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SRCE i krvni sudovi

Heart and Blood Vessels

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HEART AND BLOOD VESSELS

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SRCE I KRVNI SUDOVI
HEART AND BLOOD VESSELS

Volumen 39 Broj 1 2020. godina

Sadržaj / *Content*

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

Fifth Congress of the 34th American College of Cardiology Consortium Chapter of Serbia and Republic Of Srpska

Praktični aspekti i komparativna analiza ACC/AHA I ESC preporuka u Srbiji 2020 (PRACSIS 2020)

Practical aspects and comparative analysis of ACC/AHA and ESC guidelines in Serbia 2020 (PRACSIS 2020)

34 Ogranak ACC-a / 34th Chapter

Poštovane koleginice i kolege,

Veliko mi je zadovoljstvo da Vas pozdravim na početku Petog kongresa 34. Ogranka Američkog koledža kardiologa za Srbiju i Republiku Srpsku, koji će se održati 28-29. februara 2019. godine, u hotelu M, Beograd, Srbija. 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 , XXI I XXII Kongresu Udruženja kardiologa Srbije održanom na Zlatiboru 2015., 2017. i 2019. godine i IV Kongresu kardiologa Republike Srpske održanim 2016. godine u Tesliću. Organizovane su aktivnosti i na 65. Kongresu Američkog koledža kardiologa održanom u Čikagu u martu 2016. godine, 66. Kongresu Američkog koledža kardiologa održanom u Vašingtonu u martu 2017. i 67. Kongresu održanom u Orlandu u martu 2018. godine i 68. Kongresu održanom u martu 2019. u New Orleansu. Organizovani su Kongresi 34. Ogranka Američkog kooledža kardiologa sa temom: Praktični aspekti i komparativna analiza ACC/AHA i ESC preporuka (PRACSIS) održani u februaru 2016., 2017. i 2018. godine u Beogradu I 2019 na Jahorini, Republika Srpska. Teme Petog kongresa biće prikaz i analiza 5 novih ESC vodiča (diajbetes, predijabetes I kardiovaskularne bolesti, hronični koronarni sindrom, dislipidemije, supraventrikularne tahikardije i plućna embolija) i 2 nova ACC/AHA vodiča (primarna prevencija KVB, atrijalna fibrilacija). Predavači i moderatori će biti najistaknutiji kardiolozi Udruženja kardiologa Srbije i Udruženja kardiologa Republike Srpske. Želim da se posebno zahvalim prvom guverneru Profesoru Milanu Nedeljkoviću za izvanredno vođenje 34. Ogranka Američkog koledža kardiologa za Srbiju i Republiku Srpsku od 2015-2019. godine i podršci u organizaciji ovog Kongresa.

S poštovanjem,
Prof. dr Duško Vulić, dopisni član ANURS Predsjednik –
Guverner 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 Fifth Congress of the 34th American College of Cardiology Consortium Chapter of Serbia and Republic of Srpska, which will be held on February 28-29, 2020, at Hotel "M", Belgrade, Serbia. 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, 21st Congress of the Cardiology society of Serbia that was held on Zlatibor in 2015, 2017 and 2019, and Fourth Congress of the Cardiology Society of Republic of Srpska in Teslić in 2016. We organized activities on 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, 67th Congress of the American College of Cardiology held in Orlando in March 2018 and 68th Congress of the American College of Cardiology held in New Orleans in March 2019.
In addition, we organized congresses of 34th American College of Cardiology Consortium Chapter with following topic: Practical aspects and comparative analysis of ACC/AHA and ESC guidelines In Serbia and Republic of Srpska 2020 (PRACSIS 2016, 2017, 2018 and 2019 meeting) that were held in Belgrade and Jahorina. The main topic of Fifth Congress will be also dedicated to the analysis of the 5 most recent ESC clinical guidelines (diabetes, prediabetes and cardiovascular diseases, chronic coronary syndromes, dyslipidemias, supraventricular tachycardia and pulmonary embolism) and 2 ACC/AHA guidelines (primary prevention of cardiovascular diseases and atrial fibrillation). Speakers and moderators will be the most prominent cardiologists from the Cardiology Society of Serbia and the Cardiology Society of Republic of Srpska. I would specially like to express my gratitude to the first Governor of our Chapter Professor Milan Nedeljković for excellent leadership for the period 2015-2019 and support in organizing this Congress.
I wish you successful meeting.

Professor Duško Vulić,
Corresponding Member of ASARS Guvernor of the 34th ACC Consortium Chapter of Serbia and Republic of Srpska

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Nakon svečanog predavanja 15.3.2015. godine, na 64. Kongresu Američkog koledža kardiologa, San Diego, SAD, formiran je 34. Ogranak Američkog koledža kardiologa za Srbiju i Republiku Srpsku, čiji je prvi guverner postao Prof. dr Milan A. Nedeljković.

After inaugural lecture, on March 3 2015, during 64th ACC Congress in San Diego USA, the 34th ACC Chapter for Serbia and Republic of Srpska was established, with Professor Milan A. Nedeljkovic as a first governor.

Srce i krvni sudovi 2020; 39(1): 8-10

Case report

How would you treat: glucagon-like peptide 1 receptor analogue or sodium-glucose cotransporter 2 inhibitor in chronic coronary syndrome and heart failure in type 2 diabetes?

Tamara Kovacevic Preradovic, Zeljko Zivanovic, Bojan Stanetic, Ljiljana Kos, Nikola Sobot, Sanja Stojkovic, Dragan Uncanin[1]

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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

Introduction

Patients with type 2 diabetes mellitus (T2DM) are at high risk of vascular complications and heart failure (HF). We present a case with T2DM, coronary artery disease (CAD) and heart failure with preserved ejection fraction (HFpEF).

Case presentation

A 58 years old male with T2DM was admited to regional hospital with dyspnea and chest pain, elevated level of Troponin T and ECG changes interpreted as non-ST-elevation myocardial infarction. Invasive coronary angiography reveled diffuse epicardial coronary disease, with 50% diameter focal stenosis on all of three coronary arteries and stress echocardiography was recomended. Several weeks later, he develops hypertensive crisys and pulmonary oedema. Afterwards, a single-photon emission computerized tomography was performen and showed only 7% of ischemic myocardium in two segments: basal posterior and apical. At hospital readmission, patient had symptoms and signs of HF with elevated arterial blood pressure of 160/90mmHg and unremarkable ECG. Laboratory tests showed eleveted natriuretic peptides (NTproBNP) of 2553pg/ml, and preserved renal function by creatinine clearance (ClCr) of 74.4ml/min. Transthoracic echocardiography revealed left ventricular (LV) ejection fraction of 53%, measured from biplane images, with LV hypertrophy, left atrial enlargement and mild mitral regurgitation. LV diastolic dysfunction showed the ratio (E/e') of the peak velocity of mitral inflow (E) and the average of septal and lateral mitral annular early diastolic peak velocities (e') of 18.75 (Figure 1). Based on tricuspid regurgitation peak velocity of 3.1m/s, pulmonary artery systolic pressure was estimated to 38mmHg. Left ventricular global longitudinal systolic strain (GLS) was reduced: -14.3%. According to the current guidelines, clinical and echocardiographic features correspond to HFpEF. Dobutamin stress echocardiography with GLS analysis showed inducible ischaemia in basal segment of posterior wall and post-systolic thickening of apical segment of interventricular septum (Figure 2) with appearance of ultrasound lung comets suggestive for pulmonary congestion (Figure 3). On repeated coronary angiography an occluded posterolateral branch from left circumflex artery with collateral filling was found (Figure 4). Medical therapy

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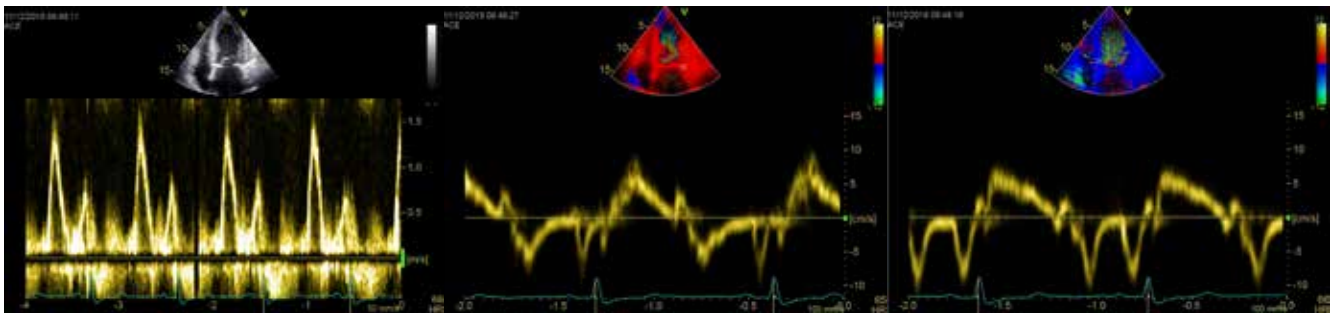

Figure 1. The ratio of the peak velocity of mitral inflow during early diastole (E), recorded by pulsed Doppler between the tips of the mitral leaflets (left), over the average of septal (right) and lateral (middle) mitral annular early diastolic peak velocities (e') recorded by pulsed tissue Doppler is equal to 18.75

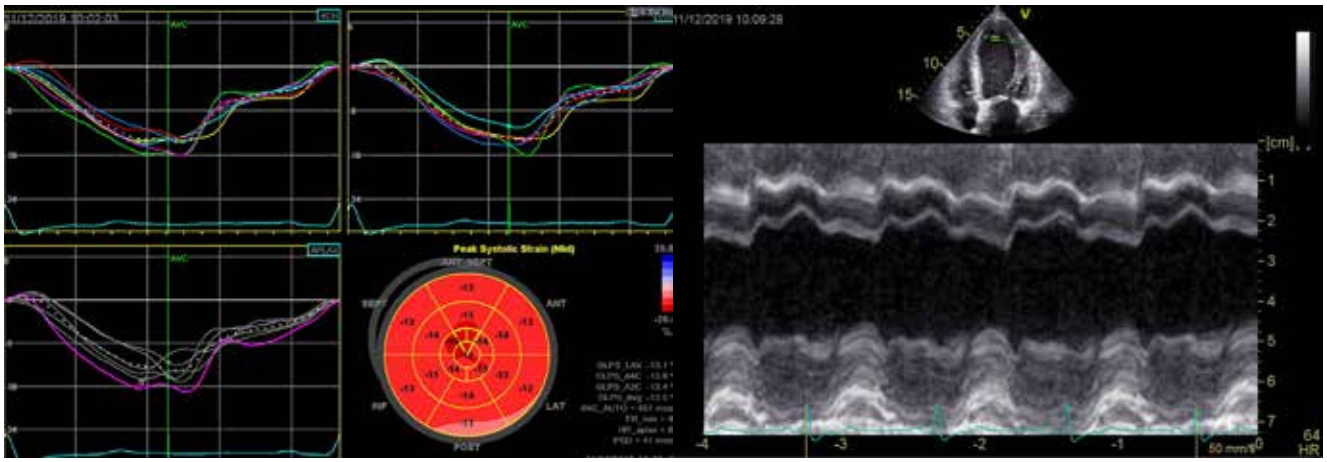

Figure 2. Postsystolic shortening (PSS) during Dobutamin stress echocardiography: speckle tracking echocardiography in basal segment of posterior wall and reduction of longitudinal strain (left); PSS on M-mode in apical segment of the septum

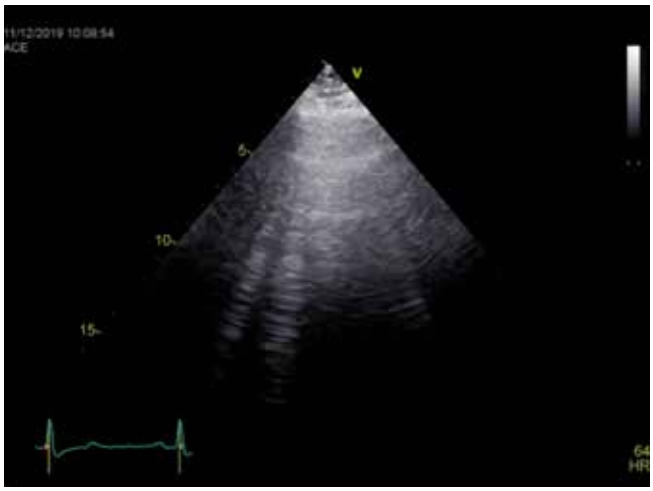

Figure 3. Ultrasound lung comets during stress echocardiography: clinically useful sign of extravascular lung water as a sign of acute pulmonary congestion during stress

was recomended for arterial hypertension, HF and CAD with upgrade of antidiabetic therapy with sodium-glucose cotransporter 2 inhibitor (SGLT2i).

Discussion

Heart failure with preserved ejection fraction is a significant clinical problem for patients with DM. Current clinical data suggest that between 30% and 40% of patients with HFpEF suffer from DM. Pathophysiological processes in HFpEF in diabetics include reduced LV compliance with increased enddiastolic stiffness, chronotropic incompetence, reduced LV long-axis systolic function with both epicardial coronary artery disease and microvascular and endothelial dysfunction.

A secondary analysis of the CANVAS trial showed similar reduction in heart failure with reduced ejection fraction (HFrEF) and HFpEF (HR: 0.83;95% CI: 0.55 to 1.25) in diabetics[1]. In the DECLARE-TIMI 58 trial, all patients with HFpEF and HFrEF had similar reduction in hospitalization, but reduced cardiovascular death was observed only in patients with HfrEF[2]. Patobiological mechanisms are still unclear, but patients treated with SGLT2i demonstrated reduction of left ventricular mass, delay in rise of natriuretic peptides as well high sensitive Troponine I[3,4]. On the other hand, therapy with glucagon-like peptide 1 receptor analogue (GLP-1 RA) in patients with T2DM who were at high risk for cardiovascular events showed lower rates of CV events and death from any cause[5] with neutral effect on HF risk in the general population of T2DM patients with established CV disease or with multiple risk factors[6]. Despite these intriguing possibilities, no clinical trials yet have evaluated the long-term effects of combined use of the two drugs. Given their commercial availability and the fact that both classes have approved indication to reduce CV risk, the dilemma remains how to

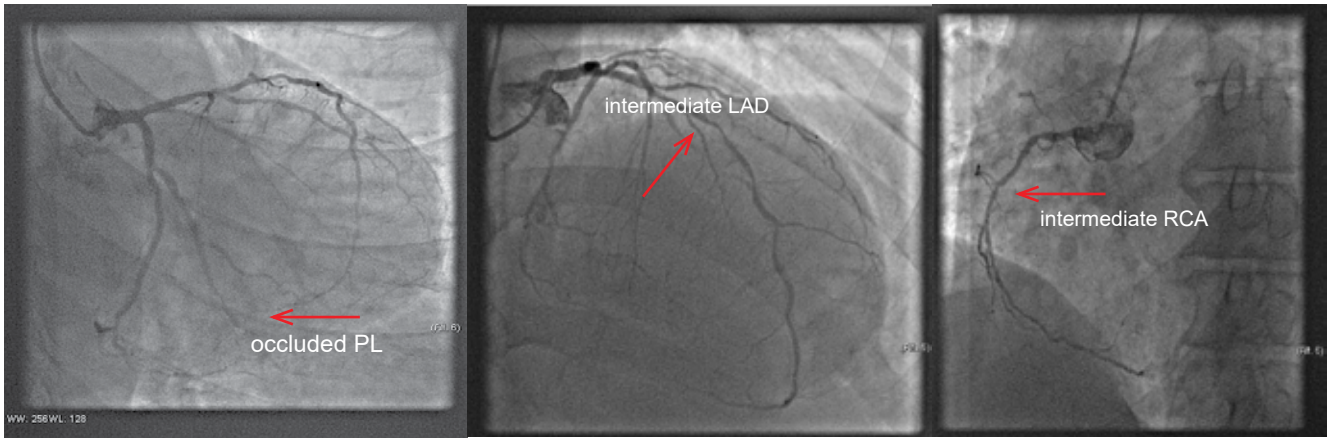

Figure 4. Selective coronarography.

choose between SGLT2i and GLP-1 RA in a T2DM patient with HF and CAD? In conclusion, ongoing trials are addressing the role of SGLT2i by reducing adverse cardiovascular outcomes in patients with HFpEF and chronic kidney disease, with and without T2DM while the role GLP-1 RA remains to be defined in individuals with established HF.

