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CARDIOLOGY SOCIETY OF SERBIA

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Časopis Udruženja kardiologa Srbije

SRCE i krvni sudovi

Heart and Blood Vessels

Journal of the Cardiology Society of Serbia



Echocardiographic and laboratory parameters in hypertensive patients with and without atrial fibrillation

Ehokardiografski laboratorijski parametri kod hipertenzivnih pacijenata sa i bez atrijske fibrilacije

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Echocardiographic and laboratory parameters in hypertensive patients with and without atrial fibrillation

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Abstract

Background. Arterial hypertension (AH) is the most common cause of atrial fibrillation (AF). During AF, the contractile function of the left atrium (LA) is lost, and structural and functional remodeling occur. AH contributes greatly to the development of this common arrhythmia. The main objective of our study was to compare echocardiographic and laboratory biomarkers in patients with AH with or without AF.

Methods We conducted a cross-sectional analysis with 97 consecutive patients (mean age, 64±9 years; 49 male) with AH, 56 patients (57.7%) with AF. All patients underwent a basic examination and measurement of blood pressure. Laboratory testing (brain natriuretic peptide (BNP), C-reactive protein (CRP)), and transthoracic echocardiography examination with assessment of the LA antero-posterior (AP) diameter from the longitudinal parasternal section, and medio-lateral (ML) and superior-inferior (SI) dimension from the four-cavity apical section was performed.

Results. In two groups, there was no difference in blood pressure values. Mean systolic arterial pressure was slightly higher in the group of patients with AF (133,1±17,4 mmHg) compared with the group without AF (129,3±20,6 mmHg; $t=0,991$; $p=0,324$). Diastolic blood pressure values did not differ between groups (with AF 77,5±12,7mmHg, without AF 78,4±10,8mmHg, $t=-0,348$; $p=0,729$). Slightly increased values of CRP were in the group of patients with AF, but the difference was not statistically significant (2.5±1.2mg/L; 3.6±2.1mg/L, $Z=-1.618$; $p=0.106$). Also, there was significant difference between groups regarding the BNP (46±23 pg/ml, 89±55 pg/ml, $Z=-3,838$; $p<0,001$). Between the two groups, all echocardiographic measurements of the LA showed significant differences (AP 45,43±5.02mm with AF; 39.37±6.05mm, $t=5.392$, $p<0,01$, ML 58.57±7.69mm with AF; 50.12±8.01mm, $t=5.253$, $p<0,001$, SI 47.43±6.35 mm with AF, 43.85±5.47 mm, $t=2.9$, $p=0.005$). As predictors of AF in hypertensive patients we found echocardiographic parameter – ML dimension of the LA and laboratory marker BNP.

Conclusion. Hypertensive patients with AF have a significantly increased LA compared with hypertensive patients in sinus rhythm. Predictors of AF in AH are ML dimension of LA and elevated value of BNP.

Key words arterial hypertension, atrial fibrillation, left atrial dimension, biomarkers

Introduction

Arterial hypertension (AH) is a disease characterized by elevated systolic and diastolic values of blood pressure (BP) $\geq 140/90$ mmHg, only elevated systolic BP (isolated systolic hypertension) or taking antihypertensive therapy¹. Arterial blood pressure is a product of minute volume and total peripheral vascular pressure resistance².

It is estimated that about 20-25% of the general population worldwide have AH and the frequency varies based on geographical, national, racial, gender, or age criteria³⁻⁵. AH is a risk factor for cardiovascular diseases (CVD) such as atrial fibrillation (AF), coronary heart disease, stroke, peripheral artery disease, congestive heart failure and sudden cardiac death^{6,7}.

A Framingham study showed that an increase in left ventricular mass (LVm 116 g/m²) significantly increased

the risk of cardiovascular (CV) events in both sexes and correlated positively with age⁸. CV events that positively correlate with left ventricular hypertrophy are: the occurrence of heart failure, arrhythmias, sudden cardiac death and cerebrovascular events⁹. Clinical studies also have shown that regression of left ventricular hypertrophy reduces the incidence of CV morbidity and mortality^{8,10}. Structural disorders heart following uncontrolled AH include myocyte hypertrophy, hypertrophy of media of intramyocardial coronary arteries as well as collagen accumulation leading to cardiac fibrosis¹¹. Furthermore, coronary flow is normal at rest, but in exertion, the coronary vasodilatory reserve becomes insufficient, which leads to subendocardial ischemia in conditions of increased myocardial oxygen demand^{10,11}. Subendocardial ischemia and cardiac fibrosis worsen diastolic relaxation leading to diastolic heart failure¹². Enlargement of the left atrium (LA) is associated with

impaired systolic and diastolic function of the LA^{13,14}. In patients with AH, the LA is chronically exposed to increased pressure during left ventricular diastole, which leads to increasing of pressure in the LA and a decrease in the conduction function of these chamber¹⁵.

The frequency of AF increases with age. It is estimated that over 6% of the population older than 75 have this arrhythmia¹⁶. In 2016, approximately 43.6 million individuals worldwide have this arrhythmia, with a higher prevalence and incidence in more developed countries¹⁶. Also, one in four adults in Europe and the United States will develop AF later in life¹⁷. Recent estimation showed that by 2030, AF will have 14-17 million patients in the European Union with 120,000-215,000 newly diagnosed patients per year¹⁸. The prevalence of AF is higher in the elderly and in patients with AH, heart failure, coronary heart disease, valvular heart disease, obesity, diabetes mellitus, and chronic kidney disease¹⁹. AF is also associated with increased morbidity from heart failure and stroke¹⁹. In controlled studies, the average annual stroke rate was about 1.5% and the annual mortality was about 3% of anticoagulated AF patients²⁰.

It is important to assess the risk of AF in hypertensive patients, since AH is the most common predisposing factor for the development of this arrhythmia²¹. In the follow-up study by Manitoba et al., the incidence of AH was 53%, and the risk of AF was 1.42 times higher in hypertensive subjects compared with normotensive subjects²². However, despite its significance as a risk factor, little data are available on the predictors of AF in individuals with essential AH without coexisting disease such as valvular disease or coronary heart disease, heart failure, disease of thyroid gland or other predisposing conditions.

This aim of our study was to show the frequency of AF in patients with essential AH, and to comparatively analyze the echocardiographic and laboratory parameters between hypertensive patients with and without AF.

Methods

We conducted prospective cross-sectional analysis of 97 consecutive patients treated for hypertension with or without AF from 2018 to 2019 at the Cardiology Clinic, University Clinical Center of Serbia.

A total of 97 (mean age 64 ± 9 years; 49 male) with AH, 56 patients (57.7%) had AF. The inclusion criteria was diagnosed essential hypertension according to the ESH (European Hypertension Association) guidelines⁴. The measurement of arterial blood pressure was performed according to the recommendations of the Joint Committee for Detection, Evaluation and Treatment of High Blood Pressure⁶. Exclusion criteria were secondary hypertension, the presence of heart failure, the presence of ischemic heart disease, and the presence of valvular heart disease.

All patients underwent a detailed physical examination with medical history exploration. Risk factors were analyzed: gender, age, previous hypertension, diabetes mellitus, hyperlipidemia, smoking, heredity, previous coronary event, previous infarction, or percutaneous

coronary intervention or coronary artery bypass graft surgery. The clinical characteristics of the patients were analyzed: arterial pressure, heart rate, the presence of signs and symptoms of heart failure.

All patients underwent a twelve-channel ECG, after 20 min of rest in a supine position at a paper speed of 50 mm-s. Based on ECG examinations, patients with AH were divided into two groups: patients with a regular heart rhythm and patients with AF.

All patients had blood sampled for analysis. of laboratory markers: brain natriuretic peptide (BNP), C-reactive protein (CRP), and uric acid.

Transthoracic echocardiography was performed on a Vivid T8 GE Healthcare device, with 3.5 and 2.5 MHz probes. The measurements were performed according to the criteria of the American Echocardiographic Association²³. Three consecutive cycles were recorded for each parameter. All subjects were examined echocardiographically by a physician who was instructed in all clinical characteristics and results.

The dimension of the LA: antero-posterior (AP) was measured in 2D mode from the longitudinal parasternal section, and the medio-lateral (ML) and superior-inferior (SI) dimension from the four - cavity apical section.

Statistical analysis

The obtained data were first processed by descriptive statistical analysis, and then the statistical significance of the difference between the examined groups was analyzed by appropriate tests depending on the distribution of data (Student's T test for parametric data, Mann-Whitney U test, Hi-square test and Fisher's test of exact probability for non-parametric data). Of the descriptive statistical methods, measures of central tendency (arithmetic mean, measures of variability, standard deviation and relative numbers expressed in percentages) were used. Statistically significant variables from individual models formed multivariate logistic regression models, on the basis of which variables were determined that significantly predict the occurrence of atrial fibrillation in the examined population. A logistic regression analysis was performed to test the correlation of the examined independent variables with the dependent AF. Statistical significance was assessed at two levels: 0.05 (statistically significant difference) and 0.01 (highly significant statistical difference).

