and cerebrovascular events following the implantation of coronary stents. We report a case of successful primary percutaneous coronary intervention (pPCI) in patient with STEMI and permanent atrial fibrillation who was on oral anticoagulant therapy with direct thrombin inhibitor Dabigatran (Pradaxa®). Our case showed example of implementation of 2017. ESC guidelines on dual antiplatelet therapy in coronary artery disease in patient with high risk for bleeding. The procedure was successful and patient was discharged from hospital in good condition without any complication.

#### **Key words**

dual antiplatelet therapy; anticoagulant therapy; atrial fibrillation; myocardial infarction; primary percutaneous coronary intervention.

#### Introduction

ual antiplatelet therapy (DAPT) present therapy consisting of aspirin and P2Y<sub>12</sub>, receptor for adenosine 5'-diphosphate (ADP), medicines which protect patients from stent thrombosis and major adverse cardiovascular and cerebrovascular events following the implantation of coronary stents<sup>1,2</sup>. We report a case of successful primary percutaneous coronary intervention (pPCI) in patient with STE-MI and permanent atrial fibrillation who was on oral anticoagulant therapy with direct thrombin inhibitor Dabigatran (Pradaxa\*) and at high risk of bleeding.

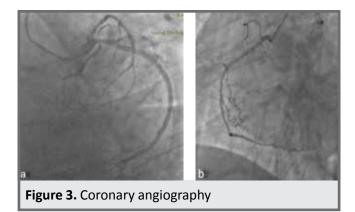
# Figure 1. ECG on admission at Cath lab

#### **Case Description**

A 74-year-old man with a history of permanent atrial fibrillation, who was on Dabigatran (Pradaxa®) therapy, received acute chest pain, started at 5 p.m. First medical contact and ECG was done at 6 p.m. in the hospital of



Figure 2. Echocardiography findings at the admission



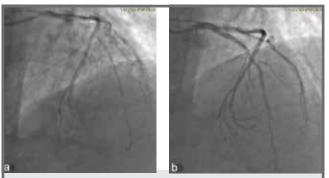
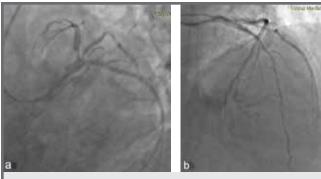


Figure 5. Stent implantation in LAD and final result

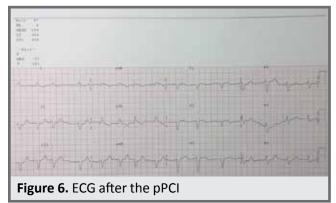


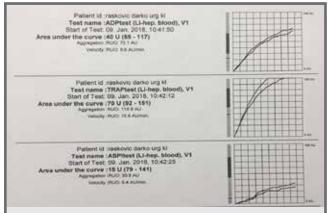
Figure 7. Echocardiography findings after the pPCI

Pozarevac. Immediately afterwards, ventricle fibrillation was registered on ECG, and patient was successfully defibrillated. After that, because acute myocardial infarction with ST elevation was diagnosed, patient received Ticagrelor (Brilique\*) 180 mg and Aspirin 300 mg, medical team from Pozarevac contacted interventional cardiologist at Military medical academy, and the patient was transferred directly to the Cath lab. The patient arrived to the Military medical academy at 19:30 hours and in Cath lab at 19:45 hours. He took the last pill of Dabigatran (Pradaxa\*) at 9 a.m. ECG revealed atrial fibrillation with heart rate of 102 per minute, wide QRS complex with ST elevation in V1 and V2 and PVC (Figure 1). In laboratory findings on admission CK was 143 and Troponin I 0,04. Echocardiography revealed akinetic wall seg-



**Figure 4.** Primary percutaneous coronary intervention on LAD





**Figure 8.** Platelets aggregability results with multiplate test on clopidogrel therapy

ment in distal part of septum, apex and distal part of anterior wall (Figure 2). Coronary angiography was done and showed occluded left anterior descending artery (Figure 3a and 3b). The procedure was continued and the primary PCI (Figure 4a and 4b) was made with implantation of two stents, one bare metal and one drug eluting stent (Figure 5a and 5b). After the procedure ECG showed complete resolution of ST segment elevation (Figure 6). Echocardiography was done after the procedure and no changes were found regarding the results on the beginning (Figure 7). Control laboratory testing showed CK 2899, CK-MB 291, LDH 549 and BNP 777.3. The patient was in acute heart failure. We administrated heparin 5000 U.I. on every 6 hours with monitoring of aPTT, ticagrelor 90 mg twice a day, aspirin 100 mg once a day, zofenopril, furosemide, bisoprolol and rosuvastatin. At the fifth day, we switched from ticagrelor to

klopidogrel with 600 mg per once, 24 hours after the last dose of ticagrelor and also started with rivaroxaban (Xarelto®) 15 mg per day. We controlled platelets aggregability on discharge (Figure 8), with multiplate test, and continued with clopidogrel and rivaroxaban therapy.

#### **Discussion**

DAPT is very important therapy in patients who's going on pPCI with or without stent implantation. In atrial fibrillation patients, the risk for bleeding is much higher because of anticoagulation therapy that patients already received.

#### Conclusion

Our case showed example of implementation of 2017 ESC guidelines on dual antiplatelet therapy in coronary artery disease in patient with high risk for bleeding. The procedure was successful and patient was discharged from hospital in good condition without any complication.

Commentary according to DAPT guidelines. A 76 year old male was admitted two hours after the onset of chest pain for the PCI under the clinical presentation of extensive anterior STEMI and with the clinical signs of acute heart failure (Killip 2 class). Patient had the history of permanent atrial fibrillation and he used dabigatran 150 mg bid for the last four months. The last dose was taken 10 hours before admission to the PCI center. Patient also recieved loading dose of ticagrelor and aspirin in the local hospital and transferred to the PCI center immediately. He did not have previous chest discomfort. The total ischemic time from the chest onset to the catheterization room was around 3 hours. There are some important points regarding the treatment of this patients:

- 1. Radial approach is recommended by the new STE-MI guidelines and it was particularly important for the patient on oral anticoagulation therapy.
- 2. Since patient had extensive STEMI and signs of acute heart failure at admission we switched him from the oral anticoagulant therapy to safer heparin therapy for the next few days because we expected worsening of the glomerular filtration rate.
- 3. For the first 5 days we continued ticagrelor therapy because this is the most vulnerable period for stent thrombosis.

- 4. However patient need DAPT and anticoagulation therapy and after STEMI it is recommended for at least 6 months. Because of the higher incidence of non-CABG major bleeding with ticagrelor compare to clopidogrel we switched the patient to clopidogrel at the fifth day after admission with the loading dose of 600 mg of clopidogrel instead the next dose of ticagrelor. The necessity for using oral anticoagulation is probable the right indication for the switching from more potent ticagrelor to less potent clopidogrel. We introduced clopidogrel at the fifth day from the STEMI avoiding possible acute resistance to clopidogrel which is very often temporary present during the ACS and the ticagrelor covered the most vulnerable time for stent thrombosis.
- 5. At the same day we stopped heparin and introduced rivaroxaban at the dose of 15 mg. Patient indeed had GFR between 50-60 ml/min during the hospital stay and we choose this dose because we planned at least one month triple therapy with clopidogrel and aspirin. Patient had CHA2DS2VASc score 5 and he obviously need oral anticoagulation therapy. Since patient had high ischemic risk (DAPT score was 3 in spite of the 75 years which takes 2 negative points) and also high bleeding risk (PRECISE DAPT score was 27) we decide to give him triple therapy for one month and to proceed with clopidogrel and rivaroxaban (15 mg) for the next 6 months, and after that we planned monotherapy with rivaroxaban very probably 20 mg per day.
- 6. DAPT score and PRECISE DAPT score are unfortunately not well suited for such severe STEMI patient because they derived from the cohorts with small number of STEMI patients especially STEMI patients on oral anticoagulant therapy.