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Case report

Risk reduction of atherosclerotic cardiovascular disease through triglycerides management: Case report

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Abstract Despite extensive studies of strategies to prevent and treat risk factors after myocardial infarction, current evidence documents disappointingly slow, and in many cases limited, implementation of these therapies in practice and daily life. Thus, secondary prevention programs were recognized by the guidelines and introduced in everyday clinical practice around Europe. Programs include a range of interventions with health education, lifestyle advice, risk factors control, stress management and physical exercise components – exercised based cardiac rehabilitation, in order to reduce risk of morbidity and mortality among cardiac patients

In 2019 new guidelines for the management of dyslipidaemias recommended drug treatment of hypertriglyceridemia in high risk individuals if triglyceride level is above 2.3 mmol/l. Through case report we aimed to present the steps in recommended risk reduction of atherosclerotic cardiovascular disease through triglycerides management.

Kew words risk factors, hypertriglyceridemia, drug treatment, secondary prevention programs, exercise based cardiac rehabilitation

Introduction

Current guidelines from the European Society of Cardiology recommend exercise-based cardiac rehabilitation (CR) for patients after myocardial infarction, as a part of secondary prevention programs. Specialized prevention programs are delivered as CR or other prevention programs for all patients with CVD or at high risk for CVD by cardiologist. The core components and goals of CR have been standardized, but the structure, length and type of program offered differs widely by country. CR is a comprehensive programmed involving exercise training, risk factor modification, education and psychological support (1-3)

In this case report we present a young patient who was referred to our cardiology department for out-patient exercise-based cardiac rehabilitation after myocardial infarction, with special emphases on triglycerides management and risk reduction of further atherosclerotic cardiovascular disease progression.

Case presentation

A 42-year-old male was referred to our Cardiology department for out-patient 12 weeks cardiac rehabilitation program after myocardial infarction. The patient was not able to attend the in-house program due to life circumflecses (unable to get paid 3 weeks leave of absence from his work, single parent)

Patient assessment on admission – mid june 2019
History of present illness and previous heart investigations

- In the end of April 2019 patient was admitted to Coronary Care Unit due to acute myocardial infarction – STEMI of inferoposterior wall, two hours after the beginning of chest pain
- PPCI was performed: two vessel diseases, RCA was infarct related artery, LAD was presented with medial stenosis of 30% and in distal segment was sub occluded, RCA was opened and drug eluted stent was implanted. POBA of LAD was scheduled and performed after 6 days of STEMI.
- Cardiac echo: Normal dimensions of chambers with wall motion abnormalities according infarction localization, EF 40%
- Lab analysis in acute settings: TC 5.27, LDL 2.13, TG 4.93mmol/l
- Risk factors for coronary artery disease: smoking, no familiar history, Wt 81kg, Ht 182cm, waist circumference 95cm

Past medical history: none

Physical activity level: sedentary lifestyle, walking up to 2 km, not on regular bases

Medications on discarge from acute hospital: ASA 100mg, Ticagrelor 90 mg 2x1, ramipril+ hidrohlotriazide 5mg+12,5mg 1x1, Bisoprolol 5 mg, , Rosuvastatin 20 mg 1x1, lansoprazol 15mg

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Discarged plan from acute hospital: TC, HDL, LDL, TRGL were order for first control scheduled in 6 weeks, plus CK, AST, ALT

Medications on admission to cardiac rehabilitation: ASA 100mg, Ticagrelor 90 mg 2x1, ramipril+ hidrohlotrtiazid 5mg+12,5mg 1x1, Bisoprolol 5 mg, Lansoprazol 15mg. Due to arise in ALT -Rosuvastatin 20 mg 1x1 were stopped two weeks before admission to Our Institution)

Vital signs on admission to secoundary prevention program:
BP 110/70mmHg • Pulse 72/min • Temp 36,6 °C • Resp 20 • Ht (1.82 m) • Wt 82 • BMI 24.8 kg/m2 • SpO2 99%, waist circumference 95cm
Labs: • WBC 5.8 • RBC 4.54; Hb 131; Ht 0,398, Na 139; K 4.0 TC 4.53, HDL 0.92, LDL 3,18, TG 3,3 • Glucose 5.14
Physical examination: no signs of heart failure, good blood pressure regulation, ECG: sin. rhythm, heart rate 72/min, q with negative T in D2, D3, aVF
Exercise capacity on entrance: estimated by exercised stress test: 10minutes and 6sec 25W, 50W, 75W and 100W for two minutes, max BP 165/105mmHg, heart rate 136/ min
Twelve weeks out-patients exercised- based cardiac rehabilitation program was created individually according to patient's age, past habits, risk factors, co-morbidities, preferences and goals, with aim to:

1. Improve exercise capacity – 30 min moderate intensity aerobic activity 3 days a week with progression to 45 minutes in follow up: continues endurance training with heart, ECG and blood pressure monitoring regarding the heart rate reserve + resistance training
2. Perform additional heart test – 24h ECG monitoring, BP monitoring, echocardiography (EF48%) and lab analysis – HBA1C
3. Optimize medical therapy:
   a. blood pressure control: doses optimized
   b. better lipid levels control: to archive not only LDL but also TG goals according the guidelines
   c. heart rate control
4. Educate the patient: diet intake, risk factors control, stop smoking, regular physical activity, limited alcohol intake

Medication during secoundary prevention program

1. ASA 100mg
2. Ticagrelor 2x90mg
3. Bisoprolol 5 mg OD
4. Ramipril 5 mg OD
5. Rosuvastatin 20 mg OD
6. Ezetimibe 10 mg OD
7. Fenofibrate 160 mg
8. Lansoprazol 15mg OD

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 46/min at 2.00am, maximal 111/min at 9.am. No episodes of atrial fibrillation were recorded; there were 11 SVES and 2 VES.
2. Echocardiography exam: left ventricle was normal in diameter with mid range ejection fraction, EF 48%
3. Lab analysis after 12 weeks: LDL 1,01 mmol/l, TG 0,73 mg/ml, HbA1C within the reference range

Exercise capacity at the end of the program: estimated by exercised stress test: 12minutes and 8sec 25W, 50W, 75W,100 W, 125 W for two minutes, max BP 190/115mmHg, heart rate 150/ min.

Secondary prevention: exercised based cardiac rehabilitation program:

1. It is recommended to initiate exercise training in a structured, supervised, centre-based program
2. It is mandatory that (sub) maximal exercise capacity is measured with a symptom-limited cardiopulmonary exercise test or exercise stress test. Based on the results:
   • training intensity and perform training adjustments were determined
   • risk and prognosis were determined
   • Re-test after exercise training program was done to objectify improvement in exercise capacity
3. A universal agreement on the best training modality in heart failure with mid range EF does not exist. An individualized approach is recommended. Training protocols vary in a number of ways: intensity (aerobic and anaerobic), type (endurance, resistance) and method (continuous and interval). Continuous endurance training is the best described form of exercise training and, because of its well-demonstrated efficacy and safety, is highly recommended in the guidelines. It is characterized by a moderate-to-high exercise intensity at steady-state condition of aerobic energetic yield, allowing the patient to perform prolonged training sessions (45-60 min duration). The exercise is usually performed on a bicycle or treadmill.
4. Resistance/strength training has been proposed to prevent the wasting syndrome and to incorporate upper body exercise, which is important to complete daily life tasks. It is important to prescribe dynamic resistive exercise training of small muscle groups and to avoid Valsalva maneuvers. The patient's preferences should be taken into account

Discussion

The previous ESC/EAS lipid Guidelines were published in August 2016.The emergence of a substantial body of evidence over the last few years has required new, up-to-date Guidelines. In 2019 ESC/EAS Guidelines were presented[3].
New evidence has confirmed that the key initiating event in atherogenesis is the retention of low-density lipoprotein (LDL) cholesterol (LDL-C) and other cholesterol-rich apolipoprotein (Apo) B-containing lipoproteins within the arterial wall[3].Several recent placebo-controlled clinical studies have shown that the addition of either ezetimibe or anti-proprotein convertase subtilisin/kexin type 9 monoclonal antibodies to statin therapy provides a further reduction in atherosclerotic cardiovascular disease (ASCVD) risk, which is directly and positively correlated with the incrementally achieved absolute LDL-C reduction.

What is new in 2019 Guidelines regarding triglicerydes?

Statin treatment is recommended as the first drug of choice for reducing CVD risk in a high –risk individuals with hypertrigliceridemia (TG >2.3 mmol/l – 200 mg/dl) as stated in new 2019 guidelines. In 2016 it was stated that statin treatment might be used as the first drug of choice in patients with hypetriglyceridemia without considering the cut off values. AHA guidelines from 2018 did not consider hypetrigliceridemia separately[4].

Since TG-rich VLDL particles and their remnants carry most of the circulating TGs, the plasma TG concentration reflects the concentration of circulating ApoB-containing TG-rich lipoproteins. According to 2019 guidelines[3] elevated plasma TG levels are associated with an increasing risk of ASCVD, but this association becomes null after adjusting for non-HDL-C, an estimate of the total concentration of all ApoB-containing lipoproteins. Lowering TG with fibrates reduces the risk of CV events by the same amount as LDL-C-lowering therapies when measured per unit change of non-HDL-C, suggesting that the effect of plasma TGs on ASCVD is mediated by changes in the concentration of TG-rich lipoproteins as estimated by non-HDL-C.

We presented the very high risk young patients (two vessel disease, STEMI recently, heart failure with mid range EF) 42 years of age that illustrate risk reduction of further atherosclerotic cardiovascular disease as part of secondary prevention programs through triglycerides management, 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 MI

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 with ASCVD. CR should be tailored according to individual risk profile, physical, psychological and social status assessed as part of medical history and examination[1].

Our patient had no possibilities to attend or 3 weeks inhouse cardiac rehabilitation program (patient-related gap). Thus, recently developed out- patients 12 weeks program in our Institution was indicated.

Patients with CVD understand poorly their disease and perceive themselves as having little control over its course, many lack interest in prevention and/or feel embarrassed about participating in preventive group sessions. Most of them do not receive robust information and/or encouragement from physicians and other health professionals regarding how to prevent recurrent events. Other factors, which hinder attendance, include lack of social support, poor psychological wellbeing, and inconvenient location with transport difficulties, competing work commitments and financial cost

Secondary prevention programs are created in order to promote physical activity, risk factors control, and adherence to therapy. Our patient was presented with normal BMI, no familiar history of CAD; with smoking, physical inactivity and inappropriate lipid profile low HDL, high LDL and high tryglicerides as risk factors. Thus our aim was to reduce risk by promote healthy lifestyle habits, appropriate physical activity and adherence to recommended drug therapy.

Lifestyle and triglyceride levels: Weight reduction improves insulin sensitivity and decreases TG levels. Regular physical exercise reduces plasma TG levels over and above the effect of weight reduction. Alcohol intake has a major impact on TG levels, particularly in individuals with HTG. Habitual consumption of significant amounts (>10% energy) of dietary fructose contributes to TG elevation, particularly in people with HTG or abdominal obesity. These effects are dose-dependent; with a habitual fructose consumption between 15–20% of total energy intake, plasma TG increases by as much as 30–40%. Sucrose, a disaccharide containing glucose and fructose, represents an important source of fructose in the diet[5-7].

Smoking cessation has clear benefits regarding overall CV risk, and specifically on HDL-C levels.[3]

Of great importance is regular exercise training. It was created according to clinical, baseline exercise capacity and prior habits. Endurance and resistance training were used. Moderate intensity aerobic endurance training composed of bicycling, walking and crossing over Nyllin steps, 3 times per week during 12 days. Exercise capacity of our patient was improved.

Lipid lowering drugs: Our goal was to achieve LDL levels beyond 1.4 mmol/l, and triglyceride levels below 2.3 mmol/l. Regarding LDL levels guidelines from both sides of the world (REF) are the same. During in patient CR program patient was educated in this term[3].

Statins reduce the synthesis of cholesterol in the liver by competitively inhibiting the enzyme HMG-CoA reductase, the rate-limiting step in cholesterol biosynthesis. The reduction in intracellular cholesterol promotes increased LDL receptor (LDLR) expression at the surface of the hepatocytes, which in turn results in increased uptake of LDL from the blood, and decreased plasma concentrations of LDL- and other ApoB-containing lipoproteins, including TG-rich particles[4]. Statins usually reduce TG levels by 10–20% from baseline values. (REF) More potent statins (atorvastatin, rosuvastatin, and pitavastatin) demonstrate robust lowering of TG levels, especially at high doses and in patients with elevated TGs (HTG), in whom the absolute risk, and therefore the absolute risk reduction, is larger.

Ezetimibe added to ongoing statin therapy reduces LDL-C levels by an additional 21–27% compared with placebo in patients with hypercholesterolaemia with or without established CHD. In statin-naïve patients, ezetimibe and statin combination therapy has resulted in around a 15% greater reduction in LDL-C when compared with the same statins and doses in monotherapy. Our patient was added ezetimibe to statin therapy to acchive target LDL[3].

Fibrates have good efficacy in lowering fasting TG levels, as well as post-prandial TGs and TG-rich lipoprotein (TRL) remnant particles as addition to statin therapy. In patients with high triglyceride levels [≥2.3 mmol/L (200 mg/dL)], lifestyle advice (with a focus on weight reduction

and alcohol abuse, if relevant) and improved glucose control are the main targets. Both the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) and ACCORD studies demonstrated that administration of fenofibrate on top of statins significantly reduced CV events, but only in patients who had both elevated triglyceride and reduced HDL-C levels If triglycerides are not controlled by statins or fibrates, high-dose omega-3 fatty acids (4 g/day) of icosapent ethyl may be used according to recently published REDUCE- IT investigators and guidelines (8-9).

Conclusion

2019 ESC/EAS guidelines for the management of dyslipidaemias differ to previous guidelines and 12018 AHA guidelines in term of risk reduction of atherosclerotic cardiovascular disease through triglycerides management. Statin treatment is recommended as the first drug of choice for reducing CVD risk in a high –risk individuals with hypertriglyceridemia (TG >2.3 mmol/l – 200 mg/dl)

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Sažetak

Redukcija rizika za aterosklerotsku bolest srca optimalnom terapijom triglicerida. Prikaz bolesnika

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Uprkos intenzivnim istraživanjima strategija za redukciju faktora rizika nakon infarkta miokarda u praksi, redukcija rizika je u mnogim slučajevima neadekvatna, a sprovođenje terapije ograničeno. Programi sekundarne prevencije prepoznati su u smernicama i uvedeni u svakodnevnu kliničku praksu širom Evrope. Obuhvataju niz mera koje se sastoje u edukaciji bolesnika, kontroli faktora rizika, optimalnoj terapiji, upravljaju strestom, fizičkoj aktivnosti kroz kardiološku rehabilitaciju baziranu na aerobnom treninigu. 2019 te godine smernice Evropskog druženja kardiologa preporučile su da u redukciji rizika za aterosklerotsku bolest terapija triglicerida zauzima značajno mesto. Kao prva terapijska linija preporučuju se statini ukloliko su vrednosti triglicerida više od 2.3 mmol/l.

Imali smo za cilj da kroz prikaz slučaja ukažemo na značaj sprovođenja svih mera sekundarne prevencije sa posebnim osvrtom na korekciju triglicerida u lipidnom statusu.

Ključne reči: *faktori rizika, hipetrigliceridemija, sekundarni preventivni programi, kardiološka rehabilitacija bazirana na fizičkom treningu*

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Case report

Optimal medical therapy in a patient with a large area of ischemia

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Abstract **Background.** Although percutaneous coronary intervention (PCI) is the gold standard in the treatment of acute myocardial infarction with ST elevation, its role in the treatment of patients with chronic coronary syndrome versus optimal medicament therapy (OMT) is not clearly defined.
Case report. We present a diabetic patient with typical chest pain and large area of ischemia on stress echocardiography and at high risk of adverse cardiac events who was on intensive OMT for 5 years with good control of the symptoms and without adverse cardiac events.
Conclusion. Despite the advances in the invasive treatment of chronic coronary syndrome, the intensive OMT has a key role in treatment of such patients.