Results

A total of 97 patients entered the study, 49 male (50.5%). The average age of the patient was 64 ± 5 years (range 20-85). Out of the total number of patients, 56 patients (57.7%) had AF. The mean value of systolic arterial blood pressure was slightly higher in the group of patients with AF, although this difference was not statistically significant ($133,1 \pm 17,4$ mmHg with AF; $129,3 \pm 20,6$ mmHg without AF; $t = 0.991$; $p = 0.324$). The mean value of diastolic arterial blood pressure was also slightly higher in the group of patients with AF, again this difference was not statistically significant (with AF $77,5 \pm 12,7$ mmHg, without $78,4 \pm 10,8$ mmHg; $t = -0.348$; $p = 0.729$).

Table 1. Descriptive statistics of CRP values in patients with and without atrial fibrillation

	N	CRP			
		Median	Perc. 25	Perc.75	
AF	No	41	2.50	1.50	4.60
	Yes	56	3.60	2.10	10.05

AF No - patients without atrial fibrillation, AF Yes - patients with atrial fibrillation, CRP - C reactive protein, N - total number of patients, Perc - percentiles

Table 2. Descriptive statistics of BNP values in patients with and without atrial fibrillation

	N	BNP			
		Median	Perc. 25	Perc.75	
AF	No	41	46.00	23.00	80.00
	Yes	56	89.00	55.50	119.00

AF No - patients without atrial fibrillation, AF Yes - patients with atrial fibrillation, BNP - brain natriuretic peptide, N - total number of patients, Perc - percentiles-

Table 3. Descriptive statistics of uric acid values in patients with and without atrial fibrillation

AF	N	A.M.	SD	Median	Minimum	Maximum
No	41	275.9	106.6	275	86	602
Yes	56	330.6	126.3	325	54	807
Total	97	307.5	120.9	305	54	807

AF No - patients without atrial fibrillation, AF Yes - patients with atrial fibrillation, N - total number of patients, A.M. - arithmetic mean, Minimum - the lowest value of uric acid levels in the blood, Maximum - the highest value of uric acid levels in the blood

There was no statistically significant difference in CRP values in patients with and without AF (Mann-Whitney U test $Z = -1.618$; $p = 0.106$), presented in Table 1. Difference of BNP values was statistically significant in investigated groups (Mann-Whitney U test $Z = -3.838$; $p < 0.001$), presented in Table 2. Also, there were significant differences in levels of uric acid between study groups ($t = 2.246$; $p = 0.027$) presented in Table 3.

In univariant regression analysis the value of the AP dimension of the LA was larger in group of patients with AF (45.43 ± 5.02 ; $t = 5.392$; $p < 0.001$). Furthermore, the ML dimension and the SI dimension of the LA were also larger in group with AF respectively (58.57 ± 7.69 ; $t = 5.253$; $p < 0.001$; 47.43 ± 6.35 ; $t = 2.900$; $p = 0.005$). Echocardiographic parameters are presented in Table 4. Significant predictors of AF in hypertensive patients were: echocardiographic parameter - ML of the LA measured from the apical four-cavity section and laboratory marker - BNP, presented in Table 5. The multivariable regression model shown in Table 6 was obtained by the Backward method, by eliminating individual predictors.

Discussion

Due to the high prevalence in the population, AH is independently responsible for the development of AF more than any other risk factor.¹ Prolonged uncontrolled AH can lead to remodeling of the heart anatomy and

Table 4. Descriptive statistics of left atrium dimension in patients with and without atrial fibrillation

AF	N	A.M.	SD	Median	Minimum	Maximum
Anteroposterior dimension						
No	41	39.37	6.05	39	28	59
Yes	56	45.43	5.02	45	34	57
Total	97	42.87	6.22	43	28	59
Medio-lateral dimension						
No	41	50.12	8.01	48	36	69
Yes	56	58.57	7.69	60	42	80
Total	97	55.00	8.84	55	36	80
Superior-inferior dimension						
No	41	43.85	5.47	43	35	64
Yes	56	47.43	6.35	46	39	69
Total	97	45.92	6.22	44	35	69

AF No - patients without atrial fibrillation, AF Yes - patients with atrial fibrillation, N - total number of patients, SD - standard deviation, Minimum - minimum value of left atrium dimension measured from longitudinal parasternal section (cm) Maximum - maximum value dimensions of the left atrium measured from the longitudinal parasternal section (cm)

Table 5. Multivariable logistics model with atrial fibrillation as dependent

	p	OR	95% IP for OR	
Uric acid	0.312	1.002	0.998	1.007
ML	0.004	1.132	1.041	1.231
SI	0.448	0.955	0.848	1.076
CRP	0.122	2.169	0.812	5.790
BNP	0.070	3.785	0.896	15.989

ML - mediolateral dimension of the left atrium measured from the apical four-cavity section, SI - superior-inferior dimension of the left atrium measured from the apical four-cavity section, CRP - C reactive protein, BNP - brain natriuretic peptide.

electrophysiological changes. Also, it can cause left ventricular hypertrophy, which leads to loading of the LA and consequently to remodeling of this chamber¹³. In our study groups, the average value of systolic pressure was slightly higher in the group of patients with AF. However, statistical analysis showed that this difference was not statistically significant ($p = 0.324$). Also, the average value of diastolic pressure was slightly higher in the group of patients with AF without significances ($p = 0.729$).

Watson and colleagues²⁴ looked for predictors of AF in natriuretic peptide and fibroinflammatory gene expression, as well as fibrosis and CD163+. As a result, peptides have been seen to increase in patients with AF. AF patients had a greater LA volume index, more valve disease, higher BNP, and altered collagen turnover markers versus controls (all $P < 0.05$).

Abhayaratna et al.²⁵ found that decreased LA reservoir function significantly increased the risk of first paroxysmal AF or atrial flutter in a population over 65 as much as 9.2-fold, regardless of left ventricular systolic function, and clinical factors. Structural remodeling, which has been shown to increase the size of the LA, is a strong predictor of atrial arrhythmia.

Table 6. Multivariable regression model obtained by predictor elimination (backward method)

	p	OR	95% IP for OR	
ML	0.001	1.114	1.045	1.188
BNP	0.049	4.410	1.006	19.336

ML - mediolateral dimension of the left atrium measured from the apical four-cavity section, BNP – brain natriuretic peptide

Most studies of inflammatory activity in AF have focused on the clinically established biomarker CRP and interleukin-6.²⁶ To date, studies with biomarkers and AF have been based on a single measurement at study entry. However, repeated measurements may provide additional information regarding the determinants for the increase of these biomarkers and the subsequent risk of AF. Continuous increases in NT-proBNP concentrations over time have been shown to be associated with cardiovascular comorbidities and give an even higher risk of stroke and mortality. It is shown that at 90 days, a higher proportion of patients with AF (89.4% vs 81.5%; $P=.002$) had an NT-proBNP level above 1000 pg/mL (to convert NT-proBNP values to pmol/L, multiply by 0.1182), and AF patients had higher NT-proBNP levels at all time points through 2 years of follow-up²⁷. In our study, the average value of CRP was higher in the group of patients with AF, however, the difference was not statistically significant as evidenced ($p = 0.106$).

Also, according to the Framingham study⁸, LA remodeling was defined as an increment of LA diameter (as a continuous variable and quartile-based analysis) and was 1 of 3 independent echocardiographic predictors for future AF development. Yoon et al²⁸ evaluated LA volume and function by strain analysis showing that the volume of indexed LA > 34 ml / m² and LA strain <31% had a two-fold and four-fold increase in the likelihood for patients with paroxysmal AF to develop permanent AF during the follow-up period of 26 months. However, the definitive cut-off for monitoring LA remodeling, as an indicator of AF development, is not clearly defined²⁹. Our findings suggest that LA dilatation in hypertensive subjects who are in sinus rhythm is valuable for identifying those individuals who are more prone to AF.

Univariate analysis of echocardiographic markers of study population showed that the average value of the LA dimension from PLAX was higher in the group of patients with AF and that there was a statistically significant difference ($p < 0.001$). It is also seen that the mean value of the ML dimension of the left atrium measured in the apical four-cavity section is higher in the group of patients with AF ($p < 0.001$). Furthermore, the average value of the SI dimension of the LA measured in the apical section of four cavities is larger in the group of patients with AF ($p = 0.005$).

Limitation of the study

This analysis had a few limitations. The number of patients recruited in our study was limited and study was conducted in single center.

Conclusion

Hypertensive patients with AF have a significantly increased LA compared with hypertensive patients in sinus rhythm. Predictors of AF in group of patients with AH are echocardiographic ML dimension of LA and elevated value of blood biomarker BNP.

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Sažetak

Ehokardiografski laboratorijski parametri kod hipertenzivnih pacijenata sa i bez atrijske fibrilacije

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Uvod. Arterijska hipertenzija (AH) predstavlja jedan od najčešćih uzroka atrijske fibrilacije (AF). Tokom AF kontraktilna funkcija leve prekomore (LP) je izgubljena, što vodi strukturnom i funkcionalnom remodelovanju ovog dela srca. AH značajno doprinosi razvoju same aritmije i daljem remodelovanju srčanih šupljina. Cilj našeg istraživanja je poređenje ehokardiografskih i laboratorijskih parametara kod pacijenata sa AH sa i bez AF uz analizu predikotora AF u AH.