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#### Sažetak

#### Antitrombocitna i antikoagulantna terapija kod bolesnika sa STEMI-jem i akutnom srčanom insuficijencijom koji je na dabigatranu zbog permanentne atrijalne fibrilacije

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Aorte stenoza je najčešća bolest valvula koja zahteva zamenu bilo operativnim lečenjem bilo transkateter interDvojna antitrombocitna terapija (DAPT) predstavlja terapiju koja se sastoji od aspirina i P2Y12, receptora za adenozin 5'-difosfat (ADP), lekova koji štite pacijente od tromboze stenta i glavnih neželjenih kardiovaskularnih i cerebrovaskularnih događaja nakon implantacije koronarnih stentova. Prikazujemo slučaj uspešne primarne perkutane koronarne intervencije (pPCI) kod pacijenta sa infarktom miokarda sa ST elevacijom i permanentnom atrijalnom fibrilacijom, koji je bilo na oralnoj antikoagulantnoj terapiji sa direktnim inhibitorom trombina Dabigatranom (Pradaxa®). Naš slučaj je pokazao primenu 2017. ESC smernica za dvojnu antitrombocitnu terapiju u koronarnoj bolesti kod pacijenata sa visokim rizikom za krvarenje. Procedura je bila uspešna i pacijent je otpušten iz bolnice u dobrom stanju bez ikakvih komplikacija.

**Ključne reči:** dvojna antitrombocitna terapija; antikoagulantna terapija, atrijalna fibrilacija; infarkt miokarda; primarna perkutana koronarna intervencija.



### The evaluation and management of patients with syncope: case report and overview of 2017 ACC/AHA/HRS Guidelines

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**Abstract** 

**Introduction:** Syncope is frequent symptom with different etiologies. Reported prevalence in general population was as high as 41%. If the etiology of syncope remain undefined after initial evaluation then an additional diagnostic tests are indicated based on clinical assessment.

**Case report:** We present a 57 year old female with ischemic cardiomyopathy with mildly reduced systolic left ventricular function who presented with recurrent syncope. The diagnosis of sustained monomorphic ventricular tachycardia was confirmed after insertion of implantable cardiac rhythm monitor and implantable cardioverter-defibrillator was implanted.

**Conclusion:** Treatment of syncope due to cardiac causes depends on the specific cause and should be based on relevant guidelines. Sometimes clinical guidelines miss selected patient groups due to lack of data, and in these cases clinical judgement is the most important part of decision making.

**Kew words** 

syncope, implantable cardiac rhythm monitor, ventricular tachycardia

#### Introduction

yncope is a sudden and temporary loss of consciousness and postural tone, with spontaneous recovery.1 It is an important clinical issue, accounting for up to 6% of hospital admissions.<sup>2</sup> Based on clinical setting and etiology, a syncope is classified to neurally-mediated (60 %), orthostatic (15 %), syncope due to cardiac arrhythmia (10%) and structural heart disease (5 %).3 In patients with cardiac syncope the risk of death is more than twofold increased. Several clinical factors for risk stratification in patients with syncope were proposed. 1-3 Patients with history of syncope on exertion or palpitation, ECG abnormalities (such as bundle brunch block, pre-excitation, myocardial scar etc.) or family history of sudden cardiac death as well as older patients with severe structural heart or coronary disease are at high risk for overall fatality and sudden cardiac death. 1-3 Although current ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death recommend an implantable cardioverter defibrillator (ICD) implantation in post-infarction patients with significantly reduced left ventricular ejection fraction (LVEF) <40 % for primary prevention of SCD, an optimal risk stratification for SCD in patients with chronic coronary disease and preserved systolic LV function is less well defined.4 Herein, we report a case of syncope due to monomorphic ventricular tachycardia (VT) in a patient with remote myocardial infarction and mildly reduced LVEF.

#### **Case report**

A 57-old woman was admitted to the Cardiology Department of Clinical Centre of Serbia due to recurrent syncope, occurring approximately five years after an acute inferior wall myocardial infarction (MI) with ST elevation. She was treated for hyperlipidemia and hypertension with beta-blocker (bisoprolol 5 mg), statin (atorvastatin 20 mg) and aspirin (100 mg daily). On examination after admission, heart sounds were normal, systolic blood pressure was 120 mmHg and there were no signs of congestive heart failure or peripheral vascular disease. Twelve-lead ECG showed normal sinus rhythm 70 bpm with old inferior myocardial scar (Figure 1). Twenty four hour Holter-monitoring demonstrated stable sinus rhythm with no ventricular or supraventricular arrhythmias. An echocardiogram showed hypokinesia to akinesia of LV inferior and posterior wall and overall EF was estimated to 45-50%. Coronary angiography revealed chronic occlusion of distal circumflex artery with non-significant stenosis of proximal part of left anterior descending coronary artery. The patient was referred to invasive electrophysiology study (EPS). However, using the standard ventricular tachycardia (VT) EP testing, consisting of programmed stimulation with 3 extra-stimuli (S<sub>1</sub>S<sub>2</sub>S<sub>3</sub>) and burst pacing from right ventricular apex, sustained VT or ventricular fibrillation (VF) were not induced. Due to high clinical suspicion for ventricular tachyarrythmias as a cause of syncope, amiodarone therapy was started before discharge and according to proposed algorithm for evaluation of pati-



**Figure 1.** Twelve-lead ECG at hospital admission showed sinus rhythm with inferior scar

ents with unexplained syncope<sup>5</sup> an implantable loop recorder (ILR, Reveal DX 9528, Medtronic) was inserted. After 21 months of clinical follow-up, interrogation of ILR revealed paroxysmal and sustained monomorphic VT of 270 bpm (Figure 2) accompanied with chest pain and near-syncope episode. Immediately, she undergone an ICD implantation. After the 2 years post implantation, the patient experienced the first appropriate and successful ICD shock for fast VT occurrence.

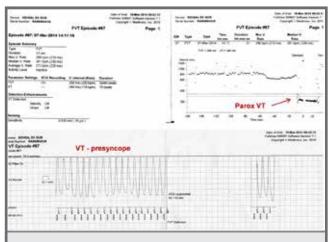
#### **Discussion**

Our patient with syncope and coronary artery disease (CAD) was a high risk patient. However, this specific group of patients with previous MI and mildly reduced LVEF were not included in large randomized ICD clinical trials so clear recommendations are lacking. An electrophysiological study (EPS) with programmed ventricular stimulation (PVS) had been used to assess the inducibility of VT, evaluate loss of consciousness and assess the indications for ICD therapy.

However the diagnostic yield varies greatly with the selected patient populations. <sup>20</sup> In CAD it may reach 50 %. Syncope associated with heart disease and reduced ejection fraction has high recurrence and mortality rates, even when EPS results are negative. <sup>21</sup> Since the likelihood of arrhythmic cause of syncope was high and the event was relatively infrequent we decided to insert an implantable loop recorder. After 21 months of follow up we made a diagnosis of VT and the patient had undergone an ICD implantation. Treatment of syncope due to cardiac causes depends on the specific cause and should be based on relevant guidelines. However sometimes clinical guidelines miss selected patient groups due to lack of data, and in these cases clinical judgement is the most important part of decision making.

#### Overview of 2017 ACC/AHA/HRS Guideline for Patients With Syncope

Clinical practice guidelines are based on systematic methods to evaluate and classify evidence, and provide a cornerstone for quality cardiovascular care. Recently, for the first time, American Collegeof Cardiology (ACC), American Heart Association (AHA) and HeartRhythm Society (HRS) have been published Guideline for the evaluation and management of patients with syncope. The goals of the present guideline were to define syncope as a symp-



**Figure 2.** ECG tracing showing paroxysmal fast sustained monomorphic VT detected by the implanted loop recorder

tom, with different causes, in different populations and circumstances; to provide guidance and recommendations on the evaluation and management of patients with suspected syncope in the context of different clinical settings, specific causes, or selected circumstances; and to identify key areas in which knowledge is lacking.<sup>6</sup>

#### Definition of syncope

These guidelines define syncope as "a symptom that presents with an abrupt, transient, complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery" with cerebral hypoperfusion as the presumed mechanism.<sup>6</sup> Furthermore, "there should not be clinical features of other nonsyncope causes of loss of consciousness, such as seizure, antecedent head trauma, or apparent loss of consciousness (that is, pseudosyncope)".<sup>6</sup> Studies of syncope report prevalence rates as high as 41 %, withrecurrent syncope occurring in 13.5 %.<sup>7</sup>

#### Initial evaluation

An initial evaluation of syncope should start with detailed history, clinical examination and 12 lead electrocardiogram (ECG) (Class I). Major categories of syncope include **neutrally mediated** (reflex) syncope (vasovagal, situational, and carotid sinus hypersensitivity), orthostatic hypotension, and cardiac syncope .Certain characteristics may help identify types of syncope based on clinical presentation. For example older age, known ischemic or structural heart disease, previous arrhythmias, palpitations before syncope or sudden loss of consciousness without prodrome, syncope during exertion or in the supine position, family history of inheritabile conditions or premature sudden cardiac death, are usually associated with cardiac causes of syncope. Younger age, no known cardiac disease, syncope in standing position or in postural changes, presence of prodrome or specific triggers, and frequent recurrence of syncope with similar characteristics, are more often associated with noncardiac causes of syncope.