Kew words chronic coronary syndrome, optimal medical therapy

Background

Although percutaneous coronary intervention (PCI) is the gold standard in the treatment of acute myocardial infarction with ST elevation, its role in the treatment of patients with chronic coronary syndrome in comparison to optimal medical therapy (OMT, which implies a lifestyle modifications and medication administration) is not clearly defined. No study has shown clearly an advantage of PCI over OMT in terms of reducing the incidence of cardiac death and non-fatal myocardial infarction (IM), although PCI has shown better symptom control in these patients (1-4). In the 2019 European Cardiac Society Guidelines for Chronic Coronary Syndrome, myocardial revascularization in addition to anatomic evaluation of stenosis by coronary angiography require also functional evaluation of stenosis (except for stenoses ≥90%), which can be achieved by invasive or non-invasive functional testing. Only then, in accordance with the comorbidities present, as well as the symptoms, a decision should be made on the further treatment of the patient (5).

Case presentation

We present a 61 year old female patient with typical chest pain who was referred to the cardiologist because of her symptoms. She had no previous cardiac events, no family history of cornary artery disease (CAD), was a non-smoker and she had diabetes type II for 20 years (treated with oral antidiabetic therapy - OAD), hypertension for 27 years and elevated levels of LDL cholesterol, BMI was 28.58 kg/m^2. She was prescribed a following therapy: Acetyl-salicylic acid 1 x 100 mg, Nebivolol 1 x 5mg, Valsartan 1 x 160 mg, Valsartan/Hydrochlorothiazide 1x 160/25mg, Isosorbide mono-nitrate 20 mg + 20 mg +0, Rosuvastatin 1 x 10 mg and previous OAD therapy (Metformin and Gliclazide). Baseline ESC was recorded (Picture 1.) with normal sinus rhythm, resting heart rate of 82 beat /min and ST depression of 0.5mm i the leads D2 and biphasic T in AVL.
Patient was referred to the echocardiography and stress echocardiography. The echocardiography showed normal dimension of left ventricle (EDV 51mm, ESV 33mm), borderline thickness of interventricular septum and posterior wall (11mm), preserved global systolic function (EF 67%), without segmental wall motion abnormalities and with preserved diastolic function. The stress echocardiography (SEHO) test on treadmill was performed according to the Bruce protocol and stopped at the third minute of first stage because of ischemic ECG changes and chest pain after achieving target heart rate. During the test and recovery period ST depression of 1mm in the leads D2, D3, aVF and V4-V6 and elevation of ST segment in the lead aVR were recorded (Picture 2.).
Echocardiography has shown worsening of the wall motion of medial and distal segment of inferior septum, distal segment of anterior septum and whole posterior and inferior wall (Picture 3.). Duke score was -6, MET 5 and heart rate recovery 23 beats/min. Based on the results of the test patient was advised to perform the coronary angiography but she refused, and decide to stay on OMT.

Amlodipine 1x5mg, clopidogrel 1x75mg, trimetazdine 2x35mg were added to current therapy. Nebivolol was switched with high dose of Bisoprolol 5mg+0+2.5mg.

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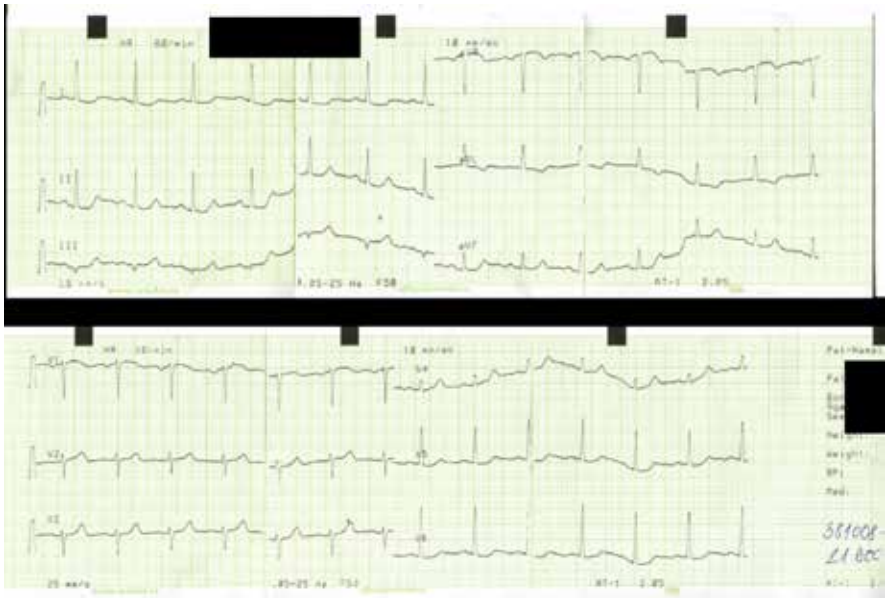

Figure 1. Baseline ECG

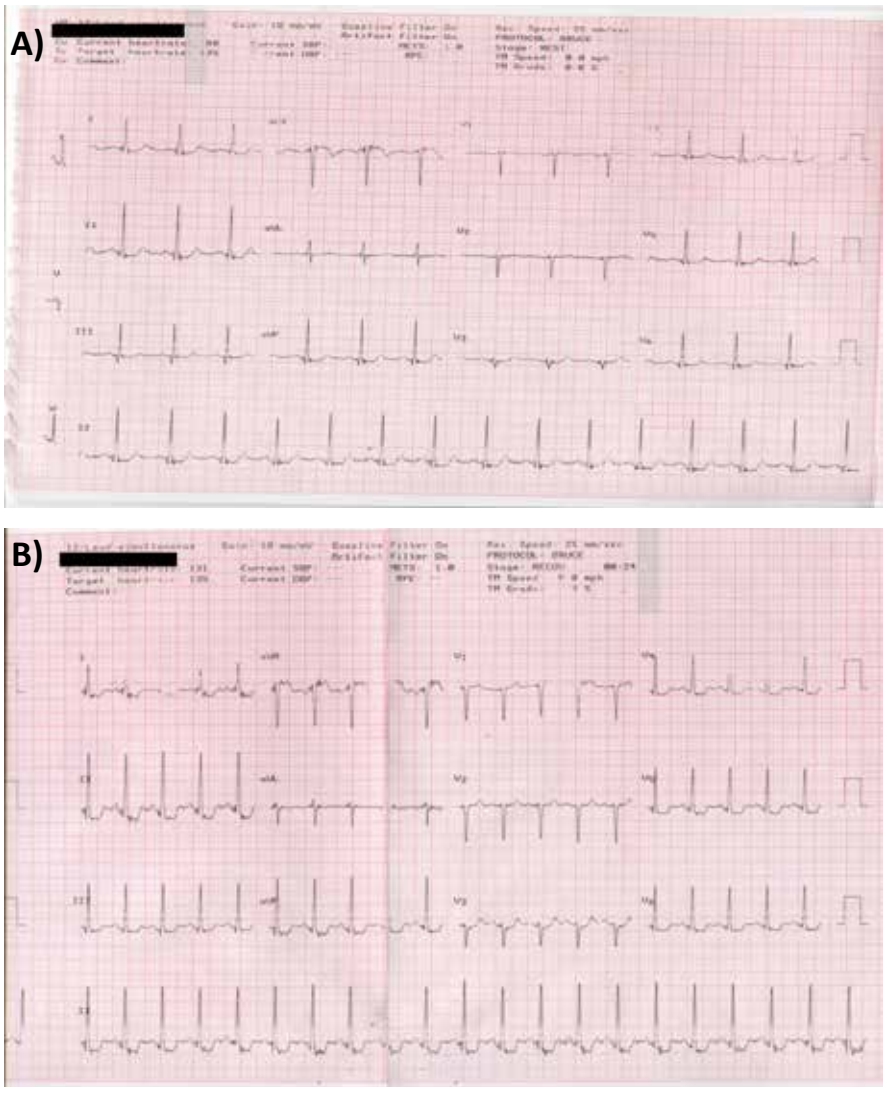

Figure 2. A) resting ECG during SEHO, B) ECG at maximum stress

The next patient visit was scheduled in 6 months. At follow up visit patient stated that she feel much better, that her anginal episodes are rare, and that she endure the effort much better and without a chest pain. The blood sample was drawn and the results showed high level of LDL cholesterol of 3.1 mmol/L and high HbA1c of 9.8%. We increased the dosage of Rosuvastatin to 20mg and sent the patient to the endocrinologist who added the insulin in the therapy. On the next visit in 6 months patient is still satisfied with control of the symptoms and the LDL cholesterol was 1.8mmol/l and HbA1c 6.9%. Patient had regular controls every 6 months without worsening of the clinical status, no new ECG changes and without adverse cardiac events. Amlodipine was increased to 1x10mg. The pharmacological dobutamine stress test was performed four years after initial test, and showed the same ECG result, and at echocardiography wall motion abnormality of inferior and posterior wall was present.
Coronary angiography (13.01.2020.) showed LM without stenosis, stenosis of proximal LAD 70%, middle LAD 90-99%, ostial D1 70-90%, proximal Cx 70-90%, proximal OM1 70-90%, proximal RCA 90-99%, middle RCA 100%. Patient was referred to the CABG operation.

Discussion

We presented a female patient with a high risk of adverse cardiac events, with significant comorbidities and with a large area of ischemia on SEHO testing. According to the new ESC guidelines for chronic coronary syndrome, the patient has a high risk for adverse events and should be referred for myocardial revascularization, (5,6). However, due to the patient's refusal to undergo coronary angiography, she received OMT. After administration of the OMT, the patient felt better and had significantly less episodes of chest pain and better tolerated effort Her cholesterol levels and glycemia were in the range recommendend by Guidelines. Also her physical activities were according to perscription. During 4 years of follow up she has no adverse cardiac event. This is in line with the results of previous studies which showed that there

was no difference in the incidence of adverse cardiovascular events between PCI and OMT in patients with stable CAD. One of the larger randomized studies on this topic was a COURAGE (*Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation*) study (n = 2287) that included patients with a positive SEHO test (proven ischemia). Patients with (previous MI, PCI, or CABG) and without previously known CAD were included in the studt which compared PCI + OMT versus OMT alone .The primary endpoint, all-cause death or non-fatal MI, did not differ between the two groups during a mean follow-up of 4.6 years. However, in patients who were invasively treated, freedom from angina was significantly better up to 3 years of follow-up. In a substudy, patients with >10% ischaemia on stress myocardial perfusion scintigraphy had a higher rate of death or MI. More PCI + OMT patients exhibited significant ischaemia reduction (33 vs. 19%; P= 0.0004).[1]

COURAGE II study, a 15-year follow-up of 1,211 patients included in the original study, also showed the same result for survival in these two groups, (PCI +OMT vs OMT, HR 0.95: 95% CI 0,79 to 1.13, p = 0.53).[7]

These results were confirmed with the prospective, multicenter, randomized ISCHEMIA (*International Study of Comparative Health Effectiveness with Medical and Invasive Approaches)* study (n=5179 pts, follow-up period 3.3 years) whose first results were published in November 2019. Similar like the COURAGE study, this study included patients without and with (previous MI, PCI and/or CABG) previously known CAD. The main criteria for inclusion was moderate to severe ischemia on stress imaging testing (≥3 of 16 segments with stress-induced severe hypokinesia or akinesia) after which patients were referred to the blinded CTA to exclude LMCA disease. The trial hypothesis is that cardiac catheterization followed by complete revascularization (based on the functional and anatomical assessment of stenosis) plus OMT is superior to OMT alone, for patients with moderate-severe ischemia on stress imaging. This study also showed no significant difference in the endpoint (all-cause mortality, non-fatal MI, hospitalization for unstable angina, resuscitated cardiac arrest, or heart failure), between two treatments. Further more, routine invasive therapy was associated with harm at 6 months (increase in periprocedural myocardial infarctions) and with benefit at 4 years (reduction in spontaneous myocardial infarction). These results do not apply to patients with current/recent acute coronary syndrome, highly symptomatic patients, left main stenosis, or left ventricular ejection fraction <35%. The effect of the revascularization on the improvement of the symptoms (quality of life) is not yet published.[8]

De Bruyne B. and al. in their study, which compared the FFR-guided PCI + OMT vs OMT alone in patients with stable CAD (n=888) also showed that there was no difference between the groups regarding the overall rate of death and non-fatal MI (7.1% vs 8.6%, p=0.56 respectively). However in this study, the PCI group had significantly lower rate of urgent revascularization triggered by myocardial infarction or ischemic changes on electrocardiography (4.0% vs. 16.3%; hazard ratio, 0.23; 95% CI, 0.14 to 0.38; P<0.001) respectively) and had better improvement of symptoms at 2 year follow up.[3]

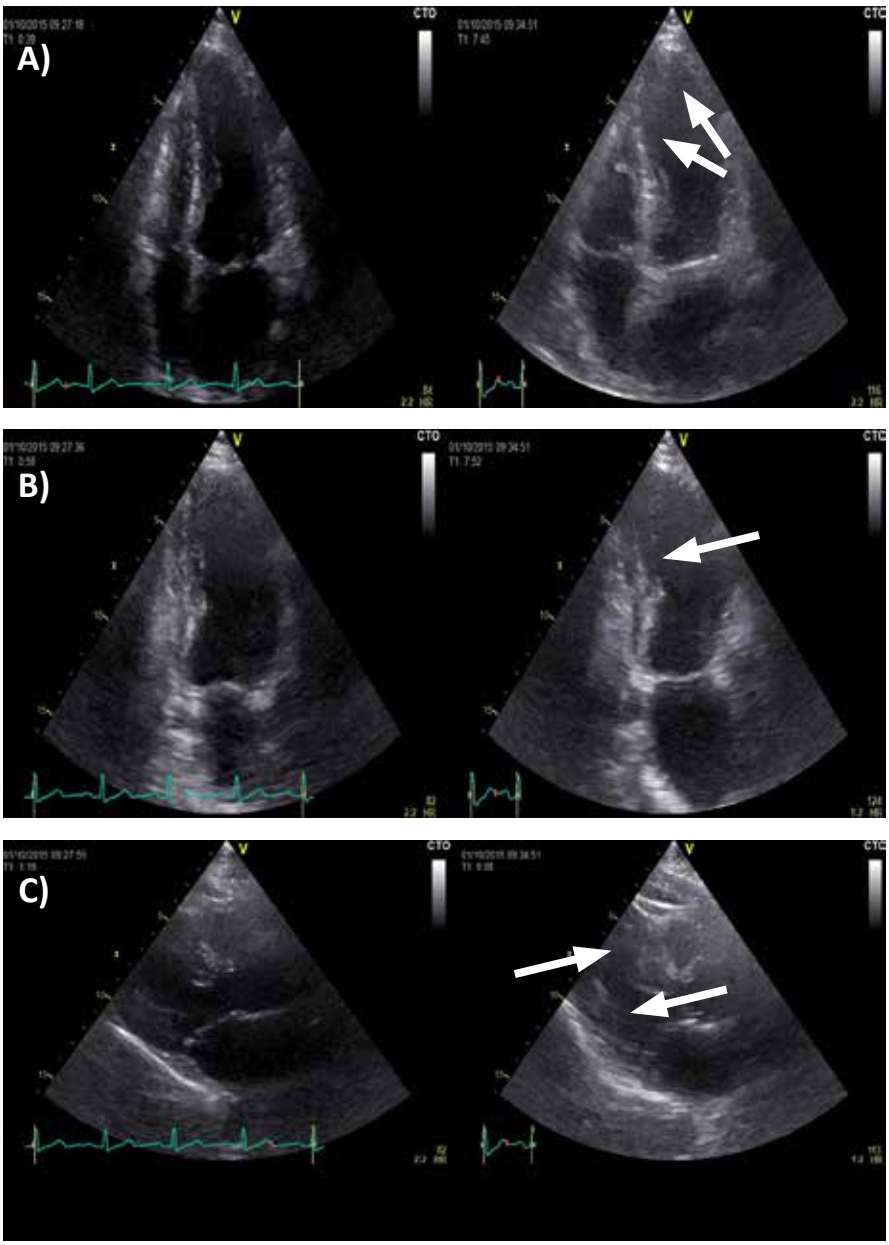

Figure 3. A) 4-chambers view at rest (left side) and on SECHO test (right side) B) 2-chambers view at rest (left side) and on SECHO test (right side) C) Parasternal long axis view at rest (left side) and on SECHO test (right side); arrows showing wall motion abnormalities

Conclusion

Our case report showed successful prevention of adverse cardiac events and improvement of symptoms in the patient with large area of inducible ischaemia and unfavorable risk profile with OMT and optimal risk factor control. This example confirms the existing guidelines on the management of chronic coronary syndrome provided only when intensive OMT is initiated and maintained. Nevertheless, clinical practice should be driven by the objective assessment of the patient's clinical status and in the case of clinical deterioration myocardial revascularization should be performed.