Metode. Sproveli smo studiju preseka sa 97 konsekutivnih pacijenata (srednjih godina 64 ± 9 ; 49 muškaraca) sa AH od čega je 56 pacijenata (57%) imalo AF. Svim ispitanicima je izvršen fizikalni pregled, izmeren im je arterijski pritisak i laboratorijske analize (brain natriuretski peptid –BNP, C reaktivni protein –CRP) uz ehokardiografski pregled sa analizom LP (merenje antero-posteriorne dimenzije (AP) iz longitudinalnog parasternalnog prozora, medio-lateralne (ML) i superiorno-inferiorne (SI) dimenzije iz prozora sa četiri srčane šupljine.

Rezultati. Analizom grupa hipertenzivnih pacijenata sa i bez AF, registrovane su nešto više vrednosti sistolnog pritiska u grupi bolesnika sa AF ali bez statističke značajnosti ($133,1 \pm 17,4$ mmHg sa AF; $129,3 \pm 20,6$ mmHg bez AF; $t = 0,991$; $p = 0,324$). Vrednost dijastolnog pritiska se nije razlikovala među grupama ($77,5 \pm 12,7$ mmHg sa AF, $78,4 \pm 10,8$ mmHg bez AF, $t = -0,348$; $p = 0,729$). Blago povišene vrednosti CRP su registrovane u grupi ispitanika sa AF, ali razlika nije bila statistički značajna ($2,51.2$ mg/L; $3,62.1$ mg/L, $Z = -1,618$; $p = 0,106$). Registrovana je značajna razlika među grupama u vrednosti BNP-a (46 ± 23 pg/ml, 89 ± 55 pg/ml, $Z = -3,838$; $p = 0,001$). Između grupa hipertenzivnih sa i bez AF svi mereni ehokardiografski parametri LP bili su značajno veći u grupi sa AF (AP $45,43 \pm 5,02$ mm sa AF; $39,37 \pm 6,05$ mm bez AF, $t = 5,392$, $p < 0,01$, ML $58,57 \pm 7,69$ mm sa AF; $50,12 \pm 8,01$ mm bez AF, $t = 5,253$, $p < 0,001$, SI $47,43 \pm 6,35$ mm sa AF, $43,85 \pm 5,47$ mm bez AF, $t = 2,9$, $p = 0,005$). Kao prediktori nastanka AF u grupi pacijenata sa AF uočeni su ML dijametar LP i vrednost BNP-a.

Zaključak. Hipertenzivni pacijenti sa AF imaju značajno uvećanu LP u poređenju sa hipertenzivnim pacijentima u sinusnom ritmu. Prediktori nastanka AF kod hipertenzivnih su ML dijametar LP i vrednost BNP-a.

Ključne reči: arterijska hipertenzija, atrijska fibrilacija, leva prekomora, biomarkeri

Ergospirometry in the assessment of cardiovascular risk and safe physical activity in obese persons

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Abstract

Background. Obesity is one of the most important health problems in the world and in our country and is the main risk factor for reduced functional capacity and therefore for cardiovascular diseases (CVD), so reducing body weight (TT) is important for a good management of the health system and impact on future adverse cardiovascular events. Therefore, a detailed assessment of the cardiopulmonary system in the obese is very important. The aim of our study was to examine the role of ergospirometry in the assessment of cardiopulmonary capacity in relation to the ordinary ECG exercise test in morbidly obese persons referred for body weight reduction in our Center for obesity.

Methods. The study was conducted in the Laboratory for Ergospirometry, Cardiology Clinic, UCCS. Obese patients with a BMI >31 kg/m² (mean BMI 45±6), aged >18 years, scheduled for the diet or bariatric surgery treatment of obesity participated in the research. The total number of patients was 196 (142 women and 54 men). All patients underwent a clinical examination and cardiopulmonary exercise test (CPET, Bruce protocol) with simultaneous gas analyses. In accordance with guidelines, we used recommended cut off for the ventilatory anaerobic threshold ≥14 ml/kg/min for increased CV risk.

Results. During CPET, there was an adequate increase in heart rate and blood pressure compared to resting values. That optimal VAT was achieved by 152 patients, while 31 obese individuals had an anaerobic threshold below 14 ml/kg/min. Persons with a lower anaerobic threshold on the test were older, and the differences were only in the achieved CPET parameters, while the classical parameters of the physical load test did not differ.

Conclusion. Cardiopulmonary capacity, as a significant predictor of mortality and morbidity, is greatly influenced by obesity. Objective assessment includes determination of cardiopulmonary capacity and ventilatory anaerobic threshold by ergospirometry which is superior to standard exercise test parameters and VAT values are also the starting point for prescribing safe physical activity. Based on the parameters of CPET we can identify a high-risk patients independently of the BMI value.

Key words obesity, ergospirometry, anaerobic threshold, cardiopulmonary capacity

Introduction

Historically, obesity is the most common and longest-known metabolic disorder, which was initially a status symbol and was not viewed as a health problem or an aesthetic defect. It is defined by the accumulation of excess body fat, as a result of an imbalance between energy intake and its expenditure, taking into account gender, age and body height. As a chronic disease, obesity has great social and economic importance, due to significant health complications that reduce the quality of life, shorten life expectancy, and the treatment of obese people has a high price¹⁻⁶.

Body mass index is the ratio of body mass in kilograms to the square of body height expressed in meters.

However, one should be careful, because it is possible to be obese and have a good body mass index, or vice versa - not to have too much weight, but have an increased BMI. This means that body composition plays a more important role than body weight measured in kilograms⁷. BMI is calculated using a formula that relates an individual's height and weight, or more precisely, it represents weight (in kg) divided by height (expressed in meters squared). So it is expressed in BMI=kg/m². The classification according to BMI is shown in Table 1. Obesity is one of the most important health problems in the world and in our country and is the main risk factor for reduced functional capacity and therefore for cardiovascular diseases (CVD), so reducing body weight

Table 1. Degree of obesity stratified according to BMI values

	Male BMI (kg/m ²)	Female BMI (kg/m ²)
Malnutrition	< 20	<19
Normal body weight	20 - 25	19 - 24
Obesity, level I (increased body weight)	25 - 30	24 - 30
Obesity, level II	30 - 40	30 - 40
Morbid obesity, level III	> 40	>40

BMI - body mass index

(TT) is important for a good management of the health system and impact on future adverse cardiovascular events¹. Therefore, a detailed assessment of the cardiopulmonary system in the obese is very important.

Ergospirometry and obesity

Peak VO₂ is the highest myocardial oxygen consumption achieved during CPET and is the most reproducible index of cardiorespiratory fitness or aerobic capacity. If the consumption curve shows a plateau at the maximum load, then the consumption can be marked as maximum VO₂max. PeakVO₂ and anaerobic threshold (AT) are also expressed according to the unit of body weight as ml/kg/min. Conversion of PeakVO₂ to MET units is achieved by dividing by 3.5 mL/kg/min. Normal consumption declines with age 8% to 10% over each decade in non-athletes, and 5% over each decade in persistent exercisers. It is also 10% to 20% higher in men, due to higher hemoglobin concentrations, greater muscle mass, and greater stroke volume. Functional capacity is decreased in obese persons, but this is not the rule, as in this population it also depends on the condition, level of obesity and age^{8,9}.

Anaerobic threshold

When the metabolic needs during exercise exceed the supply of oxygen to the working muscles, anaerobic metabolism is activated. Anaerobic - ventilatory threshold (VAT) is detected with a metabolic increase in VCO₂ and VE relative to VO₂. Typically, AT occurs between 47% and 64% of the predicted VO₂max of untrained healthy individuals and increases with training. VAT is important in prescribing training and rehabilitation because VO₂ at VAT indicates our ability to perform daily (submaximal) activities, but also the degree of fitness and decreases with deconditioning. It is also important because the activities up to the threshold are mild and that is the zone of predominantly fat consumption which is important body weight reduction. The most important parameter for evaluating risk of CV events is VAT with the cut off value for obese persons 14 ml/kg/min⁷⁻⁹.

The aim of our study was to examine the role of ergospirometry in the assessment of cardiopulmonary capacity in relation to the ordinary ECG exercise test in morbidly obese persons referred for body weight reduction in our Center for obesity.

Methods

The study was conducted in the Laboratory for Ergospirometry, Cardiology Clinic, UCCS. We analyzed 196 patients (142 women and 54 men, average age 39±10 years) with BMI 45±6kg/m² who were referred for assessment in Obesity center. All patients underwent a clinical examination and CPET. Patients with uncontrolled hypertension blood pressure, ischemic heart disease, significant valvular disease, severe chronic obstructive pulmonary disease or syncope were excluded. All patients signed an informed consent before the test. Testing was approved by the UCCS ethics committee.