#### Risk stratification should be part of initial evaluation

Obtaining a detailed history is crucial to understanding both the etiology of the syncopal eventand determining which patients are at high risk for adverse outcomes. New guidelines recommend assessment for the short- (up to 30 days after syncope) and long-term (up to 12 months of follow-up) morbidity and mortality risk of syncope, considering history, physical examination, and laboratory studies.

#### Hospital evaluation and treatment

Hospital evaluation and treatment are recommended for patients presenting with syncope who have a serious medical condition potentially relevant to the cause of syncope identified during initial evaluation. Serious medical conditions that might warrant consideration of further evaluation and therapy in a hospital setting can be arrhythmic (i.e sustained or symptomatic VT, symptomatic conduction system disease or Mobitz II or thirddegree heart block, symptomatic bradycardia or sinus pauses not related to neurally mediated syncope, symptomatic supraventricular tachycardia, pacemaker/ICD malfunction, inheritable cardiovascular conditions predisposing to arrhythmias), cardiac/vascular nonarrhythmic (i.e cardiac ischemia, severe aortic stenosis, cardiac tamponade, hypertrophic cardiomyopathy, severe prosthetic valve dysfunction, pulmonaryembolism, aortic dissection, acute HF, moderate-severe LV dysfunction), and **noncardiac** (i.e severe anemia/gastrointestinal bleeding, major traumatic injury due to syncope, and persistent vital sign abnormalities).

#### Additional evaluation

If the cause of syncope is not clear after initial evaluation then additional evaluation is indicated. A broadbased use of additional testing is costly and often ineffective. This guidelines provides recommendations for the most appropriate use of additional testing for syncope evaluation. Routine and comprehensive laboratory testing is not useful in the evaluation of patients with syncope. (Class III: No Benefit).

Routine cardiac imaging is not useful unless cardiac etiology is suspected on the basis of an initial evaluation, including history, physical examination, or ECG (Class III: No Benefit).

Transthoracic echocardiography can be useful in selected patients presenting with syncope if structural heart disease is suspected (Class IIa). Specific diagnostic tests can be useful in selected patient groups (exercise stress testing, cardiac rhythm monitoring, electrophysiological study, tilt-table testing) (Class IIa). Importantly, many patients undergo extensive neurological investigation after an uncomplicated syncope event, despite the absence of neurological features on history or examination. The evidence suggests that routine neurological testing is of very limited value in the context of syncope evaluation and management; the diagnostic yield is low, with very high cost per diagnosis. <sup>1,8-19</sup> Consequently, ma-

gnetic resonance imaging (MRI) and computed tomography (CT) of the head as well as carotid artery imaging are not recommended in the routine evaluation of patients with syncope in the absence of focal neurological findings or head injury that support further evaluation. Also rutine electroencephalography recording is not recommended in the absence of neurological features suggestive of a seizure (Class III: No Benefit).

#### Management

#### Management of cardiovascular conditions

In general, treatment strategies for cardiac causes od syncope including **arrhythmic and structural conditions** should be based on the relevant ACC/AHA Guidelines. This is so called *guideline-directed management and therapy* (GDMT). Comprehensive guidelines exist for diagnosis and management of many of these conditions, including sections on syncope.

#### Management of reflex conditions

#### Vasovagal Syncope (VVS)

Vasovagal syncope is the most common cause of syncope.<sup>3</sup> Effectiveness of drug therapy is modest.<sup>5</sup> Patient education on the diagnosis and prognosis is recommended (Class I). Physical counter-pressure maneuvers can be useful in patients with VVS who have a sufficiently long prodromal period (Class IIa). Midodrine, an alphaadrenergic vasoconstricting agent is reasonable in patients with recurrent VVS with no history of hypertension, HF, or urinaryretention (Class IIa). Dual-chamber pacing might be reasonable in a select population of patients 40 years of age or older with recurrent VVS and prolonged spontaneous pauses (Class IIb).

#### **Carotid Sinus Syndrome**

Permanent cardiac pacing is reasonable in patients with carotid sinus syndrome that is cardioinhibitory or mixed (Class IIa).

#### **Orthostatic hypotension (OH)**

Syncope suspected of OH can be mediated by **neurogenic conditions**, **dehydration**, **or drugs**. Fluid resuscitation by acute water ingestion or intravenous infusion is recommended for occasional, temporary relief in patients with neurogenic OH or dehydration (Class I). Reducing or withdrawing medications that may cause hypotension can be beneficial in selected patients with syncope (Class IIa).

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#### Sažetak

#### Evaluacija i lečenje pacijenata sa sinkopom: prikaz slučaja i pregled ACC/AHA/HRS preporuka iz 2017

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Uvod: Sinkopa je čest simptom raznovrsne etiologije. Prevalenca u opštoj populaciji iznosi čak do 41%. U koliko uzrok sinkope ostane nedefinisan nakon inicijalne evaluacije indikovani su dopunski dijagnostički testovi nakon kliničke procene.

Prikaz slučaja: Prikazujemo pacijentkinju starosti 57 godina sa ishemijskom kardiomiopatijom i blago sniženom sistolnom funkcijom leve komore sa kliničkom prezentacijom rekurentne sinkope. Dijagnoza dugotrajne monomorfne ventrikularne tahikardije je potvrđena nakon insercije implantabilnog monitora srčanog ritma, a nakon toga je ugrađen implantabilni kardioverter defibrilator.

Zaključak: Lečenje kardijalne sinkope zavisi od specifičnog uzroka i treba da bude zasnovano na relevantnim preporukama. Nekada kliničke preporuke ne pokrivaju određene grupe pacijenata zbog nedistatka dokaza iz kliničkih studija. U ovim slučajevima procena kliničara postaje najvažniji kriterijum za donošenje odluka.

Ključne reči: sinkopa, implatabilni monitor srčanog ritma, ventrikularna tahikardija



#### **Arterial thoracic outlet syndrome**

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#### **Abstract**

Arterial thoracic outlet syndrome (TOS) causes ischemic symptoms; it is the rarest type, occurring in 1-2% of all TOS cases. This paper is a case report of a 33-year-old male patient diagnosed with arterial TOS, displaying symptoms of acute critical limb ischemia caused by thromboembolism. Clinical examination revealed absent brachial, radial and ulnar pulse on the left arm. Colour Duplex Scan (CDS) was performed that showed brachial artery thrombosis and no evident flow in the radial artery. Surgical treatment was performed along with resection of dilated part of the subclavian artery that was reconstructed by interposition of Dacron tubular graft 8mm. We review the literature and elaborate on the anatomy, etiology, symptoms, diagnostic criteria and treatment modalities of arterial TOS. Arterial TOS usually remains unrecognized until a thromboembolic complication occurs. Persistent compression may cause an aneurysm in the subclavian artery.

**Key words** 

Thoracic aortic syndrome; acute limb ishchemia

#### Introduction

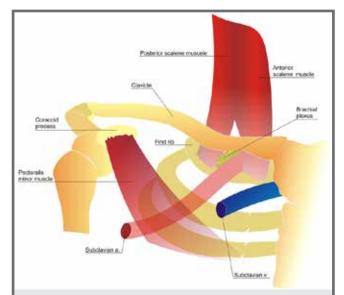
horacic Outlet Syndrome (TOS) is a name for a group of disorders characterized by the compression of the nerves, arteries or veins (or all three structures simultaneously) at the level of the upper aperture of the chest<sup>1</sup>.

The title "Thoracic Outlet Syndrome" (TOS) was introduced by Peet in 1956<sup>2</sup>. In 1958 Charles Rob defined TOS as a collective name for the compressive neurovascular disorders in the shoulder area level<sup>1</sup>. The disorder used to be described by other names as well, depending whether the emphasis was placed on the affection of neurogenic or vascular component: a description of a disorder that would fit TOS was found in the writings of Galen (2nd century A.D), Harvey (1627) and Coote (1861) described the role of repeated traumatization of the arterial segments with the first rib, in the etiology of this disorder Clagett (1962) pointed out as a dominant the role of cervical rib, Adson and Coffey (1927) were the first to conduct scalenectomy in the treatment of TOS. Ochsner, Gage and DeBakey in 1935 named it the "scalenus anticus syndrome", and made the first successful resection of the anterior scalene muscle<sup>3,</sup> <sup>4,5,6,7</sup>. Roos (1966) performed the first successful transaxillary resection of the first rib8. (Figure 1).

The aim of this case is to present interesting case of anomalous left cervical rib causing arterial TOS, subclavian artery aneurysm and brachial artery embolization.