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Sažetak

Uvod. *Iako je perkutana koronarna intervencija (PKI) zlatni standard u lečenju akutnog infarkta miokarda sa ST elevacijom, njegova uloga u lečenju pacijenata sa hroničnim koronarnim sindromom u odnosu na optimalnu medikamentnu terapiju (OMT) nije jasno definisana.*

Prikaz slučaja. *Predtavljamo slučaj bolesnice sa dugogdišnjim dijabetesom, tipičnim anginoznim tegobama i velikom zonom ishemije na stres ehokardiografskom testu koja je u visokom riziku od nastanka neželjenih kardiovaskualrnih događaja. Bolesnica je 5 godina na inzentzivnoj OMT sa dobrom kontrolom simptoma i bez neželjenih događaja.*

Zaključak. *Uprkos napretku u invazivnom lečenju hroničnog koronarnog sindroma, intenzivna OMT ima ključnu ulogu u lečenju takvih pacijenata.*

Ključne reči: *hronični kronarni sindrom, optimalna medikamentna terapija*

Srce i krvni sudovi 2020; 39(1): 19-22

Case report

A case report of an acute postoperative pulmonary thromboembolism

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Institute for Treatment and Rehabilitation Niska Banja

Abstract Pulmonary embolism (PE) is a disease that can lead to sudden cardiac death and in many patients, PE is the result of deep vein thrombosis (DVT). Surgical interventions are a significant risk factor for VTE and are the most common cause of immediate postoperative death. The paper presents a case report of a diagnosis and treatment algorithm applied in a patient who developed acute, pulmonary thromboembolism in an early, postoperative course. An acute, pulmonary thromboembolism has been diagnosed using modern diagnostic tools, according to the recommendations of the European Association of Cardiologists 2019 for the diagnosis and treatment of patients with pulmonary thromboembolism. In the acute phase in our patient, thrombotic masses in the right heart chambers were verified, fibrinolytic therapy with satisfactory therapeutic effect and no side effects was applied. The prognostic evaluation, which is also important in the further evaluation of the patient, was performed at the same time as the diagnosis of pulmonary thromboembolism and risk stratification based on the most common scoring system - the PESI index.

Kew words pulmonary thromboembolism, surgical interventions, fibrinolytic therapy

Introduction

Venous thromboembolism (VTE) is a clinical syndrome that includes deep vein thrombosis (DVT) and pulmonary embolism (PE). In terms of frequency, this disease ranks third among cardiovascular diseases, and annually, about 100-200 people in 100,000 people experience pulmonary thromboembolism (1). Pulmonary embolism (PE) is a disease that can lead to sudden cardiac death. It is caused by obstruction of the smaller or larger branches of the pulmonary artery, most commonly by thrombus, rarely by air embolus, adipose tissue, tissue particles, and amniotic fluid. Knowledge of risk factors is important in determining the likelihood of PE. Unfortunately, causing risk factors can not be identified in even 40% of patients with pulmonary embolism (2, 3). Surgical interventions, leg fractures, or replacement of the wrist with artificial, as well as spinal cord injuries are well known predisposing factors for VTE. The diagnosis is quite difficult and is only made in 50% of patients. Diagnostic evaluation in patients with suspected pulmonary embolism begins with an assessment of the likelihood of an event, which is performed by applying clinical rules known as the Vells' Rules and the Revised Geneva scoring system (4).

Case presentation

Male patient, 61 years old, admitted on May 18, 2018 to the Coronary Unit of the Niška Banja Institute for serious suffocation. This is a patient who underwent left leg amputation surgery on April 27, 2018 as a result of a chronic complication of prolonged diabetes mellitus. After six days of hospital treatment, he was discharged home without any anticoagulant therapy. Among the risk factors for cardiovascular disease are hypertension, hyperlipidemia, diabetes, obesity and a positive family history. On admission, an ECG was performed showing a sinusoidal rhythm, HR 102 bpm, S1Q3T3, ST segment elevation up to 1mm in D3 lead, incomplete right branch block (Figure 1).

On admission he was dyspneic, tachypnoic, with skin and visible mucous membranes pale in color, irrigated with cold sweat, SaO2 on admission was 62%; auscultatory lung finding: with no arrest; auscultatory heart finding: rhythmic action, tachycardia, BP=140/70mmHg, HR= 104 bpm; liver was palpable 3-4 cm below the right costal margin; pretibial swelling of the right lower leg, amputated left leg, bandaged stump. The patient was immediately suspected of pulmonary thromboembolism based on the clinical presentation, predisposing risk factors and the presence of ECG changes. Based on current European Guidelines for the diagnosis and treatment of acute pulmonary thromboembolism 2019, we used the Geneva score system, which showed that a clinical diagnosis of PTE was plausible (3 points: within one month surgery and heart rate> 95 bpm; Table 1). Upon admission, a laboratory was made that showed elevated BNP and D-dimer values (BNP was 2,420, TnI level - negative, DDIM 2900).

We also performed an initial risk assessment in patient with PTE, which is necessary and begins immediately after the suspicion of the disease and the start of diagnostic treatment is important not only for intrahospital prognosis and 30-day mortality, but also for the choice of therapeutic modality (Table 2) . Because our patient was hemodynamically stable, he was classified as not at high risk.

The therapy was started immediately (oxygen therapy, low molecular weight heparin - enoxaparin 1mg/kg body weight at 12h, antibiotic therapy (ceftriaxone 2g/24h), cardiotonic agents, bronchodilators, diuretics, strictly dosed infusion solutions. Echocardiogram (ECHO) performed on admission day revealed significant enlarged right chambers (Mc Connell's sign - positive). He was rhythmically and hemodynamically stable from admission. MSCT of pulmonary arteries was performed on May 21, 2018. MSCT showed thrombotic mass lodged in the bifurcation of the pulmonary trunk with extensions into both main pulmonary artery branches. Thrombotic masses were also seen in all lobar and segmental branches of the pulmonary artery. Conclusion: massive pulmonary thromboembolism. Follow-up ECHO was performed on

Table 1. Clinical rules for the prediction of pulmonary thromboembolism

Clinical rules for the prediction of pulmonary thromboembolism		
	Clinical assessment / scores	
Revised Geneva Score	Originally version	Simplified version
Previous DVT or PE	3	1
Heart rate		
75-95 bpm	3	1
≥ 95 bpm	5	2
Surgery or fracture within a month	2	1
Hemoptysis	2	1
Active cancer	2	1
Unilateral lower extremity pain	3	1
Localized tenderness along the distribution of the lower extremity deep venous system and one-sided swelling	4	1
Age >65 years	1	1
Clinical probability		
Three levels score		
Low	0-3	0-1
Moderate	4-10	2-4
High	≥11	≥5
Two levels score		
Low probability for PE	0-5	0-2≥
PE probable	≥6	≥3

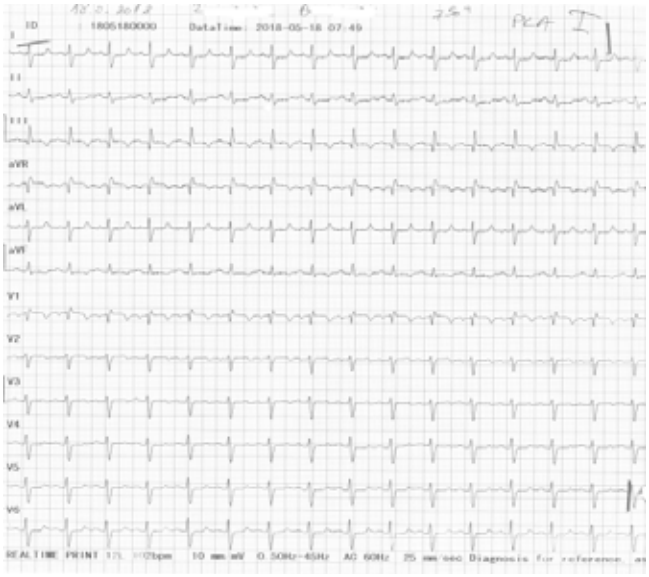

Figure 1. Admission ECG

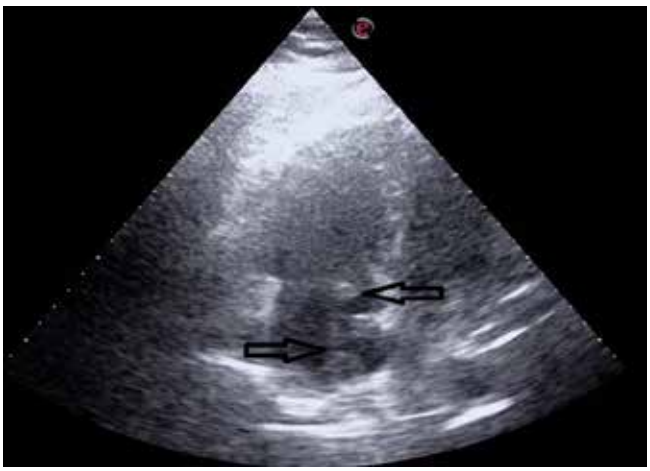

Figure 2. ECHO of thrombotic mass in the right atrium

Table 2. Classification of pulmonary embolism severity and risk of premature death (in hospital or 30 days)

Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥1	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

hospital Day 3 and revealed EFLV 60%, enlarged right chamber and, for the first time, verified striated, hyperechogenic structures (thrombotic masses - Figure 2) in the right atrium, which are fixed at the base for the interatrial septum and during the diastole prolapsed through the tricuspid orifice into the right ventricle cavity.
The patient remains rhythmically and hemodynamically stable. In the morning of the Treatment Day 4, the general condition of the patient worsens, with a blood pressure drop that soon becomes immeasurable followed with hypoxia, the patient becomes pale, flushed with cold sweat, and the decision to use fibrinolytic therapy was made, although the patient was amputated 23 days earlier; left leg was amputated above the knee (Actilisa /INN: alteplase/ 100 mg for 120 minutes). After administration of thrombolytic therapy, the patient was stabilized with introduced unfractionated heparin and warfarin therapy. On May 31, 2018, the patient was discharged as stable condition and, with conventional cardiology therapy, he received warfarin prescription.

Discussion

Venous thromboembolism (VTE) is a clinical syndrome that includes deep vein thrombosis (DVT) and pulmonary embolism (PE). In terms of frequency, this disease ranks third among cardiovascular diseases, and annually, about 100-200 people in 100,000 people experience pulmonary thromboembolism[1]. The predisposing factors for the occurrence of VTE are numerous, and they may be related to the patient himself or related to external factors. Injuries, Surgical interventions, leg fractures, or replacement of the wrist with artificial, as well as spinal cord injuries are well known predisposing factors for VTE. The use of hormone therapy in fertile women, pregnancy and puerperium, malignancies also carry the risk of VTE, and haematological malignancies have the highest thromboembolic potential. The most important predisposing factor is acquired or congenital thrombophilia. Various registries of patients who had an episode of VTE or PE during hospitalization showed that after 30 days of discharge, the overall mortality was between 9% and 11%, and after 3 months, between 8.6% and 17%[5]. Earlier studies revealed that the proportion of patients with early recurrent episodes of VTE (who were on anticoagulant therapy) increased over time, being 2% after two weeks, 6.4% after three months, and 8% after 6 months. More recent studies suggest that the highest incidence of recurrent PTE is highest within 2 weeks of discharge and declines over time. In that early period, the presence of cancer or the inability to achieve an adequate level of anticoagulant care are undoubtedly the most important predictors of an increased risk of recurrent VTE.
Later occurrence of recurrent episodes of VTE (after 6 months or after discontinuation of anticoagulant therapy) occurs in 13% of patients after one year, in 23% of patients after 5 years, and in 30% after 10 years. Factors associated with subsequent, recurrent VTE episodes are: years, male gender, family PTE, and increased body mass index. Elevated D-dimer levels, either during or after discontinuation of anticoagulant therapy, are an independent prognostic factor for late, recurrent thromboembolism[6]. Initial assessment, which depends on the patient's clinical status and its comorbidities, is very important before treatment of PE patients (Table 1). Patients with suspected PE who are in shock or have hypotension are classified as high-risk patients. They require an immediate diagnostic approach, and if the diagnosis confirms the use of pharmacological (or alternatively, surgical) reperfusion therapy. Other patients belong to the category of moderate or low risk, and they are scored (usually according to the PESI or sPESI score) after the diagnosis, to determine the risk level. Patients with PESI ≥3 or with PESI≥1 belong to the intermediate risk category. If there is right ventricular dysfunction and an increase in cardiac biomarkers (especially troponin), it is intermediate-high risk, and if only one of these two parameters is positive, intermediate-low risk7. The association of thrombotic masses in the right heart chambers and pulmonary thromboembolism is, in most cases, extremely emergency regarding the administration of therapy. These patients belong to the group of high-risk patients. The prevalence of thrombotic masses in pulmonary thromboembolism is 4% -18%[8,9] and is associated with an increase in mortality. The therapeutic option includes surgical thrombectomy in well-equipped centers or drug thrombolysis and anticoagulant therapy[8,9,10,11].
Thrombolytic therapy in these situations is the fastest and most appropriate therapeutic treatment in most situations[12]. Treatment of high-risk patients with PE involves the use of thrombolytic drugs, unless contraindications exist, together with anticoagulant medicines. If contraindications exist for the use of thrombolysis then surgical embolectomy should be considered. In intermediate- and low-risk patients in the acute phase, treatment consists in the administration of NMH or pentasaccharide, fondaparinux, together with new, non-vitamin K drugs (dabigatran, rivaroxaban, apixaban, and edoxaban)[1,13].

Conclusion

The diagnosis of PTE is a great challenge, because classic symptoms are not present in many cases. In order to make a diagnosis, it is crucial in the initial diagnostic step to suspect this disease, especially if there are well-known predisposing risk factors for PTE. Strong risk factors for deep vein thrombosis, and therefore pulmonary embolism are major trauma, surgery, low extremity fractures, artificial hip replacement, and spinal cord injury. Guidelines from the European Association of Cardiology for the Diagnosis and Treatment of Acute Pulmonary Thromboembolism significantly help in the diagnostic algorithm for PTE and the choice of therapy should be put into practice with personalized approach to the patient.

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Case report

How should we obtain a precise estimate of cardiovascular risk in asymptomatic adults?

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Abstract **Background.** A precise estimate of cardiovascular (CV) risk in asymptomatic individuals is a key factor in the primary prevention of CV disease.
Case report. In this report describe an asymptomatic individual presenting for CV status assessment. After the CV risk assessment using the SCORE risk charts and Framingham score, additional tests were performed, which provided better insight and reclassification of risk in this individual. Carotid Doppler sonography revealed plaques in the carotid arteries. Non-invasive assessment of coronary flow reserve (stress echocardiography test) demonstrated that a considerable area of the left ventricle is suffering ischemia when stressed. This was an indication for coronarography, which showed severe three-vessel coronary disease, that was later successfully treated by surgical revascularization. A year after the surgery a control stress echocardiography was performed, showing a satisfactory coronary flow reserve.
Conclusion. A precise estimate of CV risk in asymptomatic individuals opens the road leading to early diagnosis, adequate therapy, and prevention of CV disease.