Test protocol and monitoring

The Shiller CS-200 system was used for the analysis of expiratory gases during CPET. Ergospirometry was performed on a treadmill (standard Bruce protocol). During the test, oxygen consumption (VO₂) was continuously monitored and consumption at ventilatory anaerobic threshold (VAT) was determined, as well as peak consumption (peakVO₂) with monitoring of ventilatory parameters and respiratory reserve. A 12-channel ECG and blood pressure were continuously monitored. Pressure measurements and ECG recordings were performed at rest, at the end of each level and during recovery. Indications for discontinuation were: respiratory gas exchange index RER = 1.1, fatigue, dizziness, intense chest pain, horizontal or descending ST depression/elevation >1 mm lasting 0.08 s after the J point, hypertensive response (240/ 120mmHg), serious rhythm disorders.

Statistical analysis

The complete statistical analysis of the data was done using SPSS, version 17. All attributive variables were presented in the form of frequencies of individual categories, and the statistical significance between individual categories was tested with the Chi-square test. All continuous variables are presented as mean ± standard deviation, while for differences in continuous variables we will use Student's t test for independent or dependent causes or Mann-Whitney test or Wilcoxon test, depending on the normality of the distribution, which will be tested by Kolmogorov-Smirnov test. All analyzes will be evaluated at a statistical significance level of p<0.05. After the statistical processing of the data, the results will be presented tabularly and graphically.

Results

Obese patients with a BMI >31 kg/m² (mean BMI 45±6), aged >18 years, scheduled for the diet or bariatric surgery treatment of obesity participated in the research. The total number of patients was 196 (142 women and 54 men). Table 2 shows the prevalence of classic risk factors for CVD.

During CPET, there was a significant increase in heart rate and blood pressure compared to resting values. Table 3. And CPET variables are shown in table 4.

Table 2 . Risk factors in morbidly obese persons in the studied population

	n	%
Sedentary	135	68
HTN	99	50
OSA	6	3
Cigarette smoking	42	21
DM	56	28
Insulin resistance	24	12
CHO	21	10
TG	19	9
Statin therapy	17	8

HTN – hypertension; OSA- obstructive sleep apnea; DM – diabetes; CHO – cholesterol; TG- triglycerides

Table 3. Hemodynamic changes during CPET

Rest HR (bpm)	97±12
Peak HR (bpm)	165±75*
Rest SBP (mmHg)	136±12
Peak SBP (mmHg)	180±25*
Rest DBP (mmHg)	87±12
Peak DBP (mmHg)	98±10*

***p<0.0001**, HR-heart rate; SBP-systolic blood pressure; DBP- diastolic blood pressure

In accordance with guidelines, we used recommended cut off for the ventilatory anaerobic threshold ≥ 14 ml/kg/min for increased CV risk. That VAT was achieved by 152 patients, while 31 obese individuals had an anaerobic threshold below 14 ml/kg/min . Persons with a lower anaerobic threshold on the test were older, and the differences were only in the achieved CPET parameters, while the classical parameters of the physical load test did not differ.

Discussion

It is known that obesity is one of the leading risk factors for CV diseases whereas a special importance has cardiopulmonary capacity¹⁻⁶.

Chronic, morbid obesity leads to a series of changes in the CV and pulmonary system that jeopardises health and reduce the possibility of adequate supply of organs and tissues with oxygen, especially in conditions of increased needs^{8,9}. Peak VO₂ is a precise indicator of cardiopulmonary capacity and patients with low consumption have a higher risk of intervention¹⁰⁻¹². In our study, peak VO₂ was significantly higher in patients who had an optimal anaerobic threshold ≥ 14 ml/kg/min compared to the group of patients who had an anaerobic threshold lower than 14 ml/kg/min, while ventilatory efficiency was higher in group of patients who had an anaerobic threshold of less than 14 ml/kg/min. This result indicates the importance of objective assessment and the existence of a certain percentage of obese people with a reduced ability to tolerate submaximal effort^{7,10,11,12}. We have also shown that the parameters of CPET in this group of patients are superior to the classic parameters of the

Table 4. CPET parameters in obese persons

Peak VO ₂ (ml/kg/min)	19.7±3.9
VAT (VO ₂) (ml/kg/min)	17.2±3.5
VE/VCO ₂ slope	27±4

Peak VO₂ – Peak myocardial oxygen consumption; VAT (VO₂) – oxygen consumption on anaerobic threshold; VE/VCO₂ slope – ventilatory efficiency

Table 5. Ergospirometry parameters in relation to the value of the anaerobic threshold

	≥ 14 ml/kg/min N=51	<14 ml/kg/min N=14	p
Age (y)	37±10	46±9	<0.0001
BMI (kg/m ²)	46±6	47±6	0.06
Test duration (sec)	345±107	259±114	<0.0001
Rest HR (bpm)	98±12	93±15	0.09
Peak HR (bpm)	169±83	148±63	0.005
Rest SBP (mmHg)	136±12	138±14	0.277
Peak SBP (mmHg)	180±26	179±23	0.880
Rest DBP (mmHg)	87±13	87±10	0.829
Peak DBP (mmHg)	98±10	100±10	0.221
Peak VO ₂ (ml/kg/min)	20.6±3.3	15.6±2.8	<0.0001
VE/VCO ₂ slope	26±4	28±3.7	<0.0001

BMI – body mass index; rest HR- resting heart rate; Peak HR – peak heart rate; rest SBP – resting systolic blood pressure; peak SBP- peak systolic blood pressure; rest DBP- rest diastolic blood pressure; peak DBP – peak diastolic blood pressure; Peak VO₂ – peak myocardial oxygen consumption; VE/VCO₂ slope – ventilatory efficiency.

exercise ECG test which is in concordance with previous studies and guidelines^{7,9}. According to the recommendations, it is a good starting point for physical activity, because up to that level of activity, they are mild and in the zone of fat consumption, which is also an additional therapy in addition to diet therapy^{10,11}.

For patients who have an adequate threshold, more intensive activities can be prescribed, and the risk of side effects is also lower^{9,10}

Conclusion

Cardiopulmonary capacity, as a significant predictor of mortality and morbidity, is greatly influenced by morbid obesity. Objective assessment includes determination of cardiopulmonary capacity and ventilatory anaerobic threshold by ergospirometry which is superior to standard exercise test parameters and VAT values are also the starting point for prescribing safe physical activity. Based on the parameters of CPET we can identify a high risk patients independently of the BMI value.

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Sažetak

Ehokardiografija u proceni kardiovaskularnog rizika i sigurne fizičke aktivnosti kod gojaznih osoba

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Uvod. Gojaznost je jedan od najvažnijih zdravstvenih problema u svetu i kod nas i glavni je faktor rizika za smanjenje funkcionalnog kapaciteta, a samim tim i za kardiovaskularne bolesti (KVB), pa je smanjenje telesne težine (TT) važno za dobro lečenje. Zdravstvenog sistema i uticaj na buduće neželjene kardiovaskularne događaje. Zbog toga je veoma važna detaljna procena kardiopulmonalnog sistema kod gojaznih. Cilj našeg istraživanja bio je da ispita-mo ulogu ergospirometrije u proceni kardiopulmonalnog kapaciteta u odnosu na obični EKG test vežbanja kod morbidno gojaznih osoba upućenih na smanjenje telesne težine u našem Centru za gojaznost.

Metode. Istraživanje je sprovedeno u Laboratoriji za ergospirometriju Klinike za kardiologiju UKCS. U istraživanju su učestvovali gojazni pacijenti sa BMI >31 kg/m² (srednji BMI 45±6), starosti >18 godina, predviđeni za dijetu ili barijatrijski hirurški tretman gojaznosti. Ukupan broj pacijenata je 196 (142 žene i 54 muškarca). Svi pacijenti su podvrgnuti kliničkom pregledu i ergospirometriji (CPET) (Bruce protokol) uz istovremene analize gasa. U skladu sa smernicama, koristili smo preporučeni cutoff za ventilacioni anaerobni prag ≥14 ml/kg/min za povećan rizik od KV.

Rezultati. Tokom CPET-a, došlo je do adekvatnog povećanja srčane frekvencije i krvnog pritiska u poređenju sa vrednostima u mirovanju. Taj optimalni PDV postigla su 152 pacijenta, dok je 31 gojazna osoba imala anaerobni prag ispod 14 ml/kg/min. Osobe sa nižim anaerobnim pragom na testu bile su starije, a razlike su bile samo u postignutim CPET parametrima, dok se klasični parametri testa fizičkog opterećenja nisu razlikovali.

Zaključak. Kardiopulmonalni kapacitet, kao značajan prediktor mortaliteta i morbiditeta, ima veliki uticaj gojaznosti. Objektivna procena obuhvata određivanje kardiopulmonalnog kapaciteta i ventilacionog anaerobnog praga ergospirometrijom koja je superiornija od standardnih parametara testa opterećenja, a vrednosti PDV-a su takođe polazna tačka za propisivanje bezbedne fizičke aktivnosti. Na osnovu parametara CPET-a možemo identifikovati visokorizične pacijente nezavisno od vrednosti BMI.

Ključne reči: gojaznost, ergospirometrija, anaerobni prag, kardiopulmonalni kapacitet

The effect of alcohol on sports and recreation: should these pleasures be mixed?