#### **Case report**

A 33-year old male patient was admitted to our Clinic for significant pain in the left arm that appeared sev-



**Figure 1.** Schematic representation of the three compartments of the upper thoracic aperture and structures that it is comprised of

eral months prior to admission. He denied any past medical history. Clinical examination revealed absent brachial, radial and ulnar pulse on the left arm. Colour Duplex Scan (CDS) was performed that showed brachial artery thrombosis and no evident flow in the radial artery and minimal flow in the ulnar artery, with significant flow reduction in the proximal brachial artery during provocative tests and arm abduction. (Figure 2).

Invasive angiography was performed and showed aneurysm formation of the left subclavian artery 16 mm in diameter with thrombotic mass that caused distal embolization, while X-ray showed anomalous cervical



**Figure 2.** Shows reduction of flow in the proximal brachial artery during provocative tests and arm abduction



Figure 4. X-ray shows anomalous cervical first rib

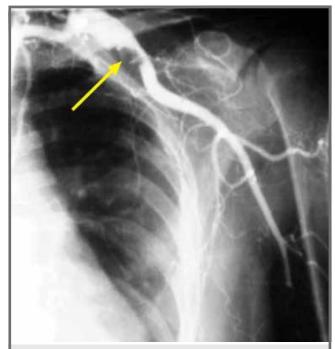
first rib with. (Figure 3, Figure 4) Thrombosis of the left brachial artery was also confirmed. (Figure 5).

Surgical treatment was indicated and resection of the anomalous left rib was performed along with resection of dilated part of the subclavian artery that was reconstructed by interposition of Dacron tubular graft 8mm. This procedure was followed by brachial artery thrombectomy with Fogarthy catheter and reconstruction with autologous vein patch. Procedure went uneventfully, brachial, radial and ulnar pulsations were present. Control CDS showed regular flow after subclavian and brachial artery revascularisation. After six months follow up the patient was doing well with left arm vascularisation well preserved.

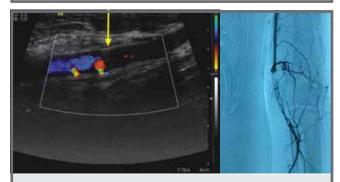
#### Discussion

The exact incidence of thoracic outlet syndrome is unknown and the majority of cases are diagnosed between the ages of 20 and 50 years, estimates range from 3-80 cases per 1000 population<sup>9, 10</sup>.

Women are three to four times more likely to develop neurogenic TOS, while the incidence of vascular



**Figure 3.** Invasive angiography shows aneurysm formation of the left subclavian artery



**Figure 5.** Acute occlusion (embolism) of brachial artery. A. Ultrasonography; B. Angiography (arrows)

TOS is equal both among non-athletic men and women<sup>11, 12</sup>.

In the vast majority of cases it is the matter of a neurogenic TOS (more than 95% of cases). Although the venous TOS (between 3 and 4%) and the arterial TOS (between 1 and 2% of cases) are significantly less frequent, their consequences are usually more serious and often require immediate surgical treatment<sup>13</sup>.

In the United States approximately 2,000 to 2,500 first rib resections are performed per year. In the last 10 years the total of 25,642 operations have been coded. 96.7% were done for neurogenic causes, 2.8% for venous issues, and 0.5% for arterial pathology<sup>14</sup>.

Morbidity and mortality is minimal, and the majority of operations are being performed by vascular surgeons<sup>15</sup>.

In the opinion of most authors, arterial TOS, occurs less frequently than venous TOS. Similarly to venous TOS it also occurs in both asymptomatic and symptomatic form. Symptomatic arterial TOS is manifested as acute or chronic. Chronic arterial TOS is manifested with pallor, cold and weakness of an arm or a hand during labor (arterial claudication). Arterial pulse is weakened

or absent. Furthermore, there is often in auscultation harsh systolic murmur over a subclaviae. Acute arterial TOS often has dramatic clinical picture: with the absence of pulses, there is pallor and coldness of arm (hands, fingers). The condition develops suddenly, progresses rapidly and often causes development of gangrene fingers.

#### Conclusion

Thoracic outlet syndrome is a complex syndrome that requires thorough knowledge of the anatomy and anatomical variants and presents management challenges to the modern cardiovascular surgeon. Arterial TOS usually remains unrecognized until a thromboembolic complication occurs. Persistent compression may cause an aneurysm in the subclavian artery.

#### Recommendation

The excellent clinical outcomes depends on the using standardized evaluation and protocol-driven treatment strategies for arterial TOS, which is emphasized in multidisciplinary approach to all forms of TOS (vascular surgeon, angiologist, interventional radiologist, and other specialiststs).

This case report suggests a distinct surgical protocol to achieve exceptional outcomes for patients with arterial thoracic outlet syndrome.

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#### Sažetak

#### Sindrom "arterial thoracic outlet"

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Arterijski sindrom gornje torakalne aperture (TOS) uzrokuje ishemijske simptome; to je najređi tip, koji se javlja u 1-2% svih TOS slučajeva. Ovaj rad je prikaz slučaja 33-godišnjeg muškog pacijenta sa dijagnozom arterijskog TOS-a, sa simptomima akutne kritične ishemije uzrokovane tromboembolijom. Klinički pregled otkrio je odsustvo brahijalnog, radijalnog i ulnarnog pulsa na levoj ruci. Izveden je Color Dupleks Scan (CDS) koji pokazuje trombozu brahijalne arterije, bez evidentiranog protoka u radijalnoj arteriji. Hirurško lečenje je izvršeno uz resekciju dilatiranog dela potključne arterije, koja je rekonstruisana interpozicijom Dacron tubularnog grafta od 8mm. Pregledom literature detaljno je elaborirana anatomija, etiologija, simptomi, dijagnostički kriterijumi i modaliteti lečenja arterijskog TOS-a.

Arterijalni TOS obično je neprepoznat dok ne dođe do tromboembolijske komplikacije. Perzistentna kompresija može izazvati aneurizmu potključne arterijie.

Ključne reči: "Thoracic aortic syndrome", ishemija donjih ekstremiteta



### Patient with coronary artery disease and hypertension

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**Abstract** 

**Background:** Cardiovascular mortality is and will be number one cause of death in years to come. Many risk factors such as hypertension, diabetes mellitus, dyslipidemias and obesity are related with increase risk of cardiovascular diseases.

Case Report: We present the case of a patient with a significant medical history of hypertension, dyslipidemia, type 2 diabetes, obesity who presented to the emergency department with atypical chest pain. Patient had uncontrolled blood pressure and high level of cholesterol. He was smoker, obese and physically inactive. He underwent a cardiac catheterization that showed a stenosis on right coronary artery originating near the anterior left coronary artery sinus and coursing between. The patient was discharged home on medical management with beta blocker therapy, ACEi , statin and antidiabetic therapy, and was instructed to restrict his physical activity and reduce body weigh. Conclusion: Treatment of patients with coronary artery disease is demanding control of the blood pressure, cholesterol and blood glucose. Many Guidelines try to find optimal treatment and goals in treatment in case to improve quality of life and complications. Any way symptomatic patients with coronary artery disease have 3 treatment options: medical management, coronary angioplasty and stent deployment, or surgical correction.

**Kew words** 

arterial hypertension, coronary heart disease, treatment

#### Introduction

ost variations of cardiovascular diseases are still number one cause of dead in a modern world. Investigators estimate that in a near future we will have slowly decrease but still leading cause and highest mortality will be related to cardiovascular disease.

However, hypertension is on the top of list of separate diseases with very high mortality anywhere in the world. Many epidemiological studies demonstrated that other factors such as diabetes mellitus, dyslipidemias, obesity and unhealthy way of leaving increase in a past decade.

#### Case report

A 65-year-old male with a significant medical history of hypertension, hyperlipidemia, type 2 diabetes, obesity, presented to the emergency department with atypical cardiac chest pain. He complained of intermittent chest discomfort that had persisted for 2 months. He described the pain as 5 of 10 in severity, substernal, lasting less than 1 minute, nonradiating, resolving spontaneously but becoming acutely worse overnight with minimal exertion. He had never taken sublingual nitroglycerin to relieve his pain, and his electrocardiogram (ECG) on presentation showed normal sinus rhythm with ST and T wave abnormalities potentially indicating

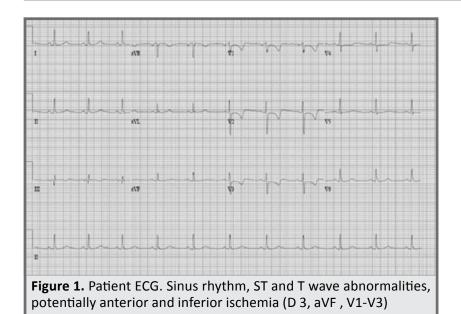
anterior and inferior ischemia seen in III, aVF, and V1-V3 (Figure 1). His 2D echocardiogram 2 months prior to admission had shown a normal ejection fraction (55%) with reduce diastolic function grade II. A bedside echocardiogram showed normal ejection fraction with severe left ventricular hypertrophy.