Kew words cardiovascular risk, prevention cardiovascular disease, carotid disease

Background

Discovery of the atherosclerotic disease in its early stages is essential in preventive cardiology. The guidelines for the prevention of cardiovascular (CV) diseases of the European and American associations of cardiology stress out the importance of CV risk assessment. The charts from which CV risk can be calculated are based on a mathematical model containing modifiable risk factors. The European Society of Cardiology has developed the SCORE (Systematic Coronary Risk Estimation)[1] system, which utilizes charts containing the variables of age, gender, smoking, systolic blood pressure value and total serum cholesterol value. The result obtained from these charts determines the total CV risk, *i.e*. the risk of dying from CV disease in the next ten years for persons aged 40-65 years. These charts are specifically adjusted for countries with low and those with high CV risk. According to the American guidelines for CV disease prevention[2], the risk is estimated based on the Framingham score[2,3]. Using the most recent version, a ten-year risk of CV event can be calculated for persons aged 30-75 years. The variables included in this score are gender, age, total serum cholesterol value, HDL-cholesterol, systolic blood pressure values, smoking habits, diabetes mellitus and hypertension treatment. In recent years, however, both guidelines suggest the need for additional methods for CV risk reclassification, and especially so in individuals for which low or intermediate risk scores are obtained initially. According to these guidelines, and also the most recent lipid guidelines, the most important is calcium score (coronary artery calcium - CAC - which is determined using the electron beam or multislice CT imaging) and the detection of carotid atherosclerotic plaques by carotid artery scanning[1,2]. Further below, we will describe how one of these methods proved valuable in the detection of severe atherosclerotic disease of the carotid arteries in an asymptomatic individual.

Case presentation

A male patient, 65 years old, presented for an examination in order to assess one's health because of the forthcoming business engagements. He denied having any heart-related symptoms and stated that he had been healthy; except for occasional propranolol, he did not take any heart medications. Regarding other modifiable risk factors, he stated that he had had elevated blood lipids but he had not taken any cholesterol-lowering medications. He was not a smoker, and his blood pressure was normal before that presentation. His office blood pressure measured at that first examination was 110/65 on the left, and 105/63 on his right arm, with heart frequency (HF) of 78/min. On auscultation, a regular heart rhythm was heard, without any additional tones and without noises at auscultatory points. A systolic ejection-type noise was heard in the carotid on the right. Electrocardiography demonstrated sinus rhythm, pathological left heart axis, and corrected QT interval was 423 ms (Fig. 1). According to the SCORE chart for European countries with high CV risk, the total CV risk was 7% (SCORE table

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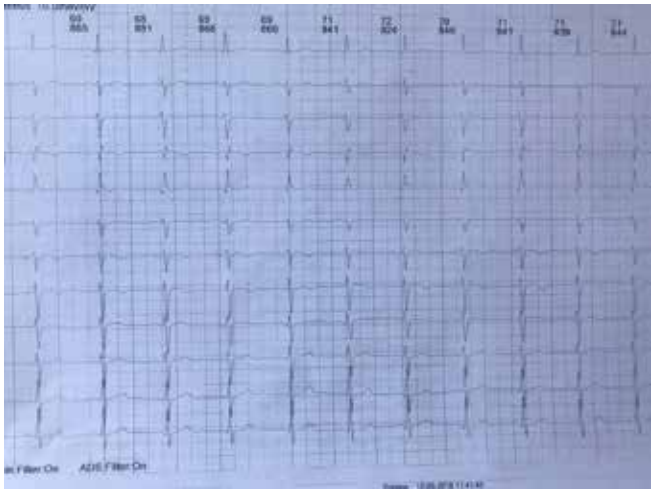

Figure 1. Electrocardiogram at the patient's first presentation - 12.05.2018

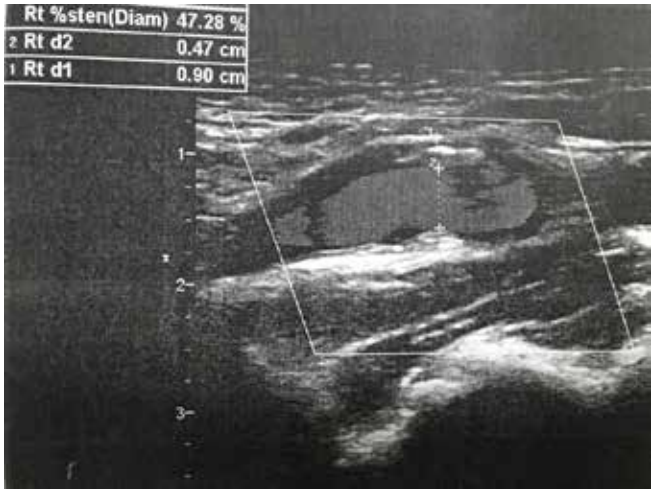

Figure 3. Doppler ultrasound of the carotids - first presentation of the patient

in Fig. 2). Such a value of CV risk categorized this patient into the group with high risk for CV death, mostly due to high cholesterol levels (total cholesterol: 6.95 mmol/l and LDL cholesterol: 4.76 mmol/l) and age (65 years), and his condition required a significant lifestyle modification and medicamentous therapy. According to the European prevention guidelines and the most recent lipid management guidelines (from 2019), a healthy lifestyle and healthy diet were recommended, together with a lipid-lowering drug, rosuvastatin (20 mg a day).

In order to improve the accuracy of risk estimation, we abided by the recommendations for risk reclassification and better CV risk consideration; these were socio-economical status (satisfactory), family history of CV diseases (negative), BMI (25.7 kg/m^2 - at the cut-off between normal and overweight), Doppler of the carotid arteries (sclerotic walls with edge plaques, mixed - predominantly fibrolipomatous with punctiform and dash calcifications (*dot-and-dash*), predominantly in the bulbs and the origins of internal carotid artery (ICA), causing segmental stenosis on the right below 46% and left below 36% (Fig. 3). The ankle-brachial index (ABI) was normal.

The finding of plaques in the carotid arteries of our patient demanded a reclassification of his status into a very

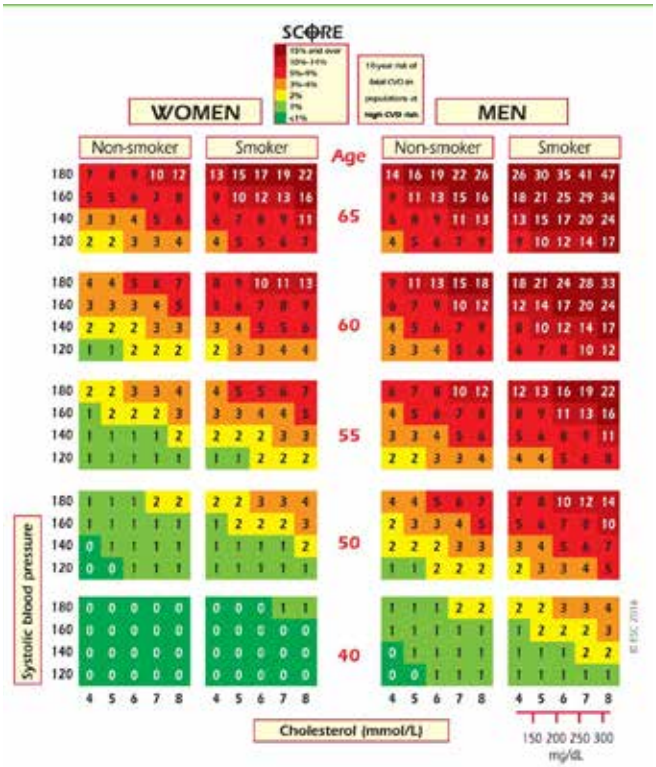

Figure 2. Cardiovascular risk estimated according to the SCORE chart - first presentation

high-risk individual, requiring additional diagnostic examinations directed towards the identification of coronary disease. The method selected was stress echocardiography, a highly specific and sensitive test to detect coronary disease.

Echocardiography demonstrated that the left ventricle had normal dimensions, normal wall thickness, and preserved regional and global contractile function. Transmitral flow suggested disturbed diastolic relaxation and mitral regurgitation in trace amounts. Mild to moderate (2+) aortic regurgitation was found. The left ventricle was at the normal cut-off. Right heart cavities had normal dimensions and functions. The pericardium had increased signal intensity, without any effusion.

Stress echocardiography was performed on a horizontal ergometer cycle (CardiowiseXrcise), with echocardiographic monitoring. At the maximum reached heartbeat of 151/min and maximum blood pressure of 165/90 mmHg, although there were no subjective complaints except for moderate fatigue, and ST segment depression of -3.32 mm was seen in the V5 lead, -2.37 mm in the V6 lead, and ST elevation in the aVR (Fig. 4). Echocardiographic monitoring, at 45° and under maximal stress, revealed worse kinetics in the basal-medial portion of the lateral wall and basal portion of the inferior wall. This test demonstrated the signs of myocardial ischemia in the inferolateral wall. After the test, the patient was referred for invasive coronarographic testing, which demonstrated three-vessel coronary disease (the main stem stenosed by 60% distally; LAD diffusely changed by 80% in the proximal segment; LCX stenosed ostially by 90%, and distally by 70-80%; RCA stenosed in the medial third by 60%; RCA was the dominant artery). Surgical revascularization of the myocardium was performed on November

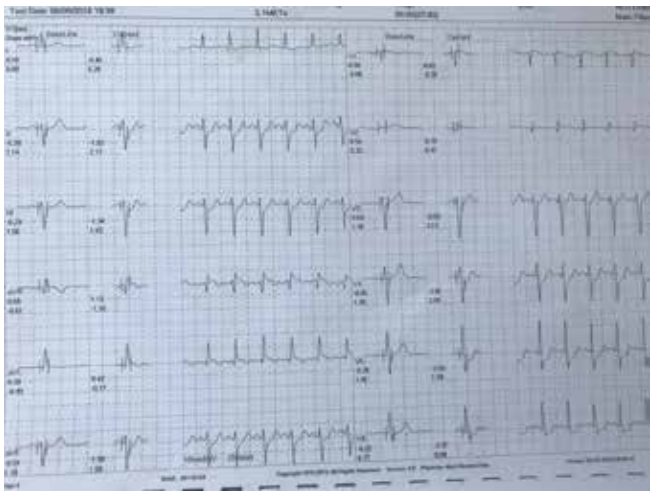

Figure 4. Electrocardiogram at stress echocardiography (physical exercise stress) - 06.09.2018

15, 2018 at the Institute for Cardiovascular Diseases "Dedinje", using the triple aortocoronary bypass approach (RIA - *a. mammariainterna sin.*, OM1 - graft autovenosum, ACDx-PD - graft autovenosum). After the heart surgery, cardiovascular rehabilitation was performed, and a year after the surgery control stress echocardiography testing was done again, which was negative for ischemia at the heart rate of 135/min and BP of 185/90 mmHg.

Discussion

CV risk estimation is one of the key aspects of CV disease prevention. The fundamental idea of the risk estimation is to detect in the simplest way the individuals exposed to high CV risk in order to reduce morbidity and mortality rates that follow CV diseases. This especially relates to asymptomatic individuals who do not have any significant heart-related complaints, but who have numerous modifiable risk factors that can accelerate the process of atherosclerosis and ultimately lead to premature CV events. The European SCORE charts and American Framingham score are the most well-known tools used in CV risk estimation[1,2]. However, although these are widely used and undoubtedly useful, they have shortcomings and limitations. In the European SCORE, the main problem is years of age, which may underestimate the total CV risk in younger patients. That is the reason why relative CV risk charts have been introduced. Another way to improve the accuracy of risk estimation is to perform some additional tests, as soon as possible, after the initial classification into four categories (low, intermediate, high and very high risk) that may reclassify the patient into a higher CV risk category. Thus, the prevention and therapeutic measures could commence as early and as aggressively as possible. These reclassification data or methods are socioeconomic status, family history of CV diseases, BMI or central obesity, coronary artery calcium (CAC) score (determined by way of electron-beam or multislice CT), detection of atherosclerotic plaques in the carotid arteries, and ankle-brachial blood pressure ratio (ankle-brachial index, ABI)[1,2,4].

In our patient, the findings of Doppler ultrasound in the carotids was shown to be essential for the use of other

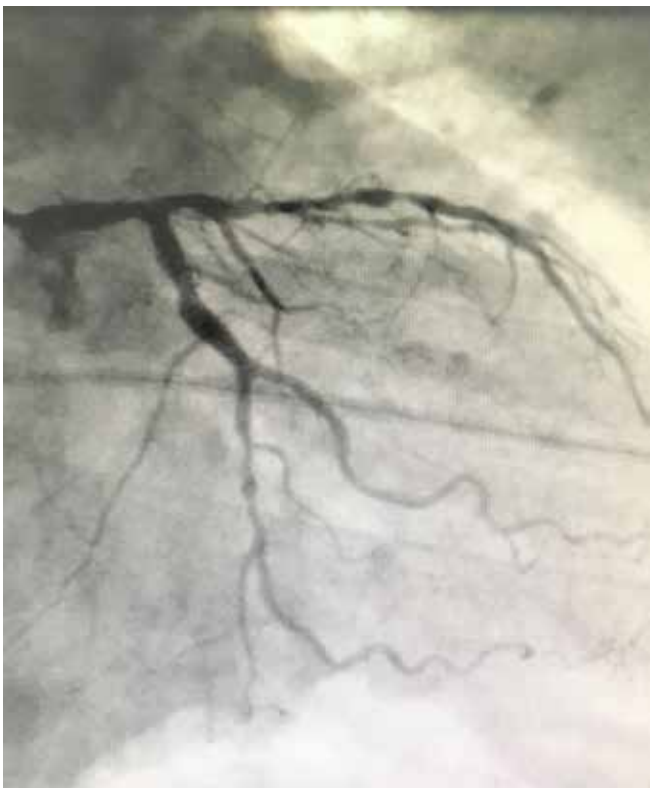

Figure 5. Coronarography finding of the patient – 21. 09. 2018

sensitive and specific methods in CV disease detection, but also for the initiation of intense statin therapy. Population studies have shown a correlation between the severity of atherosclerosis in one artery and the degree of involvement of other arteries[5]. There are two key information that can be obtained by Doppler ultrasound of the carotid arteries: intima-media thickness (IMT) and the presence of the plaque(s). The upper cut-off value for IMT is at present 0.9 mm. The risk of brain stroke and coronary events is related to IMT, but the relationship is not linear. The lack of standardization as to the definition and measurement of IMT, its considerable variability and low intra-individual reproducibility have been limiting the significance of IMT for the time being. A recent meta-analysis has failed to demonstrate any additional value of IMT compared to the Framingham risk score in the prediction of future CV disease, even in intermediate-risk groups[6]. The plaque is usually defined as the presence of a thickening in the artery core at least by 50% larger than the adjacent arterial wall, or as an injury region (IMT ≥ 1.5 mm) bulging into the arterial lumen[7]. Plaques can be characterized by their number, size, irregularity and echodensity (echolucent vs calcified). Plaques are associated with coronary and cerebrovascular events, and echolucent plaques (in contrast to calcified ones) increase the ischemic cerebrovascular event[8]. Numerous studies have stressed that plaque quality assessment (including the surface and thickness of the plaque, instead of IMT measurement) is more valuable in the prediction of CV events[1]. In our patient, IMT in a standard measurement position was 1.2 mm in the common carotid artery, and his plaques were fibrocalcified, leading to 47% stenosis. Such findings required further diagnostic procedures.

Functional non-invasive tests for the diagnosis of ob-

structive CAD are designed to detect myocardial ischemia through ECG changes, wall motion abnormalities by stress CMR perfusion or stress echocardiography[9]. We chose stress echocardiography as a visual method and were able to demonstrate significant wall motion abnormalities. Since five segments of the left ventricle had contractility changes, this definitely indicated that our patient was a high-risk one.