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Abstract

According to the recommendations, physical activity contributes to health and is both a preventive and therapeutic measure for a large number of diseases. However, there are factors that can lead to the appearance of atrial fibrillation (AF) even in healthy individuals. We presented a case of a young athlete who showed superior functional capacity during a routine ergospirometry examination, but during recovery had paroxysmal AF that was interrupted by medication. Laboratory, echocardiographic and 24 hours Holter monitoring findings were normal. Subsequent medical history indicated that he had consumed alcohol the previous night. This confirms that alcohol excess is a risk factor for paroxysmal AF.

This case indicates the importance of following the recommendations that insist on a detailed history, physical examination, and further examinations of athletes and recreationists in accordance with the existing algorithms.

Key words athletes, atrial fibrillation, alcohol intake

Case presentation

A 19 years old athlete who prefer freestyle skiing, came for a routine examination. He was completely asymptomatic, without any limitation during the sport. Laboratory blood analyses were normal. He has a negative family history for family diseases or cardiac death and he was non-smoker. He denied the use of drugs, illegal substances, occasionally consumes alcohol, and does not take any medications.

According to the recommendations for routine testing of asymptomatic athletes, echocardiography is not recommended, so the first step was an ECG (Figure 1). ECG was without pathological changes, and ergospirometry (CPET) was performed. The test showed superior functional capacity with peak oxygen consumption (peakVO₂) up to 53.5 ml/kg/min, with no signs of ventilatory limitation (which excludes diastolic dysfunction due to cardiomyopathies), and without ST segment changes and rhythm disturbances. Hemodynamic response during the test was normal (Table 1).

However, during the 1st minute of recovery phase, sudden dyspnea and palpitations occurred accompanied by the significant drop of blood pressure from 170/98 mmHg to 100/60 mmHg. ECG showed atrial fibrillation, with a ventricular response of about 100/min with premature ventricular beats (Figure 2).

According to guidelines this was the first time diagnosed AF as AF was not diagnosed before, irrespective of its

duration or the presence/severity of AF-related symptoms. We administered i.v. Propafenone 120 mg (1.5 mg/kg over 10 min) which resulted in prompt termination of AF and restoration of normal sinus rhythm. We did not use anticoagulants as this was a paroxysmal AF in person with low risk of thromboembolic events (stroke). However, predischage conversation with the patient disclosed that previous night the athlete was at a party and consumed a large amount of alcohol.

As a part of further assessment and prevention of the new onset of AF we performed echocardiographic examination which revealed a normal left ventricular morphology and function, as well as normal left atrial structure without dilatation and signs of increased pressure. Also we performed 24 hours ECG monitoring which did not show rhythm or conduction disturbances. Control ergospirometry confirmed excellent functional capacity without the occurrence of rhythm disorders during exertion.

He was recommended to perform routine control examinations and to avoid use of alcohol and other pro-arrhythmic substances.

Discussion

According to the recommendations, moderate, regular physical activity (PA) is beneficial to health and represents the cornerstone of prevention of cardiovascular diseases, including AF. It is not only the effect of PA on the state of fitness, but also through the modification



Figure 1. Baseline ECG: sinus rhythm, 61 bpm, incomplete right bundle branch block



Figure 2. ECG during the 1st minute of recovery: atrial fibrillation, with a ventricular response of about 100/min with premature ventricular beats

of many of its predisposing factors¹⁻³. Patients at risk of AF should therefore be motivated to exercise, but the dosing of PA is very important. AF is more common in active and former elite athletes as well as recreational athletes who perform high-intensity endurance training. This effect of sports on the occurrence of AF as well as other adverse events is described by the *U* curve. At the beginning of playing sports, in men, the risk of CV events decreases, but over time, with the length of the sports activity and proportionally with the intensity of the training, the risk of AF and atherosclerotic complications increases. This association was not confirmed in women^{4,5}. There is relationship between AF and vigorous physical activity, mainly related to long-term or endurance sport participation. Based on these data, patients should be encouraged to undertake moderate-intensity exercise and remain physically active to prevent AF incidence or recurrence, but maybe avoid chronic excessive endurance exercise (such as marathons and long-distance triathlons, etc.), especially if aged >50 years⁶. Thus, in persons with paroxysmal AF it is important to recommend a moderate intensity of aerobic sports activity and a moderate level of strength exercises (with weight). In hypertensive athletes, physical activity is a

Table 1. Hemodynamic changes during cardio-pulmonary exercise test (CPET)

Rest HR (bpm)	61±12
Peak HR (bpm)	177±75*
Rest SBP (mmHg)	120±12
Peak SBP (mmHg)	170±25*
Rest DBP (mmHg)	70±12
Peak DBP (mmHg)	98±10*

* $p < 0.0001$

HR=heart rate; SBP=systolic blood pressure; DBP= diastolic blood pressure

measure of treatment and prevention of AF. In addition to other non-pharmacological measures including: restriction of salt intake, weight reduction if applicable, balanced diet (eg Mediterranean diet) and smoking cessation, there is a strong recommendation to avoid alcohol intake during exercise^{1,7}.

In persons with known AF, underlying structural heart disease or preexcitation should always be ruled out before advising sports activity. It is also important to exclude hyperthyroidism, (forbidden) drug use as well as alcohol abuse. Intensive sports should be temporarily stopped until the identified cause is eliminated (IA recommendation)^{1,3}.

Exercise recommendations for individuals with arrhythmias and implantable cardiac devices are also very clear. Prior to exercise, evaluation and management of structural heart disease, thyroid dysfunction, alcohol or drug abuse, or other primary causes of AF is recommended¹. Alcohol abstinence reduced arrhythmia recurrence in regular drinkers with AF⁶.

However at the same times there is some gaps in evidence in the terms of the threshold lifetime sports activity for increasing the risk of developing AF is unknown. It is also unknown whether ongoing participation in vigorous exercise at the same intensity after successful AF ablation is associated with a higher risk of AF recurrence¹. Further trials will give more answers.

Conclusion

Alcohol excess is a risk factor for incident AF. This case indicates the importance of following the recommendations that insist on a detailed history, physical examination, and further examinations of athletes and recreationists in accordance with the existing algorithms.

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Sažetak

Dejstvo alkohola na sport i rekreaciju: da li se ova dva zadovoljstva mogu kombinovati?

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Prema preporukama, fizička aktivnost doprinosi zdravlju i istovremeno je preventivna i terapijska mera za veliki broj bolesti. Međutim, postoje faktori koji mogu dovesti do pojave aatrijalne fibrilacije (AF) čak i kod zdravih osoba. Prikazali smo slučaj mladog sportiste koji je tokom rutinskog ergospirometrijskog pregleda pokazao superiorni funkcionalni kapacitet, ali je tokom oporavka imao paroksizmalni AF koji je prekinut lekovima. Laboratorijski, ehokardiografski i 24-časovni nalazi Holter monitoringa bili su normalni. Naknadna medicinska istorija je pokazala da je prethodne noći konzumirao alkohol. Ovo potvrđuje da je višak alkohola faktor rizika za paroksizmalnu AF. Ovaj slučaj ukazuje na važnost poštovanja preporuka koje insistiraju na detaljnoj anamnezi, fizičkom pregledu, kao i daljim pregledima sportista i rekreativaca u skladu sa postojećim algoritmima.

Ključne reči: sportisti, aatrijalna fibrilacija, unos alkohola

Echocardiography in the prevention of sudden cardiac death in athletes

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Abstract Sudden cardiac death (SCD) in an athlete is always shocking. It is of the utmost importance to better understand the causes of SCD in athletes and to discover optimal strategies for prevention. Echocardiography is a noninvasive first-line imaging technique in the identification of structural heart disease and is also irreplaceable in distinguishing an athlete's heart from cardiomyopathy. Therefore echocardiography is important in the prevention of sudden cardiac death during sports activities.

Key words sudden cardiac death, sport, echocardiography

Sudden cardiac death (SCD) is defined as unexpected, non-traumatic death during and shortly after training, usually within 1 h, in a person considered healthy¹. That is a very rare event. Current estimates of the incidence of SCD in competitive athletes range from almost 1 in a million to 1 in 5000 athletes per year. It affects male athletes 10 times more than female^{2,3}. After trauma SCD is the most frequent cause of death in sportsmen and two times more often than in the general population⁴.

Otherwise, athletes are individuals of young and adult age, either amateur or professional, who are engaged in exercise training on a regular basis and participate in official sports competitions. The problem with that definition is that persons who do regular physical exercise, and at times very intense, but never participate in organized competitions are left out. Although the general opinion is that professional athletes are at higher risk of SCD considering they aim to win which can lead to exaggerated training, one must remember that individual exercisers often practice very intense training totally unsupervised⁵. In older athletes (>35y) the most frequent cause of SCD is coronary artery disease and in young structural heart diseases. Many structural heart diseases are clinically silent and preparticipation evaluation of athletes is of the utmost importance. In presumably healthy young athletes prevalence of SCD-related structural malformations is 0,3%⁶.