He was taking medicaments for blood pressure, diabetes and dyslipidemia but on his examination he had elevated blood pressure 155/95 mmHg, with heart rate 65 per minute. Blood glucose was 118 mg/dl, cholesterol 151 mg/dl, HbA1C 6,7%, LDL 68 mg/dl, triglycerides 101 mg/dl, urea 39 mg/dl and creatinine 1,0 mg/dl.

He was admitted to cardiology for unstable angina and underwent a cardiac catheterization that showed an anomaly of RCA. Patient then received medical therapy and was discharged home on a stable condition.

#### **Discussion**

Epidemiological studies have established a strong association between hypertension and coronary artery disease (CAD). Hypertension is a major independent risk factor for the development of CAD, stroke, and renal failure. The optimal choice of antihypertensive agents remains controversial, and there are only partial answers to important questions in the treatment of hypertension for the prevention and management of ischemic heart disease (IHD).



The prevalence of hypertension is thus directly proportional to the age of the population, with more than half of people >65 years of age having a high BP. The Framingham Heart Study has estimated the remaining lifetime risk of developing hypertension at ≈90% for men and women not yet hypertensive by middle age.¹ In addition; there is a change with age in the relative importance of SBP and DBP as risk indicators. Before 50 years of age, DBP is the major predictor of IHD risk, whereas after 60 years of age, SBP is more important.⁵ It is important to note that, in this population ≥60 years of age, DBP becomes inversely related to CAD risk and pulse pressure becomes the strongest predictor for CAD.

Randomized trials have shown that BP lowering in patients with hypertension produces rapid reductions in cardiovascular risk that are highly consistent with data from observational studies  $^{2,3}$ . For example, a 10-mm Hg lower usual SBP is associated with a 50% to 60% lower risk of stroke death and a  $\approx$ 40% to 50% lower risk of death resulting from CAD

Several studies (Heart Outcomes Prevention Evaluation [HOPE], Survival and Ventricular Enlargement [SAVE], and European Trial on Reduction of Cardiac Events With Perindopril in Stable Coronary Artery Disease [EUROPA]) have shown a beneficial effect of angiotensin-converting enzyme (ACE) inhibitors on CVD outcomes in individuals. <sup>4,5,6</sup>

In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, with a mean follow-up of 4.7 years, a target BP of <120 compared with <140 mm Hg was not associated with a reduced risk of a composite of CVD events (heart attack, a stroke, or a cardiovascular death).<sup>7,8</sup>

Meta-analyses of antihypertensive trials have demonstrated that BP lowering is more important than the particular drug class used in the primary prevention of the complications of hypertension. Combination antihypertensive drug therapy is typically needed to achieve and to sustain effective long-term BP control.

The overall goal of therapy is to reduce excess morbidity and unnecessary deaths. In the case of hypertension, dyslipidemia, and diabetes mellitus have been established therapeutic targets. A commonly cited target for

BP is <140/90 mm Hg in general and <130/80 mm Hg in some individuals with diabetes mellitus or CKD. The first AHA scientific statement from 2015 on the treatment of hypertension in the prevention and management of IHD also recommended a goal of <130/80 mm Hg in individuals with established CAD, with CAD equivalents, or with a Framingham Risk Score of ≥10%. 11,12,13

New AHA guidelines , published in November 2017, suggest blood pressure <130/80 mmHg as a target values in control of blood pressure in patients with CAD. To achieve these targets in adults with DM and hypertension, as useful and effective group of drugs are recommended beta blockers, diuretics, ACE inhibitors, ARBs, and CCBs.<sup>14</sup>

Except hypertension, it should be emphasize effect of dyslipidemia, diabetes mellitus, cigarette smoking, obesity, and chronic kidney disease (CKD) as independent determinants of CVD risk. As indicated previously, hypertension represents an independent risk factor for CVD, and evidence indicates that the concomitant presence of other recognized cardiovascular risk factors results in a multiplicative increase in risk for cardiovascular events. Some current guidelines call for more aggressive BP management in the presence of other cardiovascular risk factors, and BP reduction without attention to other risk factors is inadequate to reduce cardiovascular risk.<sup>15</sup>

It should to emphasize that there is general consensus that smoking increases the risk of cardiovascular events. Many studies have shown a correlation between smoking and death. Life expectancy is reduced by 13.2 years in male smokers compared with nonsmokers, and this trend is stronger in female smokers, with a 14.5-year decrease in life expectancy.<sup>15</sup>

The prevalence of obesity, defined as a body mass index  $\geq 30 \text{ kg/m}^2$ , has increased in recent years, with  $\approx 30\%$  of the adult falling into this category. The positive relationship between obesity and BP is well documented. Obese adults are  $\approx 3$  times more likely to be hypertensive compared with non obese adults, and increased adiposity may explain > 60% of hypertension in adults. <sup>15</sup>

The management of dyslipidemia was the subject of a recent ACC/AHA guideline.

The guideline advocates the use of a 10-year risk calculator determine the appropriate intensity of statin therapy to reduce CVD risk in those most likely to benefit. Those patients with CVD and age  $\leq$ 75 years, with LDL cholesterol  $\geq$ 190 mg/dL, or with a 10-year CVD risk  $\geq$ 7.5% should receive high intensity statin therapy (eg, atorvastatin 40–80 mg/d or rosuvastatin 20–40 mg/d to reduce LDL cholesterol by approximately  $\geq$ 50%). Those with CVD who are >75 years of age or those with diabetes mellitus but with a 10-year risk of <7.5% should receive moderate-intensity statin therapy such as simvastatin 20 to 40 mg/d, atorvastatin 10 to 20 mg/d, or rosuvastatin 5 to 10 mg/d to decrease LDL cholesterol by 30% to 50%.  $^{16,17}$ 

Patients with type 2 diabetes mellitus is defined as a fasting plasma glucose ≥126 mg/dL, a 2-hour oral glucose tolerance test value ≥200 mg/dL, hemoglobin A1C ≥6.5%, or random plasma glucose ≥200 mg/dL in a patient with classic symptoms of hyperglycemia. Type 2 diabetes mellitus is a strong and independent risk factor for coronary heart disease. So strong is this association that a diagnosis of diabetes mellitus could be considered a coronary heart disease risk equivalent, although this is controversial. Hypertensive patients with type 2 diabetes mellitus are also at increased risk for diabetes mellitus—specific complications, including retinopathy and nephropathy

#### **Conclusion**

This case illustrates an example of an patient with history of hypertension and coronary diseases in a elderly patient presenting with chest pain. The preferred treatment for these patients is conservative medical therapy with good control of blood pressure and other factors.

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#### Sažetak

#### Pacijent sa koronarnom bolešću i hipertenzijom

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Smrtnost od kardiovaskularnih oboljenja, kao masovna nezarazna oboljenja, biće i u narednim godinama vodeći
uzrok smrti. Mnogi faktori rizika kao što su hipertenzija, dijabetes melitus, dislipidemije i gojaznost povećavaju
rizik za kardiovaskularnu smrtnost

Prikaz slučaja: Pacijent sa dugogodišnjom istorijom hipertenzije, i povećanim masnoćama u krvi, tip 2 dijabetesom, gojazan javlja se na pregled sa atipičnim bolom u grudima. Pacijent ima nekontrolisan krvni pritisak i visoke vrednosti holesterola u krvi, pušač, gojazan i fizički neaktivan. Podvrgnut je kateterizaciji koronarnih arterija koja je pokazala stenozu desne koronarne arterije blizu račve sa levom koronarnom arterijom. Pacijent je nakon detaljnih analiza i pregleda otpušten na kućno lečenje uz medikamentoznu terapiju beta blokator, ACI inhibitor, statin i terapija za regulaciju šećera u krvi. Savetovana mu promena načina života i primena nefarmakoloških mera.