Coronarography confirmed the findings and high-risk patient status (the high-risk criteria were three-vessel disease with proximal stenosis, LM disease, or proximal anterior descending disease)[9]. Our patient fulfilled these criteria: the main stem stenosed distally by 60%; LAD in the proximal segment 80% diffusely changed; LCX ostially stenosed by 90%.

The next question would be how to treat this patient? The indications for revascularization in patients with stable angina or silent ischemia are left main disease with stenosis over 50%; proximal LAD stenosis over 50%; and a large area of ischemia (over 10% of the left ventricle. The decisions for revascularization by percutaneous coronary intervention or coronary artery bypass grafting (CABG) are based on clinical presentation (symptoms present or absent) and prior documentation of ischemia (present or absent).

The superiority of CABG over a strategy of initial medical therapy was established in a meta-analysis of seven RCT[6,8] more than two decades ago, demonstrating a survival benefit of CABG in patients with SCAD and left main (LM) or three-vessel disease, particularly when the proximal LAD coronary artery was involved, and has been confirmed in more recent studies[10].The coronarography finding and the estimation of functional ischemia led our heart team to decide in favor of CABG in our patient. The intervention was performed without any complications, followed by a specialized cardiovascular rehabilitation program. A year after, stress echocardiography demonstrated preserved coronary reserve.

Conclusions

An asymptomatic adult person does not always mean a healthy adult person. A patient was presented in whom a high CV risk was demonstrated already by using the CV risk estimation charts/scores. His further diagnostic management took place in accordance with the current guidelines, involving the methods for CV risk reclassification (in our case, Doppler ultrasound imaging of the carotid arteries). Identifying a patient with vascular disease and even a higher degree of risk, significant areas of ischemia were demonstrated by non-invasive functional testing - stress echocardiography. Coronarographic testing showed that the patient had a multivessel disease with severe three-vessel coronary disease, which was successfully treated by surgical revascularization.

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Case report

Treatment challenges in a very high-risk diabetic patient with coronary artery disease

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Abstract We present 58-year woman with T2 diabetes mellitus and multiple cardiovascular risk factors who was addmited to our clinic due to unstabile angina. Coronary angiography revealed bifurcation lesion of medial left anterior descending coronary artery (LAD) with 90% stenosis and first diagonal branch (D1) with a vessel diameter of 2 mm, and percutaneous coronary intervention (PCI) with implantation of one drug eluting stent (DES) in medial LAD was performed. During the follow-up optimal blood pressure control was achieved with combination of antihypertensive drugs and poor glycaemic control was managed with adding empagliflosin to metformin. Trimetazidine was initiated as a second-line treatment to reduce angina symptoms. Repeated coronary angiography due to angina one year later showed patent stent in mid LAD, but gracile periphery of LAD and D1 branch, not suitable for PCI. Optimal medical tretment was indicated. Lifestyle changes were also recommended. Ezetimibe was added to statin therapy due to high levels of LDL cholesterol. Further multifactorial aproach and tighter control of risk factors is needed in order to prevent other vascular complications in this patient.

Kew words diabetes mellitus, acute coronary syndrome, unstabile angina, risk assesment, cardiovascular risk factors

Introduction

Diabetes mellitus (DM) increases the risk of coronary heart disease two times independent of other risk factors. Women and younger patients have higher relative risk of vascular events. Patients with long duration of DM and microvascular complications will have higher both relative and absolute risk levels[1].

Case presentation

We present an obese 58-year-old woman (body mass index 34 kg/m^2) who was admitted to our clinic in November 2018 due to crescendo angina. She has DM type 2 duration of 8 years on metformin therapy, hypertension, dyslipidemia diagnosed when she was 28 years old, positive family history of coronary artery disease (her father and uncle both had myocardial infarction at 42 years of age) and history of light smoking. The patient also has inflammatory myopathy and receives hormone therapy for hypothyroidism and inhalatory corticosteroids for asthma. Two weeks before admission she performed excercise electrocardiogram (ECG) because of suspected anginal symptoms, which showed low exercise tolerance and 2 mV ST-depression in leads DII, DIII, aVF, V3, V4, V5, V6 during rest.

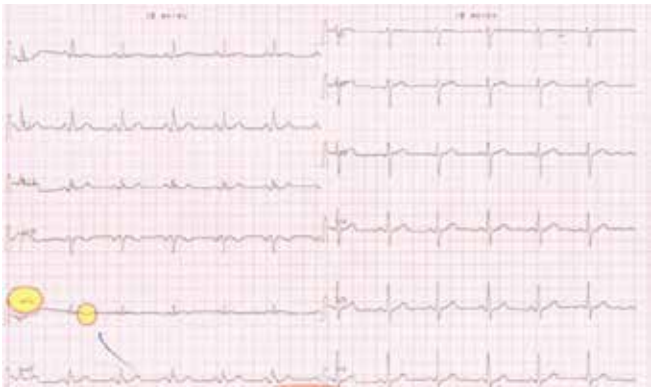

Figure 1. Resting electrocardiogram showed negative T wave in lead aVL.

On admission she was eupnoic, in sinus rhythm, heart rate 75 b.p.m, blood pressure was 130/80 mmHg and without clinical signs of heart failure (HF). Biochemistry testing showed normal values of high sensitive troponin I and creatin kinase (CK)-MB, with elevated values of CK (318 [26-200 U/l]), normal renal function and normal blood gas analyses. Resting ECG showed negative T wave in lead aVL (Figure 1). Transthoracic echocardiography (TTE) revealed normal left ventricle (LV) systolic function with no regional wall motion abnormalities. Invasive coronary angiography was performed and showed bifurcation lesion (Medina classification 0,1,1) of medial left anterior descending coronary artery (LAD) with 90% stenosis and first diagonal branch (D1) with a vessel diameter of 2 mm, 99% stenosis and muscular bridge in distal segment of D1

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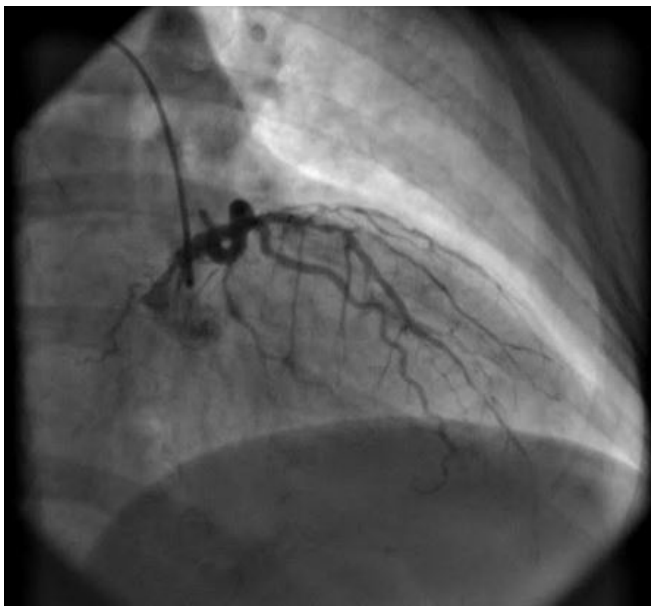

Figure 2. Bifurcation lesion of medial left anterior descending coronary artery (LAD) with 90% stenosis and first diagonal branch (D1) with a vessel diameter of 2 mm, 99% stenosis and muscular bridge in distal segment of D1

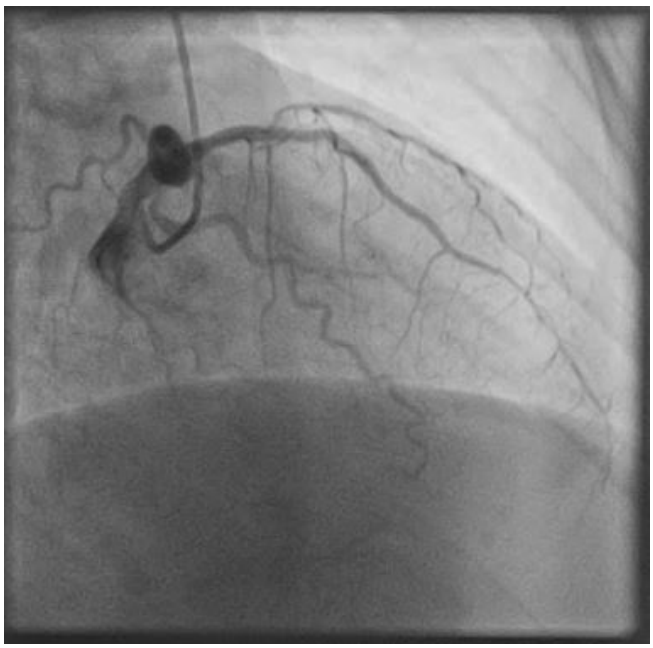

Figure 3. Repeated coronary angiography (Figure 3) showed patent stent in mid LAD, diameter of LAD peripherally <1.5 mm and narrow D1 branch with diameter ≤2 mm

(Figure 2A). Percutaneous coronary intervention (PCI) with implantation of one drug eluting stent (DES) in medial LAD was performed and followed by „POT-side-POT" with D1 branch (Figure 2B). TIMI 1 was achieved in D1 branch, although stent was not implanted because of narrow vessel diameter. The patient was discharged with dual antiplatelet therapy, bisoprolol 2,5 mg, perindopril 5 mg, rosuvastatin 20 mg, pantoprazol 40 mg and metformin 1000 mg b.i.d.

During the 6-months follow-up she was without ischaemic symptoms, however she experienced anginal symptoms again. Optimal blood pressure control was achieved by adding calcium channel blocker (amlodipin 5 mg) and thiazide-like diuretic (indapamid 1,25 mg). Statin dose was reduced (rosuvastatin 10 mg) due to increased levels of CK. In November 2019 the values of HbA1c were checked indicating poor glycemic control. Since HbA1 raised from 7.4 to 9.8% and the patient was considered as very high-risk, sodium-glucose co-transporter 2 inhibitor (SGLT2i) (empagliflozin 10 mg) was introduced into therapy. Excersise ECG revealed ST-depression in leads DII, DIII, aVF, V4, V5, V6 during rest. TTE showed preserved global systolic function, without wall motion abnormality. Repeated coronary angiography (Figure 3) showed patent stent in mid LAD. As part of negative remodeling, LAD periphery was gracile, diffusely atherosclerotic altered with vessel diameter <1.5 mm and narrow D1 branch with diameter ≤2 mm not suitable for PCI. Optimal medical tretment was indicated. Trimetazidine was initiated as a second-line treatment to reduce angina. Lifestyle changes were also recommended.

Three months after initiating SGLT2i therapy, control value of HbA1c is 8.2%. Considering persistent high LDL cholesterol (LDL-C) values (3.24 mmol/l), ezetimibe was added to therapy. Screening for microvascular complications of DM has been performed. Eye examination did not show signs of diabetic retinopathy, estimated glomerular filtration rate was 66 ml/min/1.73 m^2, microalbuminuria was not detected, and neurological investigation did not show signs of neuropathy. Value of ankle-brachial index (1,2 for right leg and 1,1 for left leg) and normal biphasic continuos wave Doppler curves excluded lower-extremity artery disease.

Discussion

Chest discomfort that meets criteria for crescendo angina (prior typical ischaemic symptoms escalate and appear at a lower threshold and over a short period of time) falls under the unstable angina which is managed according to the ESC guidelines for acute coronary syndromes (ACS)[2]. Glucose abnormalities are common both in patients with ACS or chronic coronary syndromes (CCS) and worsen the prognosis of these patients[3]. A meta-analysis including 5 324 patients with non-ST-segment elevation ACS and DM, an early invasive compared to delayed strategy showed reduced mortality at a median follow-up of 6 months (HR 0.67, 95% CI 0.450.99)[4]. Coronary revascularisation techniques should not differ among patients with and without DM (e.g. use of DES and radial approach for PCI). PCI is recommended for patients with DM and one- or two-vessel CAD without proximal LAD stenosis (class Ia) and has similar outcomes to CABG in diabetic patients with low complexity CAD (SYNTAX score ≤22)[5]. DM is already diagnosed in up to one third of patients with CAD and more than two third of patients with CAD have newly detected glucose abnormalities[6]. The values of HbA1c and fasting plasma glucose (FPG) are used to diagnose T2DM and when these values are inconclusive, oral glucose tolerance test (OGTT) is performed. In ACS

the OGTT should be done after four to five days, to minimize false-positive results[3,7].

According to the 2019 ESC Guidelines on Diabetes, Prediabetes and Cardiovascular Diseases (CVD) our diabetic patient was at very high-risk considering the fact she had DM with established cardiovascular disease and more than three major risk factors. The 10-year risk of CVD death for these patients is more than 10%. Female gender is also considered not to be protective for premature CVD in diabetes. Control of potentially modifiable risk factors to reach recommended targets is crucial for very high-risk diabetic patients. Lifestyle changes are cornerstone of prevention DM and its vascular complications and consider smoking cessation, reduction in calorie intake in order to reduce BMI, physical activity and a Mediterranen diet. Recommended value of blood pressure (systolic ≤130 mmHg, but not <120 mmHg and diastolic ≤80 mmHg, but not <70 mmHg) according to ESC guideline on Diabetes was achieved with combination of four group of antihypertensive drugs in our patient[3,8].

The recommended target values of HbA1c for patients with diabetes are <7% or <53 mmol/ml in order to reduce microvascular complications and the same values should be considered for preventing macrovascular complications[3]. In diabetic patients, FPG, post-prandial glycaemia and glucose variability were less strongly associated with CVD risk factors than HbA1c and mean blood glucose[9]. Although the role of glucose variability still needs to be defined, studies report that FPG variability is a strong predictor of all-cause and CVD-related mortality in individuals with DM[10]. Newer oral glucose-lowering drugs (glucagon-like peptide-1 receptor agonists (GLP1-RAs), dipeptidyl peptidase-4 (DPP4) inhibitors, and SGLT2i) reduce post-prandial glucose rise and might be appropriate tool for management of glucose variability[11]. Both GLP1-RAs and SGLT2i have also shown BP-lowering effects[12,13].

Data derived from several cardiovascular outcome trials recommend use of GLP1-RAs (liraglutide, semaglutide, or dulaglutide) and SGLT2 inhibitors (empagliflozin, canagliflozin, or dapagliflozin) in patients with T2DM who have atheroscrerotic CVD or high/very high CV risk, whether they already use metformin, like our patient, or are metformin naïve, as first line therapy (3). A meta-analysis of three trials (EMPA-REG OUTCOME, CANVAS, DECLARE-TIMI 58) with SGLT2 inhibitors showed reduced composite of HF hospitalisation or CV death, reduced progression of kidney disease (regardless of atheroscrerotic CVD presence) and reduction of MACE in individuals with established CVD[14]. The CREDENCE trial[15] with canagliflosin compared to placebo showed relative reduction of the primary renal outcome of 30% in patients with T2DM and albuminuric chronic kidney disease. Favorable results in these trials are probably due to reduction in HF-associated events and can be explained with impact of SGLT2i on hemodynamic parameters (e.g. reduced plasma volume)[16]. American Diabetes Association still prefers metformin as initial pharmacologic agent for the treatment of T2DM and the second medication added to metformin is based on the clinical characteristics of the patient (e.g. established ASCVD or indicators of high ASCVD risk)[17].

Statin therapy is first-line lipid-lowering treatment and if the target LDL-C is not achieved, addition of ezetimibe is recommended[18,19]. Our patient received reduced dose of rosuvastatin, which is considered to has a lower rate of side effects[20]. In patients on maximal tolerated dosages of statin therapy, when LDL-C was above 1.8 mmol/L, addition of proprotein convertase subtilisin/kexin type 9 (PCSK9) additionaly lowered the LDL-C. This result showed the strength of PCSK9 compared to statin therapy. Reduction of LDL-C led to lowering the incidence of CV endpoints, especially in those patients who had LDL-C >2.6 mmol/l. Therefore lowering of LDL-C after acute coronary syndrome from previously suggested 1.8 mmol/l to 1.4 mmol/l is now recommended[21]. In very high-risk patients, with persistent high LDL-C despite treatment with a maximum tolerated statin dose, in combination with ezetimibe, or in patients with statin intolerance, a PCSK9 inhibitor is recommended to target an LDL-C of <1.4 mmol/L (<55 mg/dL) or at least 50% LDL-C reduction[3].