Basic cardiovascular screening encompasses history, physical exam, and ECG and it has unique challenges and limitations. Transthoracic echocardiographic exam (TTE) is recommended when there is a justified clinical suspicion (athletes who are symptomatic, who have abnormal physical findings including abnormal electrocardiogram (ECG), and/or positive family history for SCD). It is estimated that nearly 30% of potentially fatal structural heart diseases cannot be discovered without echocardiography. Diseases like aortic dilatation, bicuspid

aortic valve, mitral valve prolapse, Ebstein anomaly, congenital anomalies of coronary arteries, congenitally corrected transposition of the great arteries as well as 10-30% cardiomyopathies can not be detected without echocardiography. Still, echocardiography which can identify all these structural malformations is still not included in routine screening².

Coronary artery (CA) anomalies are rare congenital malformations, potentially fatal, and sometimes asymptomatic. Coronary vessels can have an abnormal origin, course, destination, size and number. Anomalous origins can have right CA from left coronary or noncoronary sinus, and left CA when it originates from the right coronary sinus of the aorta or the non-coronary sinus. Besides, coronary arteries can originate directly from the ascending aorta or pulmonary artery⁷.

Key to the recognition of anomalous CA origin is absence of typical echocardiographic visualization during meticulous screening.

Athletic training promotes structural and functional heart adaptation. These changes are considered benign but they may overlap with the phenotypic manifestations of a cardiomyopathy which are the commonest cause of SCD in young competitive athletes. Echocardiography, especially in elite athlete, is necessary in differentiating physiologic from pathologic remodeling⁸.

Information needed for interpretation of echocardiographic exam are^{9,10}

- gender (female athlete rarely have findings that are out of normal range)
- Age (heart of young athlete also show adaptive changes but in lesser degree compared to older athlete)
- Ethnicity (heart of black athlete sportista always show greater degree of hypertrophy and left atrial enlargement. Left ventricular wall thickness greater than 12mm in Caucasian and greater than 14mm in black male athlete and 13mm in black female athlete always requires further functional examination)



Figure 1. Bicuspid aortic valve



Figure 2. Dilated thoracic aorta



Figure 3. Ebstein anomaly



Figure 4. CCTGA (Congenitally corrected transposition of the great arteries)

- Body surface area (BSA). In extreme big BSA $>2.3\text{m}^2$ non indexed left ventricular wall thickness and enddiastolic dimension should not exceed 14mm and 65mm respectively)

- Symptoms (special attention should be paid to exertional chest pain, fainting and blurred vision, irregular heart beat, tiredness disproportionate to the intensity of training)

- ECG changes

- Type of sport

If TTE is done, it is wrong to do quick targeted exam. One should perform comprehensive standard echocardiographic exam with assessment of left ventricle diastolic function and right ventricle structure and function¹¹⁻¹³. Echocardiographic clues to differentiate athlete's heart from cardiomyopathies are symmetrical enlargement and normal function of both left and right ventricle in healthy athletes.

Examples of some structural heart diseases which can be missed if screening of athlete if done without echocardiography are presented in Figures 1-4.

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Sažetak

Ehokardiografija u prevenciji iznenadne srčane smrti kod sportista

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Iznenadna srčana smrt (ISS) kod sportiste je uvek užasavajuća. Izuzetno je važno bolje razumeti uzroke ISS kod sportista i razviti najbolje strategije za prevenciju. Echokardiografija je neinvazivna tehnika prvog izbora u identifikaciji strukturne bolesti srca i takođe nezamenljiva u razlikovanju sportskog srca i kardiomiopatije. Zbog svega navedenog ehokardiografija je važna u prevenciji iznenadne srčane smrti tokom sportskih aktivnosti.

Ključne reči: iznenadna srčana smrt, sport, ehokardiografija

Sport and recreation after revascularization, pacemakers implantation or valve replacement: Insights and future perspectives

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Abstract

In the last few years, numerous recommendations of the European Association of Cardiologists and guides of the European Association for Preventive Cardiology - Sports Cardiology section and Secondary prevention/Cardiac rehabilitation section pointed the importance and positive effects of physical activity on functional capacity improvement, reduction of mortality and reduction of re-hospitalization rates. Physical activity and playing sports are recommended for individuals in accordance with personal affinities, age, comorbidities, cardiovascular risk factors, and for cardiology patients after prior evaluation and classification of the underlying disease and associated risks. Sports cardiology is a field that is constantly developing. Till today, there are no unique registries or documents with unique recommendations for patients after revascularization, after the implantation of a pacemaker and replacement of valves. We analyze the available data from the literature, recommendations and guides, the basic algorithms for sports and recreation of these patients and highlight the necessity and importance of future research in the field.

Key words

sports and recreation, myocardial revascularization, valve replacement

Introduction

We are witnessing the time when physical activity and sports activities are recommended to all individuals in accordance to personal affinities, age, comorbidities, and for all cardiac patients with prior evaluation and classification of the underlying disease and associated risks.

In the last few years, numerous recommendations of the European Society of Cardiology (ESC) and position papers of the European Association for Preventive Cardiology (EAPC), Sports cardiology and Secondary prevention/cardiac rehabilitation sections, indicate the importance and positive effect of physical activity. Generally, higher levels of physical activities and fitness are associated with lower all-cause mortality, lower rates of cardiovascular diseases, and lower prevalence of several known malignancies¹⁻⁶.

Despite the substantial health benefits provided by regular physical activities, intense exercise may paradoxically act as a trigger for life-threatening conditions¹. Sports cardiology is a field that is constantly evolving, there are no unique registries or documents that would indicate exact recommendations for individuals after coronary artery revascularization, after pacemaker implantation and valve replacement, we aimed to review the available recommendations and literature and high-

light the necessity and the importance of future research in this area.

Cardiovascular pre-participation screening in athletes to detect the diseases lies outside the scope of this article and is discussed elsewhere¹.

Athletes: Competitive and Recreational

The ESC defines an athlete as 'an individual of young or adult age, either amateur or professional, who is engaged in regular exercise training and participates in official sports competition'⁷. A recreational athlete engages in sports for pleasure and leisure-time activity, whereas a competitive athlete is highly trained with a greater emphasis on performance and winning (*elite* or *competitive* athletes). Nevertheless, sporting discipline is in relation to the predominant component (skill, power, mixed and endurance) and intensity of exercise. Intensity of exercise must be individualized after maximal exercise testing, field testing and/or after muscular strength testing¹. Thus, it will be of great importance for physician to indicate the type of sport, frequency and duration of exercise and intensity to provide the advice and make shared decision with patients, especially after revascularization, pacemaker implantation or after valve replacement.



Figure 1. Sporting discipline in relation to the predominant component and intensity of exercise (Adopted from ESC – EAPC, see reference 1).

Sport and recreation in patients after myocardial revascularization

The major cause of myocardial ischemia in subjects >35 years of age, including athletes, is coronary artery disease⁸. Major cardiovascular risk factors, in addition to age and sex are family history of coronary artery disease, hypercholesterolemia, hypertension, diabetes mellitus and smoking, particularly if combined². Coronary artery disease in subjects below 35 years is rare (most often caused by familial hypercholesterolemia). Physical inactivity is an additional cardiovascular risk factor, and conversely, regular physical training reduces the risk of accelerated atherosclerosis, as well as the risk of sudden cardiac death or arrest during vigorous exertion⁹.

Coronary artery disease includes the entire spectrum of acute and chronic clinical syndromes caused by myocardial ischemia in the field of obstructive or non-obstructive atherosclerotic disease of the epicardial coronary arteries. From a clinical point of view, it is not a simple and homogeneous group, but is expressed by a series of subgroups in a variety of clinical forms that can proceed not only typically, but also atypically, with different levels of risk and complications, often unpredictable in course and prognosis. Patients with established atherosclerotic cardiovascular disease require timely clinical monitoring with risk stratification and treatment to stop or delay the further progression of disease, preserve quality of life, maintain or improve functional capacity and prevent the occurrence of recurrent events, which is why prevention programs in highly specialized centers are recommended.

The ESC Guidelines on CVD prevention in 2021² gave the stepwise approach for prevention. All patients with established atherosclerotic cardiovascular diseases are recommended to stop smoking, adopt a healthy lifestyle

and control all risk factors in Step 1. Further intensification of therapy to lower therapeutic targets is defined in Step 2 (depending on residual risk, comorbidity, lifetime risk, benefit from therapy, presence of frailty, and patient preference).

In general population, physical activity is recommended to everybody - adults of all age groups are recommended to strive for moderate-intensity physical activity for 150 to 300 minutes per week or 75-100 minutes per week of intense aerobic physical activity or their combinations in order to reduce all-cause mortality and morbidity, or in some cases, to the extent that their abilities and their health condition.

In athletes, the EAPC position paper from 2019⁶ and ESC recommendations 2020¹ singled out a group of patients with chronic coronary syndromes:

- all patients with stable angina
 - asymptomatic and symptomatic persons within one year after an acute coronary syndrome
 - persons who recently underwent revascularization
 - asymptomatic and symptomatic persons more than one year after the initial diagnosis or revascularization.
- Inclusion in intensive activities and participation in competitive sports in these individuals depend on numerous factors among which are: the type of competitive sport, fitness level of the patient, cardiovascular risk profile, presence of ischemia and arrhythmias indicated by physical activity, or evidence of myocardial dysfunction. All these factors may be determined by: assessment of previous history of the disease, testing with physical load (cardiopulmonary exercise testing) or functional imaging methods and echocardiographic examination. Guidelines suggests that asymptomatic persons with normal tests and preserved left ventricular systolic function belong to the category with a *low risk* for the occurrence of adverse events induced by myocardial ischemia, and therefore can be involved in competitive sports on an individual level. There are no restrictions in low-risk patients for skills sports regardless of age (Figure 1).