Zaključak: Lečenje pacijenata sa koronarnom arterijskom bolešću zahteva adekvatnu kontrolu krvnog pritiska, holesterola i šećera u krvi. Mnogi vodiči relevantnih Udruženja pokušavaju u proteklim godinama da na osnovu rezultata kliničkih studija i dostupnih dokaza, preporuče optimalne ciljeve u lečenju, a sa ciljem da poprave kvalitet života i spreče komplikacije. U svakom slučaju, pacijenti sa koranarnom bolešću imaju tri opcije u lečenju: medikamentozna terapija, koronarna angioplastika i ugradnja stenta ili hirurška korekcija (by pass).

Ključne reči: arterijska hipertenzija, koronarna bolest, tretman



# Complex treatment of patient with STE myocardial infarction – according to New ESC STEMI guidelines 2017.

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#### **Abstract**

**Introduction:** In many aspects of STEMI patient treatment there are the clear guideline according to many scientific evidence from excellent designed and performed large randomized clinical studies. However there is still some gray zones of knowledge and scientific fields in which exist no answered questions.

Case report: Male patient age 68 has been admitted to Cardiology Clinic, Institute for Cardiovascular Diseases of Vojvodina, Sremska Kamenica due to typical chest pain and electrocardiography (ECG) signs of STEMI anterolateral region. The patient is hospitalized in center for PPCI with time delay of 210 minute, dominantly due to no adequate organization of medical service. Immediate after the admission primary percutaneous intervention (PPCI) was performed at distal tip of venous graft for obtuse branch of LCx with drug eluting stent (DES) implantation with the minimum intrahospital time delay. Hospital course was complicated by heart failure, atrial fibrillation, and thrombus in the left ventricle.

**Conclusion:** Timely diagnosis of STEMI and good organization of medical service at all level is the key to successful care, and the prevention of time delay in establishing diagnosis and adequate therapeutic activities remains an imperative in the treatment of patients with STEMI.

**Key words** 

STEMI, percutaneous coronary intervention, time delay, treatment

#### Introduction

oronary artery disease (CAD) is the leading cause of death worldwide. Incidence of this form of heart disease is still increasing. However in some of European countries in the past three decades is noticed decrease mortality from CAD.<sup>1,2</sup>

New modalities of diagnostic workup and protocols of treatment for patients with acute myocardial infarction with permanent ST elevation (STEMI) is susceptible for many changes according to many scientific achievements. The new Guidelines for treatment patients with STEMI announced and published in September 2017 give us some new insight in this field of cardiology praxis.

In many aspects of STEMI patient treatment there are the clear guideline according to many scientific evidence from excellent designed and performed large randomized clinical studies. However there is still some gray zones of knowledge and scientific fields in which exist no answered questions. Some treatment options are under observation and provide doubtful questions.

How to shorter the time delay to make diagnosis, reperfusion strategy, optimal approach to perform coronarography, how to treat patient with acute heart fail-

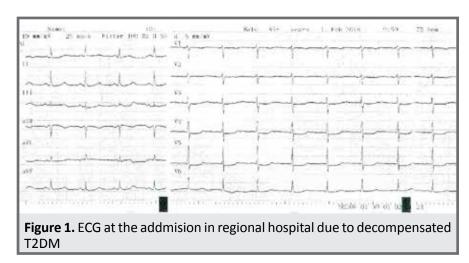
ure, optimal duration of dual and introduction triple antithrombotic therapy if thromboembolic event appears and its duration, how to treat non culprit vessel and many more questions are the possible problems to deal with.

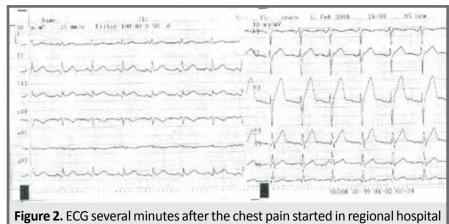
#### Case report

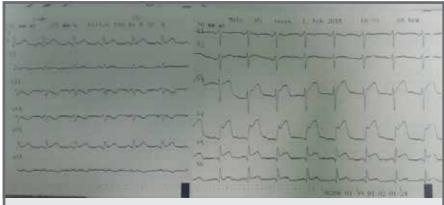
Male patient age 68 has been admitted to Clinic of Cardiology in our Institution due to typical anginal chest pain and electrocardiography (ECG) signs of STEMI anterolateral region. Patient was transferred from regional hospital where he was previously admitted due to acute metabolic decompensation of diabetes mellitus. The patient confirmed history of hypertension and type 2 diabetes mellitus (T2DM) more than a decade.

Due to angina complains the patient has been treated in the year of 2010 with surgical revascularization procedure with double aorto-coronary by pass, with grafting right coronary artery (RCA) and obtuse branch of left circumflex coronary artery (LCx).

The first symptoms of typical chest pain start on  $1^{\rm st}$  February 2018 at around 18.00. The chest pain was associated with profuse swelling and dyspnea. ECG at the time of admission in regional hospital at  $1^{\rm st}$  February







**Figure 3.** ECG after 1,5 hour from the start of chest pain sent by Viber technology to on duty cardiologist

2018 at 9.59 hour and 6 p.m. as well as at 19.30 hour our display at Figures 1,2 and 3. During the period of observation in regional hospital some diagnostic work up was performed. Laboratory tests performed after the chest pain started revealed enlarged level of high sensitive troponin I and CPK MB isoenzyme (TnI 33639 ng/l, CK-MB 246,9 ng/ml). According to this clinical scenario the patient gets 300 mg of aspirin oral.

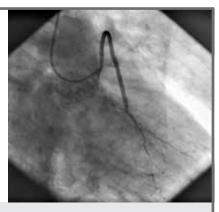
According to ECG displayed at Figure 2 and 3, at 19.39 hour by telephone has been consulted on duty cardiologist in our institution. During telephone consultation ECG recordings has been presented to our on duty cardiology via Viber technology. Immediate transfer to our cardiology Clinic was suggested.

The patient arrived to our emergency department (ED) at 21.30 hour or some 3.5 hour or 210 minutes after the symptoms of STEMI started.

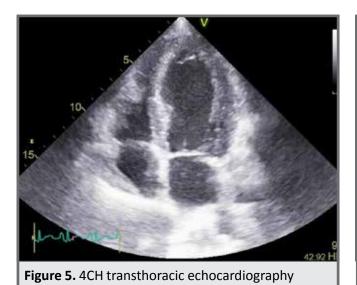
At the admission in our hospital the patient was dyspnoic with mild increased respiratory rate of 18-20/min., with basal rales on lungs with oxygen saturation of 91%. Blood preassure 140/80 mmHg, sinus rhythm rate 90/min. According to this findings patient at the moment at admission was in Killip 2 functional class.

The patient was pretreated in our ED with loading dose of ticagrelor of 180 mg oral, 20 mg of i.v. furosemide. Immediate after he was transferred to catheterization laboratory for emergency coronarography.





**Figure 4.** a) occlusion of obtuse marginal branch LCx and b) final results after stent implantation



10. 15. 16:65 H

**Figure 6.** 4CH transthoracic transpulmonary contrast echocardiography

At 21:46 hour the patient was in catheterization laboratory and 5 minutes later 6 Fr arterial sheet was introduced in right radial artery. Coronarography revealed significant stenotic lesions of native left anterior descending coronary artery (LAD) with 70-90% stenosis. The native RCA and obtuse marginal branch were with chronic total occlusions (CTO). Venous graft for RCA was patent with no stenotic lesion and infarct related artery was targeted as distal segment of venous graft for obtuse marginal branch of LCx at the point of attachment to obtuse marginal branch.

Immediate after was performed primary percutaneous intervention (PPCI) at distal tip of venous graft for obtuse branch of LCx with drug eluting stent (DES) implantation, with optimal result. TIMI flow 3 was achieved. During the procedure 380 ml of contrast agent has been used, 24 minute of X-ray exposure and total irradiation of 703 mGy.

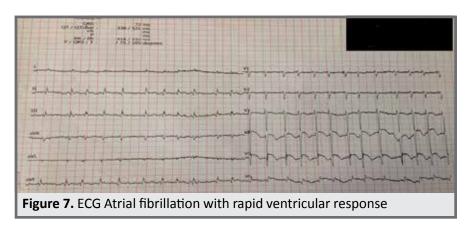
After the procedure due to progression of heart failure to level of acute pulmonary oedema, the patient was transferred to intensive coronary care unit (ICCU). His vital signs deteriorate rapidly, respiratory rate 25-28/min., heart rate of 100/min., oxygen saturation to 88 %, and lactate level of 2.2 mmol/l. With additional 40 mg of furosemide, spironolactone of 50 mg, oxygen via facial mask with flow of 4 l/min. was added.

All this measures gives the results and rapid clinical stabilisation was achieved. After 12 initial hours of treatment the patent was clinical stabile enough and transferred to semi-intensive intensive department.