Further multifactorial aproach and tighter control of risk factors is needed in order to prevent microvascular and other macrovascular complications in this patient.

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Sažetak

Prikaz slučaja: Izazovi u lečenju veoma visoko rizičnog pacijenta sa dijabetes melitusom i koronarnom arterijskom bolešću

Žena starosti 58 godina sa T2 dijabetes melitusom i mnogobrojnim kardiovaskularnim faktorima rizika je primljena na našu kliniku zbog nestabilne angine. Urađena je koronarografija kojom se registruje bifurkaciona lezija 90% sužene prednje silazne koronarne arterije (LAD) i prve dijagonalne grane (D1) sa dijametrom krvnog suda 2mm, i u istom aktu perkutana koronarna intervencija (PCI) sa implantacijom jednog lekom obloženog stenta u medijalni segment LAD. Tokom daljeg praćenja je kontrola krvnog pritiska postignuta kombinacijom antihipertenzivnih lekova, dok je loša glikemijska kontrola tretirana dodavanjem empagliflozina metforminu. Trimetazidin je uveden u terapiju kao druga linija antianginoznih lekova. Ponovljena je koronarografija godinu dana kasnije zbog anginozih tegoba i registrovan je prohodan stent u LAD i gracilna periferija LAD i D1, nepogodna za PCI. Indikovan je optimalni medikamentni tretman. Preporučene su promene životnih navika. Ezetimib je dodat statinskoj terapiji zbog povišenih vrednosti LDL holesterola. Neophodan je nastavak multidisciplinarnog lečenja i stroža kontrola faktora rizika kako bi se prevenirale dalje vaskularne komplikacije kod ove pacijentkinje.

Ključne reči: *dijabetes melitus, akutni koronarni sindrom, nestabilna angina, procena rizika, kardiovaskularni faktori rizika*

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Clinical review

Supraventricular tachcycardia practical guide for diagnosis and management

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Abstract Supraventricular tachycardia (SVT) is any atrial tachyarrhythmia with heart rate exceeding 100 bpm in rest. The simplest and clinically simple to apply is a division according to QRS duration (width), to SVT with narrow QRS (less then 120ms duration) and wide QRS tachycardias (over 120ms QRS duration). Diagnostic algorithm for SVT differentiation is started by a 12 lead ECG which is interpreted by its QRS duration as a fisrt step in SVT diagnostics. The second step is regularity assessment of the RR interval , while the third step is P wave identification. The last step is assessment of the P wave to QRS frequency ratio. ECG interpretation in these four steps enables SVT identification in most of the patients. In some patients a vagal maneuver or i.v application of Verapamil or Adenosin are needed in order to distinguish the SVT type. The therapy of SVT patients is divided into acute, which goal is to cease the tachycardia onset, and chronic, or ongoing whose goal is to maintain sinus rhythm. The acute therapy is administrated based on the QRS duration and hemodynamic state of the patient. Conclusions: everyday, clinically orientated approach to patients with supraventricular tachycardias is based on simple ECG criteria and not on complex mechanisms of tachycardia origin. The approach based on QRS duration, or QRS morphology divided into wide and narrow QRS complexes is simple and efficient approach for practical diagnostics and therapy of supraventricular tachyarrhythmias.

Kew words supraventricular tachycardia, QRS duration and width, tachycardia induced cardiomyopathy.

Introduction

Supraventricular arrhythmias are common and patients are often symptomatic, requiring management with drugs and electrophysiological procedures. In the general population, the Supraventricular Tachycardia (SVT) prevalence is 2.25/1000 persons and the incidence is 35/100 000 person-years. Women have a risk of developing SVT that is two times greater than that of men, and persons aged ≥65 years or have more than five times the risk of developing SVT than younger individuals[1]. In specialized centers, AV nodal reentry tachycardias (AVNRT) is the most frequently treated substrate after Atrial Fibrillation (AF), followed by atrial flutter and AV reentry tachycardias (AVRT), in patients referred for catheter ablation[2-4]. Women are more likely to be affected by AVNRT than men (ratio 70:30),[5-6] while the converse is true for AVRT (ratio 45:55)[7]. A relationship with the monthly cycle has been suggested,[8] and episodes are more frequent during pregnancy in women with pre-existing SVT[9].

How to recognize

Supraventricular tachycardia (SVT) is any atrial tachyarrhythmia with heart rate of more than 100 bpm at rest[1]. Supraventricular tachycardias can be divided according to their electrophysiological origin and QRS width.

Table 1. General electrophysiology division.

Atrial tachycardias
• Sinus tachycardia • Focal Atrial Tachycardia • Multifocal Atrial Tachycardia • Macro Reentry Atrial Tachycardia • Atrial Fibrillation
AV junctional tachycardias
• Atrioventricular nodal re-entrant tachycardia (AVNRT) • Non-re-entrant junctional tachycardia
Atrioventricular re-entrant tachycardia (AVRT)
• Orthodromic • Antidromic

The General electrophysiology division is based on pathophysiology/electrophysiology approach and mechanism of origin. In the remainder of this text we will base our focus on a clinically based approach to division of tachycardias. This approach is based on a simple wide vs narrow QRS morphology, or should we say "worry or not to worry morphology". As a border mark, a 120ms QRS width was taken. All further diagnostic and therapy approach in patients with supraventricular tachycardias featured in this article will be based on this value.

Diagnosis

In everyday clinical practice a 12 lead ECG is the simplest way ahead, but we also have additional simple tools like vagal maneuvers and some intravenous injection of medications. SVT diagnosis can be made based on three basic steps which represent the basis of diagnostic algorithm, using 12 lead ECG , vagal maneuvers and intravenous administration of Adenosine (or in our everyday clinical situation/s intravenous administration of Verapamil)

1. 12 leads ECG

In exam protocol all patients should have a 12 lead ECG done.
We divided a ECG interpretation into four steps in order

Table 2. QRS width division

Narrow tachycardias ≤120 ms QRS width
Regular rhythm narrow QRS tachycardias
• Sinus tachycardia • Focal Atrial Tachycardia • Atrial flutter with fixed AV conduction • Atrioventricular nodal re-entrant tachycardia (AVNRT) • Orthodromic AVRT • Idiopathic VT (especially high septal VT)
Irregular rhythm narrow QRS tachycardias
• Atrial Fibrillation • Focal Atrial Tachycardia or atrial flutter with varying AV block • Multifocal Atrial Tachycardia
Wide tachycardias >120 ms QRS width
Regular rhythm wide QRS tachycardias
• Ventricular Tachycardia or flutter • Ventricular paced rhythm • Antidromic AVRT • Supraventricular tachycardias with Bundle Branch Block (pre-existing or rate-dependent during tachycardia) • Atrial tachycardia with pre-excitation • Wide QRS Supraventricular tachycardias due to electrolyte disturbance or antiarrhythmic drugs
Irregular rhythm wide QRS tachycardias
• Atrial fibrillation or atrial flutter with varying block conducted with aberration • Antidromic AV re-entrant tachycardia with variable Ventricle-Atrial conduction • Pre-excited Atrial Fibrillation • Polymorphic Ventricular Tachycardia • Torsade de pointes • Ventricular fibrillation

to make a diagnosis of supraventricular tachycardia easier.
Step one: First comes first, it is necessary to measure the width of the QRS with the boundary being 120ms.
Step two: according to the RR intervals check the regularity/irregularity of the tachycardia
Step three: P wave presence/absence, the best way to see it is in the V1 lead.
Step four: See the relationship of P frequency and QRS frequency.
After step one, if we have **narrow QRS tachycardia**: we judge the regularity of the same. If the tachycardia is irregular, we probably are encountering atrial flutter, fibrillation or atrial tachycardia. If the tachycardia is regular, we search for P waves and their relationship with QRS complexes and frequency of the QRS.
Back to step one, **wide QRS tachycardia**: If we have wide QRS tachycardia, this brings out the old dilemma weather this tachycardia is supraventricular or ventricular in origin. On the other hand, this new division of narrow and wide QRS tachycardias gives a non-electrophysiologist a unique opportunity to be relatively safe and efficient in therapy regardless of the electrophysiological origin of the tachycardia.

2. Vagal maneuvers

There are several possibilities of reaction to these maneuvers (1):

- **Slowing of AV node conduction**: thus, unmasking atrial electrical activity and revealing P waves.

This happens in atrial fibrillation, flutter or focal Atrial tachycardia

- **Temporary decrease in the atrial rate:** sinus tachycardia and focal atrial tachycardia
- **Tachycardia termination:** AVRT and AVNRT
- **No effect**

3. Intravenous administration of Adenosine or Verapamil in regular narrow QRS tachycardia[1]:

- **Slowing of AV node conduction:** thus, unmasking atrial electrical activity and revealing P waves. This happens in atrial fibrillation, flutter or focal Atrial tachycardia
- **Temporary decrease in the atrial rate:** sinus tachycardia and focal atrial tachycardia
- **Tachycardia termination:** AVRT and AVNRT
- **No effect** if the dose or delivery is inadequate

Management

All therapeutic approaches in SVT are generally divided into acute and ongoing (chronic). Acute management is dependent on the QRS width and hemodynamic compromise at the presentation patients with supraventricular tachycardia. Acute management has as its objective to cease the tachycardia. Chronic or ongoing has as its goal prevention of tachycardia or at least making the probability of it happening much lower.

Acute management of supraventricular tachycardias

Narrow QRS tachycardias without established electrophysiological origin[10-15]

Hemodynamically stable patients

- **A 12 lead ECG** during tachycardia is mandatory
- **Vagal maneuvers**
- **Adenosine** (6-18 mg intravenous bolus) if vagal maneuvers fail
- **Verapamil** (intravenous) if vagal maneuvers and adenosine fail (or adenosine not available)
- **Metoprolol** intravenous if vagal maneuvers and adenosine fail (or verapamil was not applied)
- **Synchronized direct-current cardioversion** if everything above mentioned fails.

Hemodynamically unstable patients

- **Synchronized DC cardioversion.**

Wide QRS tachycardias without established electrophysiological origin[16-18]

Hemodynamically stable patients

- **A 12 lead ECG** during tachycardia is mandatory
- **Vagal maneuvers**
- **Adenosine** (6-18 mg intravenous bolus) if vagal maneuvers fail, and with no preexcitation on resting ECG (if available) in this case verapamil is not recommended!
- **Procainamide (**intravenous) if vagal maneuvers and adenosine fail
- **Amiodarone** intravenous administration, if vagal maneuvers and adenosine fail
- **Synchronized direct-current cardioversion** if everything above mentioned fails.

Hemodynamically unstable patients

- **Synchronized DC cardioversion.**

The majority of failures in intravenous therapy come with erroneous application of the drug.
Adenosine: The mean dose required for termination is 6 mg. To achieve efficient rhythm correction, injection should be as a rapid bolus with immediate saline flush. Large, centrally located (e.g. antecubital) veins are likely to deliver more effective drug concentrations to the heart. Dosing should be incremental, starting at 6 mg in adults followed by 12 mg. An 18 mg dose should
be considered, also taking into account tolerability/side effects in the individual patient. Adenosine has a very short plasma half-life measured in seconds, with end-organ clinical effects complete within 20-30 s.
Repeat administration is safe within 1 min of the last dose.
Calcium channel blockers (verapamil intravenous) and beta blockers (metoprolol intravenous) are of value, particularly in patients with frequent atrial or ventricular premature beats.
Verapamil: 0.075 - 0.15 mg/kg intravenous (average 5 - 10 mg over 2 min), on the other hand is associated with a risk of hypotension. These drugs should be avoided in patients with hemodynamic instability, HF with reduced LV ejection fraction (<40%), a suspicion of VT, or pre-excited AF.

Metoprolol: 2.5-15 mg given intravenous in 2.5 mg boluses. Beta blockers are contraindicated in patients with decompensated heart failure. Caution is needed with concomitant use of intravenous calcium channel blockers and beta-blockers, because of possible potentiation of hypotensive and bradycardic effects.
Valsalva maneuver: Carotid sinus massage is performed with the patient's neck in an extended position, with the head turned away from the side to which pressure is applied. It should always be unilateral as there is a potential risk with bilateral pressure, and it should be limited to 5 s. The patient should be monitored. This technique should be avoided in patients with previous transient ischemic attack or stroke, and in patients with carotid bruits. Other maneuvers, such as facial immersion in cold water or forceful coughing, are rarely used[1].

Chronic management of supraventricular tachycardias
Two points should be made regarding the practical chronic management of supraventricular tachycardias[19-29].
First is the fact that the agent that stopped the acute onset does not necessarily is the agent of choice for the prolonged management.
Second, the ongoing management is quite often therapy orientated (medical or interventional) and then electrophysiological in nature.
In that light our points will be made according to agents and procedures used:
Beta blockers: are used for heart rate slowing and thus for SVT cessation. Today, Bisoprolol, Nebivolol, and Metoprolol are recommended for oral therapy.
Sinus tachycardia
- Atrial tachycardia/s
- AV nodal reentry tachycardias
- Manifest preexcitation

Calcium channel antagonist (Non dihydropyridine type): Verapamil or Diltiazem are recommended for oral therapy.
- Sinus tachycardia
- Atrial tachycardia/s
- AV nodal reentry tachycardias

I_f Channel blockers (Ivabradine): is used as a second line therapy when a full dose of beta blocker does not achieve sinus rhythm slowing. They are introduced along with beta blocker. On the other hand, they can be used as a single therapy agent in patients where beta blocker use is contraindicated. The are used only in patients with sinus rhythm, they are not of any use in patients with atrial fibrillation.
Sinus tachycardia
- Atrial tachycardia/s other than atrial flutter of fibrillation

Ic Vaughan-Williams group of antiarrhythmic drugs (Procainamide, Propafenone, Flecainide): These medication should not be used in patients with manifest coronary artery disease or in patients with heart failure.
- AV nodal reentry tachycardias
- Macro reentrant tachycardias-AVRT
- Manifest preexcitation

III rd group Antiarrhythmic drugs: Amiodarone, Dronedarone, Sotalol
- AV nodal reentry tachycardias
- Macro reentrant tachycardias-AVRT
- Manifest preexcitation

Catheter ablation: It is rarely used as a first choice therapy, almost by rule when other therapy options are exhausted.
- Sinus tachycardia (rarely)
- Atrial tachycardia/s
- AV nodal reentry tachycardias
- Macro reentrant tachycardias-AVRT
- Manifest preexcitation

Tachycardia induced cardiomyopathy like long term consequence of sustained untreated and uncontrolled supraventricular tachycardia/s

Definition

It is a reversible cause of impaired LV function due to persistent tachycardia or very frequent ventricular premature beats that can lead to HF and death[30-32].
However, it has not been fully established how the majority of patients with frequent premature ventricular contractions have a benign course, whereas ≤30% of them may develop cardiomyopathy.

Diagnosis

This sort of cardiomyopathy should be considered[33]:
1: In any patient with new onset of LV dysfunction. Typically, in LV ejection fraction is <30%, LV end-diastolic diameter is <65 mm, and LV end-systolic diameter is <50 mm.
2. In the presence of persistent or frequent tachycardia, or frequent premature ventricular contractions.
3. The diagnosis is made by excluding other more plausible causes of cardiomyopathy (NMR, MDCT, invasive angiography, biopsy etc.)
4. Recovery of LV function after cessation of the arrhythmia or control of the ventricular rate.
5. Serial assessment of N-terminal pro-B-type natriuretic peptide (NT pro BNP) and comparing it to the baseline level during follow-up can help differentiate it from irreversible idiopathic dilated cardiomyopathy.
6. ECG long term monitoring (24-72h Holter ECG, Telemonitoring, Cardiac Implanted Electronics Devices (CIED) in reaching diagnostic thresholds for arrhythmic events frequency).

Therapy

Medicament or interventional (ablation) intervention in stopping or reducing the frequency of the arrythmia events[34-37].