Some restrictions may apply for high-intensity power, mixed, and endurance sports (Figure 1) and for older patients (>60 years old) with chronic coronary syndromes - age is an additional, strong predictor of adverse events during exercise. Individuals with high-risk coronary features may gradually return to sport 3–6 months after successful revascularization pending a normal maximal exercise or functional imaging test.

When ischaemia cannot be treated despite adequate therapy, including revascularization, the individual should be restricted from competitive sports, with the possible exception of individually recommended low-intensity skill sports. Such individuals may engage in regular recreational exercise of low and moderate intensity provided risk factors and symptoms are treated adequately and there is regular clinical surveillance (Figure 2). These individuals may also participate in leisure sports, 2–3 times/week, in selected cases, if the intended activity is below (around 10 beats) the ischemic threshold and below the level of arrhythmias.

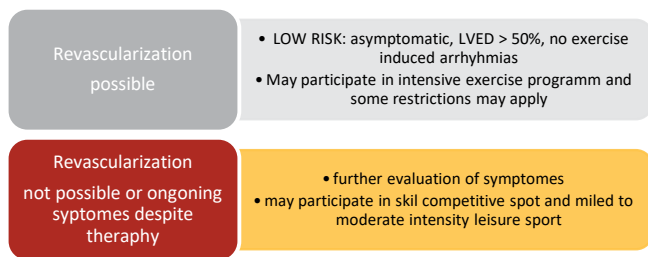


Figure 2. Clinical evaluation and recommendation in ASCVD (adopted from ESC, reference 1)

Secondary prevention after revascularization: Return to sport and recreation

Secondary prevention through comprehensive cardiac rehabilitation (CR) has been recognized as the most cost-effective to ensure favorable outcomes across a wide spectrum of cardiovascular disease, reducing cardiovascular mortality, morbidity and disability, and to increase quality of life. The delivery of a comprehensive and ‘modern’ cardiac rehabilitation program is mandatory both in the residential and the out-patient setting to ensure expected outcomes.

Individuals who have experienced cardiac surgery, or percutaneous intervention should be referred to an early exercise-based CR program, soon after the discharge, for 8–12 weeks after the cardiac event¹¹. Several controlled cohort studies and meta-analyses have found a survival benefit for patients receiving cardiac rehabilitation after acute event compared with no cardiac rehabilitation (26% reduction of cardiac mortality, 18% recurrent hospitalization), even in the modern era of early revascularization and statins¹².

Campos et al recently analyze the effects of exercise-based cardiac rehabilitation on physical performance after myocardial revascularization (coronary artery bypass grafting and percutaneous coronary intervention)¹³. Their systematic review and meta-analysis indicated that exercise-based CR increases physical performance after myocardial revascularization with an emphasize that aerobic and combined training lasting at least 8–12 weeks might be more effective in improving physical performance. Every week that exercise is delayed requires an additional month of exercise to accomplish the same level of benefit¹⁴.

Exercising individuals with coronary artery disease may start performing low- to moderate-intensity recreational sporting activities in parallel with participation in the structured progressive exercise program. All types of sports activities may be considered, at an appropriate intensity level; however, careful attention should be paid to the development of new symptoms. In general, structured outpatient exercise program, for 3–6 months, are required to achieve the appropriate level of activity for sports participation.

In competitive athletes, an echocardiogram, maximal exercise test with 12-lead ECG recording or cardiopulmonary exercise (CPET) test is recommended for risk stratification before return to sports. CPET specifically adds information on aerobic and anaerobic thresholds,

guiding exercise intensity prescription and progression **In recreational athletes** (and leisure-time activity), similar principles apply regarding risk stratification. A symptom-limited/maximal exercise test or CPET should precede the return to sports. If aerobic exercise is not tolerated, predominantly strength-related sports with a small amount of muscular work are recommended.

Sport and recreation after device implantation

Currently, millions of people with cardiac implantable electronic device live in Europe and hundreds of thousands join them every year. According to a 2017 report of the European Heart Rhythm Association, a total of 547 586 pacemakers, 105 730 implantable cardioverter-defibrillators (ICDs), and 87 654 cardiac resynchronization therapy devices were implanted in the ESC area in 2016^{11,15,16}.

Pacemakers (PM) are common and individuals with PM have less severe disease and comorbidities than patients with an ICD. For that reason, patients with a PM may participate in competitive or recreational sports in the absence of structural or other heart disease for which exercise may be prohibited as recommended in recent guidelines¹. It is of great importance to avoid sport activities within first weeks after device implantation (eg. strong upper extremity movements might increase risk of lead dislocation). Late lead damage due to subclavian crush (with insulation or conductor failure) can be seen in sports with pronounced arm movements (such as volleyball, basketball, tennis, golf, climbing etc). In these individuals, implantation on the contralateral side of the dominant arm, fixation within the pocket, or submuscular placement may improve durability of the system. Exercise testing and/or Holter monitoring during sports may improve individualized programming of the upper sensor and the tracking rate and exclude inappropriate rate acceleration in other circumstances (e.g. horse riding)^{1,17}.

Implantable cardioverter defibrillators

The burden of sudden cardiac death in the young is disproportionately larger because of their greater life expectancy and the tragic effect on families and communities. Since 1980, the ICD is proven to be effective in preventing sudden cardiac death in patients of all ages, including children and adolescents, with cardiac disease at high risk of ventricular arrhythmia^{18–20} and for patients with risk factors, ICDs are more cost-effective for the young recipients because of the greater life expectancy²¹. However, prior recommendations disqualified young patients with ICDs from competitive and high-intensity sports except those with low cardiovascular demand, such as billiard, bowling, or golf.

In the study of Saarel et al, shocks for ventricular arrhythmias occurred during sports, but all were successful at termination of arrhythmia without harm. Authors showed that many young athletes with ICDs could participate in competitive and high-intensity sports with-

out failure to terminate arrhythmias or injury, despite the shocks, confirming results of a smaller single-center registry of 21 young people^{22,18}. The rate of appropriate shocks during sports was low—1.5 per hundred person-years, and of the total shocks received, less than one-quarter occurred during sports. This finding suggested that restriction from the activity would not have a large impact on the overall burden of treated arrhythmias. Only 4 athletes received appropriate ICD shocks during sports, precluding the identification of meaningful and statistically significant predictors of risk. Although hours spent in competition or practice were greater for the 4 athletes who received shocks during sports, there was a wide variation; whether longer hours spent in competition or practice significantly increase the likelihood of appropriate shock during sports cannot be determined from this study. All of the athletes who received shocks (appropriate or inappropriate) during sports were prescribed β -blockers. It remains unclear whether they were adherent to prescribed therapy.

This large multinational ICD Sport Safety Registry on 440 athletes and additional analysis in 82 non-professional recreational athletes pointed out that shared decision making is appropriate when deciding whether or not to continue sports in ICD receivers.

In some patients, sport might be contraindicated, predominantly due to progression of underlying disease (eg arrhythmogenic cardiomyopathy). In case of inappropriate shocks, sinus tachycardia or supraventricular arrhythmias may occur due to underlying disease.

Further, in some cases, participation in moderate and high intensity exercise should be discouraged, as in ICD shocks in general (eg 30 to 40% of athletes who experienced shocks in ICD registry stopped participation). In case of moto sports, diving, cycling loose of focus could cause harm to a third party or athlete and informed decision making is needed to reevaluate all options.

For all patients with cardiac devices (PM, cardiac resynchronization therapy, and ICD), sports activities associated with a risk of chest trauma should be avoided.

Exercise-based cardiac rehabilitation after ICD implantation

It was recently proposed that cardiac rehabilitation for all patients with cardiac implantable electronic device can be a unique opportunity to optimize medical treatment, to increase exercise capacity, and to improve their clinical condition and to supervise the correct functioning of the device^{10,15}.

This is not only related to the underlying heart disease but also to specific issues, such as psychological adaptation to living with an implanted device and, in ICD patients, the risk of arrhythmia, syncope, and sudden cardiac death.

Clinical and laboratory evaluation is the first step in evaluating ICD patients in the setting of comprehensive CR. Minimally, history and clinical examination, device interrogation, chest X-ray, echocardiogram, CPET, and Holter should be performed before starting exercise-based CR.

As the basis for exercise advice and prescription, a symptom-limited exercise test, preferably CPET, is mandatory. Endurance training intensity zones can be determined on the ventilatory thresholds, peak VO₂, or, in absence of a CPET, on heart rate and heart rate reserve. Exercise prescription may include both endurance and resistance training. Endurance training may use continuous and/or interval or intermittent training models, 3–5 days/week, during 30–60 min, associated with dynamic exercises. For continuous aerobic training, prescription may be similar to that used in heart failure patients, keeping in mind upper limits of the device. In case of chronotropic incompetence, rate-adaptive pacing should be programmed. Resistance training sessions (2–3 sessions/week) may be tailored according to a preliminary evaluation of strength, but special attention is required with shoulder movement in order to avoid important strain in the side of implant, particularly in the early phase after device placement.