Echocardiography at the first day revealed significant reduction of both systolic diastolic function of left ventricle. Initial estimation was on about 25-30 % left ventricle ejection fraction (LVEF) with highly suspicious apical thrombotic material (Figure 5). According to that finding additional transpulmonal contrast echocardiography was performed (Figure 6). Contrast echocardiography enable more accurate endocard visualization and confirmed thrombotic material in apical segment of left ventricle and even worse systolic function of left ventricle with approximate EFLV around 20 %.

Due to visualized thrombus with high embologenic potential, low molecular weight heparin (LMWH) was introduced in therapeutic dose. First dose of beta blocker was introduced in dose of 1,25 mg oraly bisoprolol and zofenopril 3,25 mg twice daily.

At the second day or 30 hour after the admition clinical state deteriorate. The patient start to be mental agitated and atrial fibrillation with rapid ventricular rate appeared (Figure 6). After the introduction of amiodarone and additional beta blocker therapy successful conversion to sinus rhythm has been achieved. How-



ever paroxysmal events of atrial fibrillation and flluter were noticed and at 3<sup>rd</sup> and 4<sup>th</sup> day of hospitalization. All those rhythm disturbances have been successfully converted with medicament interventions. By estimating the thrombotic and potential bleeding risk with CHA2DS2-VASc score value of 4, and HAS-BLED score of 2, triple antithrombotic therapy was introduced according to at least two indications, atrial fibrillation and visualized thrombus in left ventricle. The antiplatelet therapy was switched to klopidogrel 75 mg, and LMWH followed by oral anticoagulant therapy with warfarin.

Further clinical course went without complications. According to lack of evident ongoing ischemia there was no indication for repeat coronarography or additional revascularization procedure. Heart team indicate additional functional investigation for eventual rest coronary ischemia in the follow up by stress echocardiography examination.

The patient was discharged from hospital after 11 days of hospital stay, with no clinical complains in stabile heart- sinus rhythm. Triple antithrombotic therapy (clopidogrel, aspirin, warfarin) was proposed for at least1 month. Other therapy consists beta blockers (bisoprolol), amiodarone, ACE inhibitor (zofenopril), statin (rosuvastain), diuretic (furosemide + spironolactone) and insulin and proton pump inhibitor (pantoprasol).

#### **Discussion**

Timely diagnosis of STEMI is key of successful treatment, starts with first medical contact (FMC). In accordance with modern European guidelines, 12-channel ECG must be done at the place of FMC, with ten minutes of delay. In addition, ECG monitoring is recommended with all patients with suspicious for STEMI. Routine blood samples for cardiac-specific enzymes is also recommended, but its results or not needed to start reperfusion therapy.<sup>2-7</sup>

In this case, patient had immediately reported chest pains, and time from FMC to first ECG was less than ten minutes. However, clearly ECG signs of STEMI was not recognized and caused delay initial time delay added with not necessary laboratory diagnostic workout, not recommended in case of evident ECG changes such as ST elevation.

Considering that PPCI was feasible within 120 min, transfer to primary PCI center was indicated. Patient was admitted at ED after 3.5 hours from reported chest

pains. Patient was transferred from ED, directly to catheterization laboratory. This approach is strongly recommended according to some data from hospitals with high volume in PPCI in United States.<sup>8,9</sup>

From the above, we can conclude that total ischemic time was 3 hour and 45 min, whereby patient delay in this case was minimal. Delay to establish definite diagnosis and transportation time was unacceptable too long. According to guidelines recommendations for intra hospital delay in PCI center have to be as shorter as possible. In our case the longest time delay was due to adequate analysis of ECG records and the transport organization of the patient to PPCI center. Knowing that nearest PPCI center is within 7 km away from regional hospital, the total time delay due to medical system of 210 minutes was extreme long.

Coronarography, graftography and in the same act PPCI, was performed by radial approach, with implantation of DES in venous graft for obtuse branch of LCx . Transradial approach in PPCI is feasible and safer in patients with aorto-coronary by-pass grafts. Percent of positive outcome of intervention is similar between transradial and transfemoral approach, but transradial approach is connected with lower rank of severe vascular complications. <sup>10</sup>

Interventional cardiologists often choose radial approach because of experience and smaller risk of bleeding complications. 11-14

Decision of DES implantation is made according to relevant guidelines. Latest generations of DES showed grater safeness and even better efficiency, especially when it comes to reducing risk of stent-thrombosis and re infarction.<sup>2,15</sup>

Based on meta-analysis results, routine thrombus aspiration during PPCI is not recommended, but in case of larger thrombus mass after opening of coronary artery one should consider.<sup>16</sup>

The use of GP IIb / IIIa inhibitors should be considered as an auxiliary treatment strategy before, during and after the PCI, if there is no flow in the open artery or thrombotic complications are present.<sup>17</sup> In this case, after the intervention an optimal result was achieved and without thrombotic complications, the therapy was not applied.

According to relevant guidelines, patients with STE-MI and multi vessel disease, revascularisation of lesions on non-infarction arteries should be considered before discharge. Because of significant changes of LAD,

in this case, ambulatory functional estimation is indicated in irrigation area of LAD.

A further course of patient hospitalization is complicated by heart failure, the onset of stagnant blood in the left ventricle and the presence of microthrombus between trabecula, and then by the onset of paroxysm of atrial fibrillation.

In accordance with relevant guidelines, therapy for the treatment of acute heart failure was applied, with the use of therapeutic doses of parenteral anticoagulant therapy.

Following guidelines for STEMI 2017. within treatment of heart failure, oxygen therapy is recommended with SpO2 < 90%. Although the benefit of oxygen therapy in patients with STEMI, who are hypoxic is undisputed, the use of oxygen in non-hypoxic patients is still controversial.<sup>21</sup> A new randomized study showed that routine oxygen administration in normoxic patients with STEMI did not show any benefit over a one-year mortality.<sup>22</sup> There are practically no clear randomized studies that support the routine use of oxygen in patients with acute IM, and the harmful effect cannot be excluded.<sup>23</sup>

Because patient had several episodes of paroxysmal atrial fibrillation and suspected microthrombus in the left ventricle, in addition to the application of dual antiplatelet therapy, oral anticoagulant therapy (OAT) was also added, which is confirmed by calculated scores (HAS-BLED and CHA2DS2-VASc). According to relevant guidelines, triple therapy should be considered - (aspirin, clopidogrel, OAT) for one to six month to patients who have an indication for taking OAT, and who have been under PCI, regardless of the type of stent.

If there is a large ischemic risk due to acute coronary syndrome or other anatomic/procedural characteristics, it is necessary to consider giving triple therapy for more than a month, up to 6 months.<sup>24</sup> Suspension of antiplatelet therapy should be considered after 12 months.<sup>25</sup>

However, despite a large number of studies, it remains unclear what is the best decision of antithrombotic therapy in patients who have indication for OAT and antiplatelet therapy at the same time.

#### **Conclusion**

Timely diagnosis of STEMI, and good organization of medical service at all level is the key to successful care, and the prevention of delay remains an imperative in the treatment of patients with STEMI, in order to reduce the occurrence of complications and to improve the clinical course and outcome of the disease.

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#### Sažetak

## Lečenje kompleksnog bolesnika sa infarktom miokarda sa ST elevacijom - prema ESC preporukama za tretman bolesnika sa STEMI iz 2017

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**Uvod:** U mnogim aspektima tretmana STEMI pacijenata postoje jasna uputstva prema mnogim naučnim dokazima iz odlično dizajniranih i izvedenih velikih randomizovanih kliničkih studija. Međutim i dalje postoje tzv. sive zone u saznanjima i naukom neodgovorena pitanja.

**Prikaz slučaja:** Muškarac starosti 68 je primljen na Kliniku za kardiologiju, Instituta za kardiovaskularne bolesti Vojvodine, Sremska Kamenica zbog tipičnih bolova u grudima i elektrokardiografskih (EKG) znakova STEMI anterolateralne regije. Pacijent je hospitalizovan u centru za PPCI sa kašnjenjem od ukupno 210 minuta nakon početka simptoma STEMI-a, dominantno zbog kašnjenja u organizaciji zdravstven službe. Urađenom primarnom perkutanom koronarno intervencijom (PPCI) na distalnom kraju venskog grafta za LCx sa implantacijom lekom obloženog stenta (DES) ostvaren je sa minimalnim gubitkom intrahospitalnog vremena zbrinjavanja. Bolnički tok je komplikovan srčanom insuficijencijom, atrijalnom fibrilacijom i trombom u levoj komori.