Conclusion

Clinical, everyday approach to supraventricular tachycardias and arrythmias should be based how much is possible on clinical and ECG criteria rather than complex arrythmia origin assessment. The approach based on narrow vs wide QRS morphology and duration is reliable

and efficient for practical diagnosis and treatment of supraventricular tachycardias.

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Sažetak

Supraventrikularna tahikardija (SVT) je bilo koja atrijalna tahiaritmija sa srčanom frevencom preko 100/min, u mirovanju. Najjednostavnija i klinički lako primenljiva je podela SVT prema širini QRS kompleksa, na SVT sa uskim QRS kompleskima (manje od 120ms) i na SVT sa širokim QRS kompleksima (preko 120ms). Dijagnostički algoritam za prepoznavanje SVT podrazumeva 12 ovdvodni EKG kod koga se interpretira širina QRS kompleksa kao prvi korak u dijagnostikovanju SVT. Drugi korak je određivanje regularnosti ili iregularnosti RR intervala, treći korak je identifikacija P talasa. Poslednji korak je odreživanje međusobnog odnosa frekvence P talasa I frekvence QRS. Interpretacijom EKG u ova četiri koraka kod najvećeg broja pacijenata omogućiće nam identifikaciju SVT. Kod nekih pacijenata biće potreno sprovesti Vagalni manevar ili intravenski primeniti Adenosin ili Verapamil. Terapija pacijenata sa SVT deli se na akutnu, sa ciljem da se prekine SVT i hronična, terapija održavanja sinusnog ritma. Akutna terapija primenjuje se u zavisnosti od širine QRS kompleksa i hemodinamskog statusa pacijenta. Zaključci: Svakodnevni, klinički pristup pacijentima sa Supraventrikularnim tahikardijama baziran je na jednostavnim EKG kriterijumima a ne na kompleksnim mehanizmima nastanka aritmija. Pristup baziran prema širini QRS kompleksa, morfologija širokih i uskih QRS kompleksa je jednostavan i efikasan pristup za prkatičnu dijagnostiku i terapiju supraventrikularnih tahiaritmija.

Ključne reči: *Supraventrukularna tahikardija, dužina trajanja QRS kompleksa, tahikardijom indukovana kardiomiopatija*

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Case report

Cryoballoon catheter ablation of atrial fibrillation

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Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice, affecting up to 2% of global population[1] and accounts for more than 30% of hospital admissions for cardiac rhythm disorders[2]. It is associated with increased morbidity and mortality[3]. Catheter ablation of AF has emerged from investigational procedure to the most effective procedure for symptomatic patients with promising outcome data[1,4]. Patients with heart failure can benefit from the procedure[5] and it improves quality of life[6].

The most commonly used procedure for AF ablation is a point by point ablation via a single tip catheter usually combined with a three-dimensional 3D mapping system and the most commonly utilized energy source is radiofrequency energy.[7,8]

The second most common form of catheter ablation is by cryoballoon technology, a variant of single shot ablation, which revolutionized treatment of AF.

First cases of cryothermal technology were successfully applied in 1970s,[9] but it was in 2003 when we saw the introduction of balloon based cryogenic catheter for pulmonary vein isolation (PVI)[10]. Today, cryoballoon (CB) catheter ablation is recognized ablation method, mainly because of reproducible and fast procedures[11-20].

Case presentation

A 66 years old female was presented in our outpatient clinic due to recurrent attacks of atrial fibrillation. She is on antihypertensive drugs for more than ten years which include beta blockers and on Class Ic antiarrhythmic drugs since the diagnosis of AF five years ago. She was also on warfarin for thromboembolic risk reduction. CHA2DS2-VASc score was 3. During the course of evaluation, an echocardiogram was done, normal dimension for cardiac chambers, LV EF was estimated to 55%, left atrial dimension was measured as 39 mm.

Coronary angiogram was performed two years ago, with no stenosis found.

Approximately three times a year she had to presented to emergency clinic for parenteral drug conversion of symptomatic AF. Sometimes, the episodes subside spontaneously.

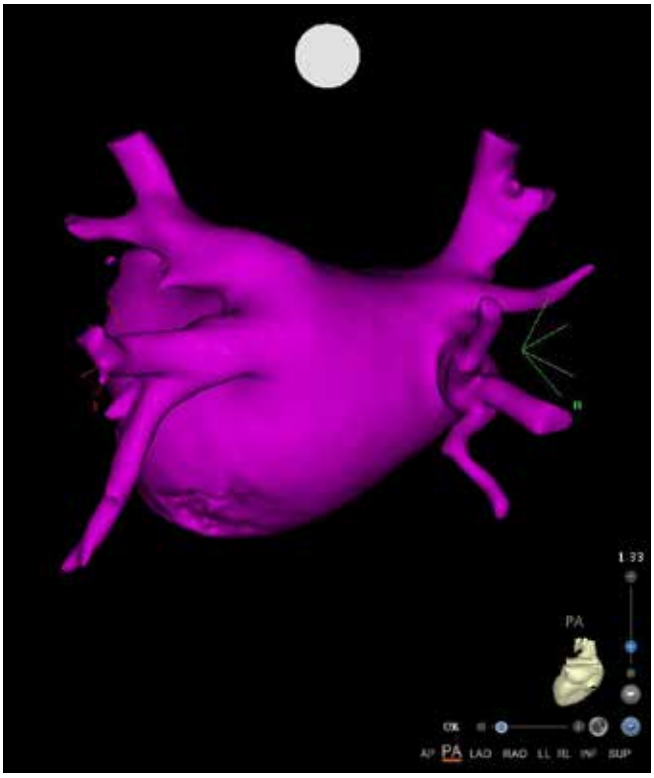

Figure 1. Chest CT scan of left atrial anatomy.

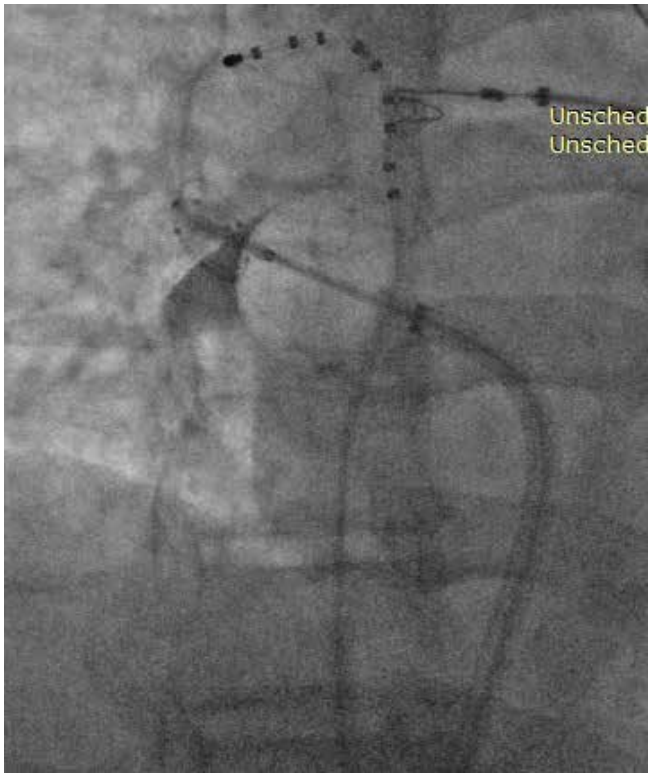

Figure 2. Fluoroscopy of cryoballoon vein occlusion.

Physical examination was unremarkable. TA 135/80 mm Hg, pulse 66/min, sinus rhythm on ECG. Laboratory findings as well as thyroid gland function tests were in normal range.
The indication for catheter ablation of atrial fibrillation was made.
Protocol for preparing the patients at Institute for Cardiovascular disease Dedinje is to perform transesophageal echocardiography (TEE) to all patients preparing for catheter ablation of AF due to exclusion of left atrial appendage (LAA) thrombi and computer tomography (CT) chest scan to delineate left atrial anatomy.
TEE did not show any thrombi in LAA.
After preparation of the patient, cryoballoon catheter ablation of AF was preformed as pulmonary vein isolation (PVI) with a single transseptal punction. All 4 pulmonary veins were isolated at the end of the procedure. Occlusion of all the veins during the ablation was estimated to be 4/4. Approximate time to isolation (TTI) was around 60 seconds, the temperature at the time of isolation was - 27 to -37°C. The minimal achieved temperature during the ablation was - 52° C. The procedure time was 55 minutes. The ablation was performed on uninterrupted warfarin therapy and using conscious sedation.
The patient was discharged home the second day after the procedure, in sinus rhythm and with no pericardial effusion.
6 months after the procedure, the patient did not have any symptomatic episode of atrial fibrillation, and no sustained atrial arrhythmia was registered at 1, 3 and 6 months 24h ECG holter monitoring.

Discussion

The primary selection criterion for ablation of AF is the presence of symptoms, such as palpitations, fatigue and dyspnea. Current guidelines recommend that additional variables should be considered because if they are present, they could result in higher complication rate and reduced success of the procedure such as obesity, sleep apnea, concomitant heart disease, left atrial size, type of AF and patient age[1,11].
Catheter ablation of AF is recommended as a second-line therapy for patients with symptomatic paroxysmal AF (PAF) or persistent AF for whom therapy with antiarrhythmic drugs (AADs) (Class I) has failed and for patients with long-standing persistent AF with a Class IIb indication. Although invasive cardiac procedures involve the potential for life-threatening complications, long-term AAD therapy has been shown to be more commonly associated with considerable side effects compared to ablation (17 vs. 8%).[25]

The success of catheter ablation

The multiple procedure success rate of pulmonary vein isolation (PVI) in patients with PAF after a 5-year follow-up period has been reported to be approximately 80%, failing to about 60% after 10 years[26,27]. For patients with persistent AF, stable sinus rhythm (SR) after successful PVI was reported in 25% after a single procedure and in 68% after multiple procedures, during a median follow up of approximately 7 years[28].
Estimation of the real success rate after catheter ablation of AF remains difficult due to inconsistencies in the definitions pf procedural success and post procedural rhythm monitoring and differences in the analysis of outcomes after single or multiple procedures. To date, the electrophysiology community has defined AF recurrence as the occurrence of any symptomatic or asymptomatic atrial tachyarrhythmia after the procedure lasting for > 30 seconds. Newer studies have presented a novel definition focusing on the AF burden which may represent a more relevant parameter for risk stratification and efficacy assessment after AF ablation.
While RF based PVI in combination with a 3 D mapping system was long considered to be the " gold standard", the CB has emerged as the most commonly used alternative ablation tool for PVI and is now established as the second gold standard in patients with paroxysmal atrial fibrillation in the current guidelines[1,21].
CB based ablation is associated with a low incidence of major complications, specifically driven by a low number of pericardial effusions or tamponades[22]. In addition, the incidence of phrenic nerve palsy, which is the most common balloon associated complication, can be kept considerably low by implementing safety algorithms, such as phrenic nerve pacing and monitoring of the compound motor action potential. Furthermore, the incidence of PV stenosis is a rare finding in patients undergoing CB ablation and has only been mentioned in incidental case reports[22,23]. Most data on CB ablation have been collected from patients suffering from PAF, with the data showing encouraging outcomes. The multicenter FIRE AND ICE trial, which prospectively randomized PAF patients to either RF or CB based PVI, demonstrated non-inferiority of CB ablation versus RF ablation in terms of efficacy and safety[21]. However, the positive findings from recent analyses encourage the application of CB based catheter ablation to patients with persistent AF also. The Cryo4persistent study focused not only on the recurrence of AF after previous CB based PVI but also on the symptoms and demonstrated a significant improvement in patients' quality of life following CB ablation in those with persistent AF[24]. These findings were confirmed in the analysis of two large prospective registries (the AF Ablation Long-Term registry within the EURObservational Research Programme [AFA EOPR] and the Swedish catheter ablation registry with reported lower EHRA (European Heart Rhythm Association) score, a measure of AF related symptoms and a lower rate of AF related symptoms and a lower rate of continued antiarrhythmic drugs after CB based AF ablation.
Catheter ablation is a well-established treatment option for patients with symptomatic AF and more effective at maintaining SAR than antiarrhythmic drugs. Currently, the most effective technique for AF ablatio is circumferential isolation of the PVs, irrespective of AF type. RF based and CB ablation are equally effective in patients with PAF.

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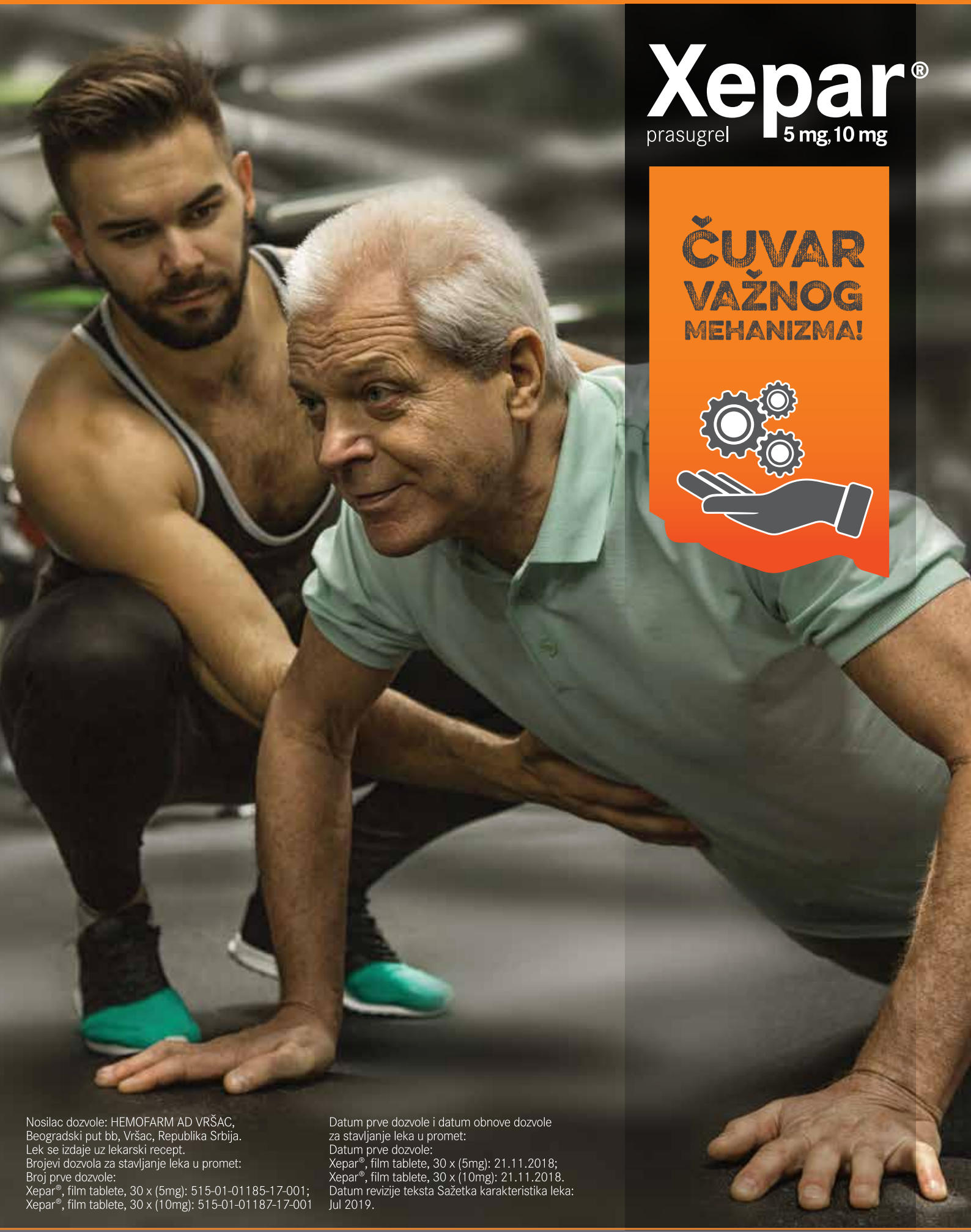

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