Implantable cardioverter-defibrillator patients, following exercise-based CR, achieved a better exercise capacity. The impact on all-cause mortality, serious adverse events, and health-related QoL remained unclear¹⁵.

ICD patients, however, still have low referral rates and poor adherence to CR (due to the high incidence of anxiety (18–38%) and depression (28–32%) and to the fear of ICD discharges,²³ highlighting the importance of psychoeducational component of CR^{15,16}).

Future research and registries should focus on the sport and recreation in real life ICD recipients.

Sports and recreation after valve replacement

Valvular heart disease is usually an age-related degenerative process, predominantly affecting individuals in their fifth decade and onwards. There is a pertinent population of younger individuals with congenital valvular heart disease. Exercise recommendation in individuals with valvular heart in 2020 ESC Guidelines on sport cardiology and exercise in patients included general principles in assessment and risk stratification of those individuals prior to leisure exercise or competitive sports¹. Till today, little is known on sports and recreation after valve replacement. In 2021, a position statement of the Sport Cardiology Section of the European Association of Preventive Cardiology on Athletes with valvular heart disease and competitive sport added a valuable data²⁴.

Although patients improve clinically after heart valve replacement, the long-term mortality is higher than in a healthy control population. Patients with normal haemodynamic patterns at rest may have abnormal values under physical stress. A proportion of individuals warranting surgical correction for mitral regurgitation may undergo valve repair instead of replacement. There are no data on the natural history of a valve replacement or repair in individuals who exercise intensively, therefore the current consensus recommendations are relatively conservative. Therefore, exercise testing should be performed up to the intensity consistent with that of the

sport the athlete wishes to pursue. Given that artificial valves are associated with some flow limitation, it is recommended that athletes who have had valve replacements have the same exercise limitations as asymptomatic athletes with moderate native valve disease provided ventricular function is preserved and pulmonary artery pressure is within normal limits. Anticoagulation is mandatory for mechanical prosthesis and those with atrial fibrillation which further limits their choice of competitive sports. As with native valves, athletes with prosthetic valves or valve repair should undergo annual re-evaluation^{24,25}

Blank et al recently conducted retrospective cohort the study on one hundred twenty-one patients aged 18 to 65 years who underwent a first-time mitral valve replacement for primary mitral regurgitation in a tertiary care center with an aim to examine the impact of sports on outcomes after mitral valve replacement in a 34 month follow up²⁶. Participation in sports was quantified by the number of hours per week during the past 6 months, classified according to the Mitchell classification and assessed with the International Physical Activity Questionnaire (IPAQ) short form. Fifty-six patients participated in sports regularly (median of 3 h/week), 17% patients reached the primary composite endpoint with no correlation with participation in sports, IPAQ categories in any of the Mitchell classification subgroups and a high level of participation in sports ≥ 6 hours. According to these results, sports seem to be unrelated to the worst outcome after mitral valve replacement.

Exercise- based cardiac rehabilitation after valve replacement

Cardiac rehabilitation programmes should be available for all patients undergoing valve surgery, including those after minimally invasive cardiothoracic surgery or aortic valve replacement in order to improve short-term physical capacity. Core Components of cardiac rehabilitation following valve heart surgery include: patient assessment (wound healing, comorbidities, complication and disabilities; special focus on perioperative congestive heart failure, atrial fibrillation, pleural and pericardial effusion, and diaphragmatic paralysis etc), evaluation and appropriate treatment of postoperative pain; echocardiography (pericardial effusion, prosthetic function and disease at other valve sites); exercise capacity to guide exercise prescription - symptom limited exercise stress test as soon as possible and a maximal exercise test about four weeks after surgery¹⁰.

Exercise training should be individually tailored according to the clinical condition, baseline exercise capacity, ventricular function and different valve surgery. After mitral valve replacement exercise tolerance is much lower than that after aortic valve replacement, particularly if there is residual pulmonary hypertension. Upper-body training can begin when the chest is stable, i.e. usually after six weeks.

The actual exercise prescription for patients with recent valve replacement or repair is the same used for CABG surgery patients. The physical activity of these patients

may have been more restricted for an extended period of time prior to the surgical intervention. Early after valvular surgery, the spontaneous exercise capacity improvement is weak and consequently, the resulting low functional capacity may require these patients to initiate with exercise in a conservative fashion. Exercise intensities may vary according to the patient's needs using interval training such as in heart failure patients or a steady state modus in the light or light to moderate domains and it should be supervised by the target heart rate and the rate of perceived exertion. Exercise-based cardiac rehabilitation after heart valve surgery positively impacts VO₂ peak after 4 months, but recently no long-term benefit was found after 12 months²⁷. Future research should focus on defining the risks of returning to exercise following valvular intervention.

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Sažetak

Sport i rekreacija posle revaskularizacije, implantacije pejsmejkera ili zamene valvule: Pregled sadašnjih saznanja i perspektive

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U poslednjih nekoliko godina brojne preporuke Evropskog udruženja kardiologa i vodiči Evropske asocijacije za preventivnu kardiologiju - Sportsku kardiologiju i Sekundarnu prevenciju/kardiološku rehabilitaciju ukazuju na značaj i pozitivan efekat fizičke aktivnosti na poboljšanje funkcionalnog kapaciteta, redukciju mortaliteta i redukciju stope rehospitalizacije. Fizička aktivnost i bavljenje sportom preporučuju se pojedincima u skladu sa ličnim afinitetima, godinama života, komorbiditetima, prisutnim faktorima rizika, a kardiološkim pacijentima, uz prethodnu evaluaciju i klasifikaciju osnovne bolesti i pridruženih rizika.

S obzirom da je sportska kardiologija oblast koja se nesporeno razvija, i da ne postoje jedinstveni registri ni dokumenta koja bi ukazivala na jedinstvene preporuke kod osoba koje su podvrgnute revaskularizaciji, nakon ugradnje pejsmejkera i zamene valvula imali smo za cilj da kroz dostupne podatke iz literature i preporuka i vodiča ukažemo na osnovene algoritme za sport i rekreaciju ovih bolesnika i istaknemo neophodnost i značaj budućeg istraživanja u oblasti.

Ključne reči: sport i rekreacija, revaskularizacija miokarda, veštačke valvule

SPONZORI SIMPOZIJUMA
UDRUŽENJE ZA SPORTSKU KARDIOLOGIJU SRBIJE

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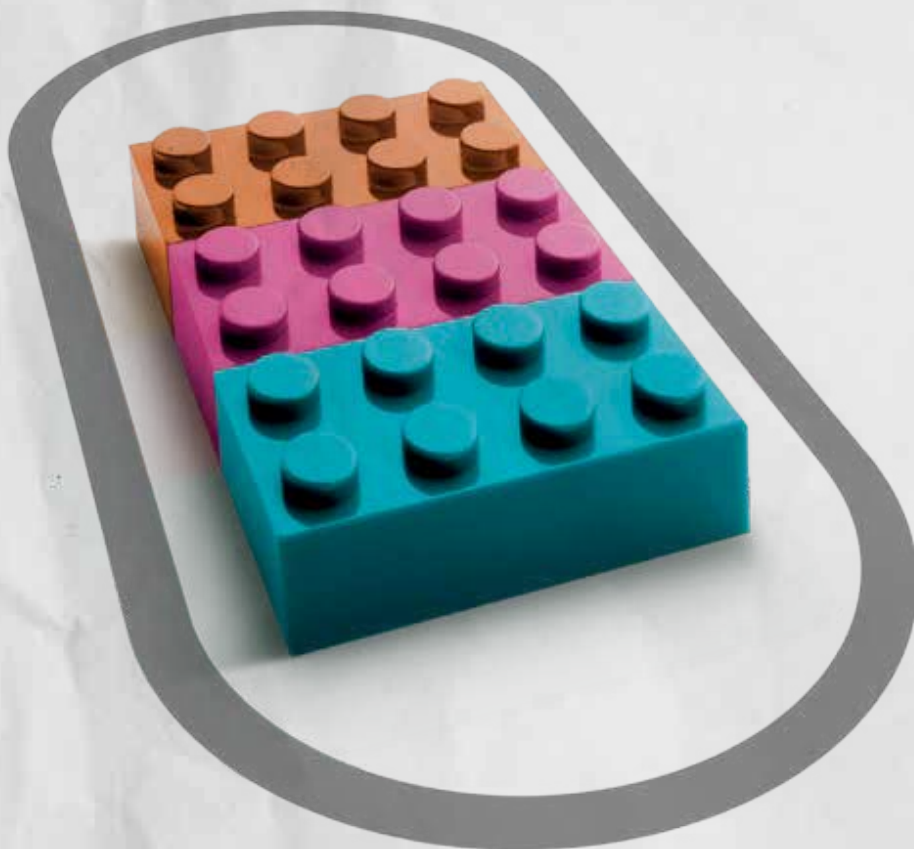
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