**Zaključak:** Pravovremena dijagnoza STEMI- i dobra organizacija svih delova zdravstvenog sistema je ključ uspešnog lečenja, a prevencija vremena odlaganja postavljanja dijagnoze i ispravnih terapijskih postupaka, ostaju imperativ u lečenju bolesnika sa STEMI.

Ključne reči: STEMI, perkutana koronarna intervencija, vreme odlaganja, lečenje

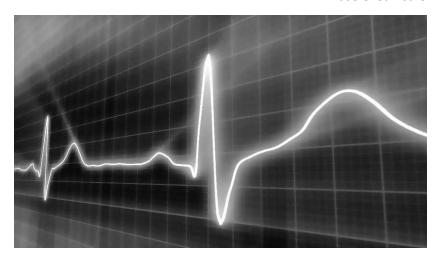
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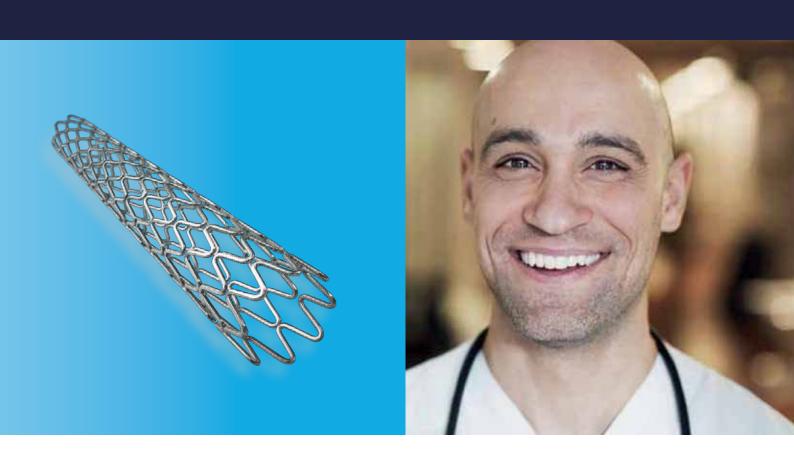


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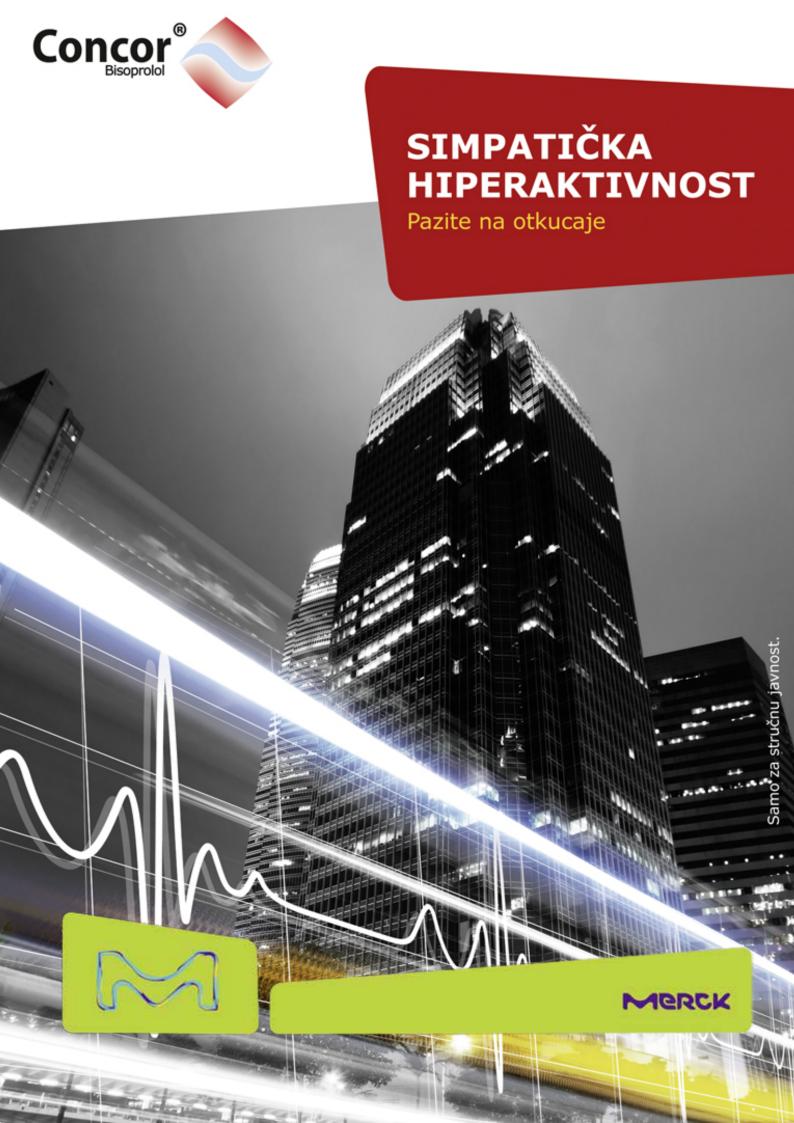
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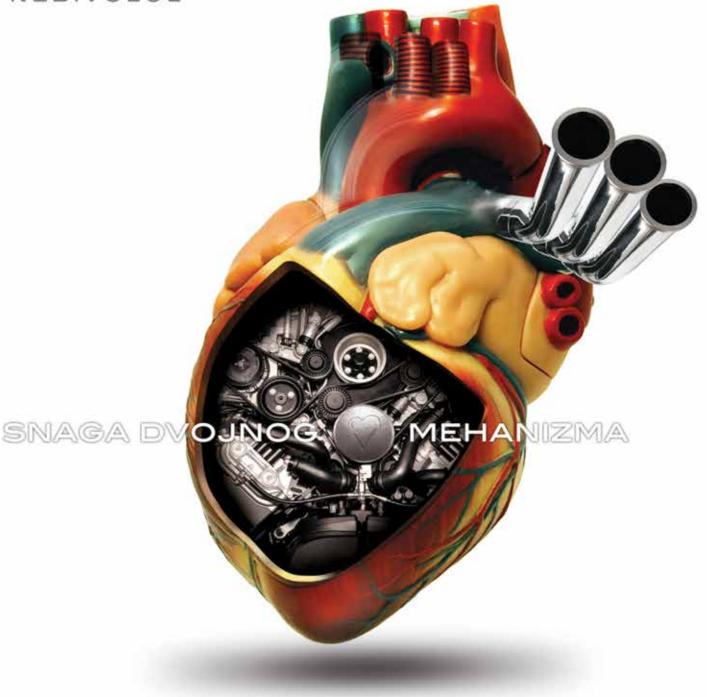
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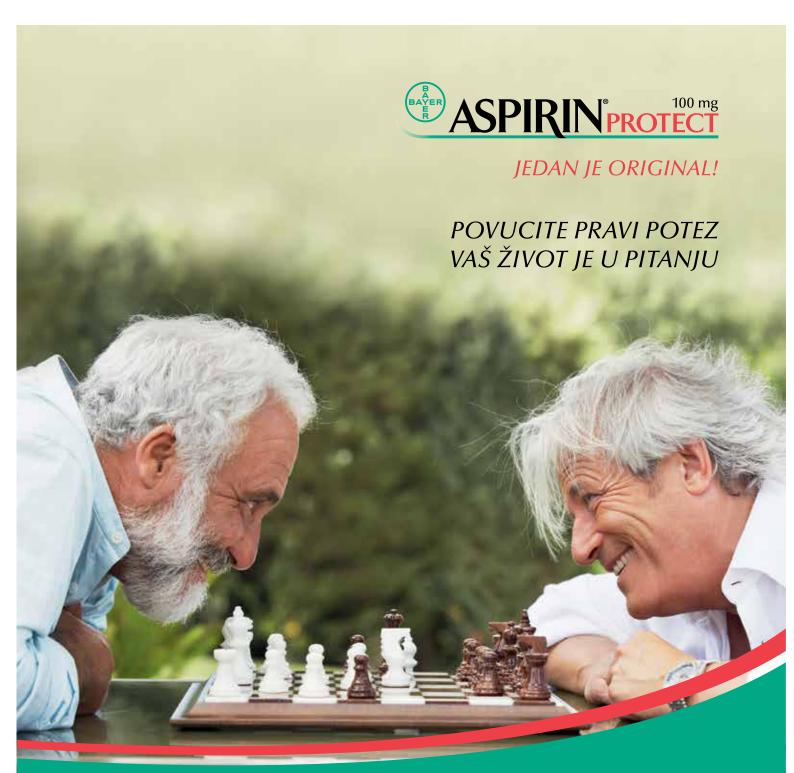








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