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Pathophysiological aspects and therapeutic effects of permanent cardiac pacing

Obesity and hypercholesterolemia in open urban population (simultaneous epidemiological study)

Assessment of mechanical dyssynchrony during patient's selection for cardiac resynchronization therapy by speckle tracking echocardiography

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Contents

Editor's Welcome

Dear colleagues!

In the 24th issue of the International Heart and Vascular Disease Journal, there are the leading article, original, review articles and case report.

The leading article section presents literature review on permanent cardiac pacing that is an issue of modern cardiology. It has been shown that even the use of "physiological" cardiac pacing modes does not always lead to adequate electromechanical conjugation and maximum restoration of the heart; therefore, not all successful heart rhythm and conduction disturbances corrections with PM implantation are associated with life quality and long-term prognosis improvement.

Three articles are published in the "Original articles" section. Two studies are from Tyumen Cardiology Research Center on the risk factors prevalence in population. The results of the first research showed that every second examined citizen has hypercholesterinemia and excessive body mass /obesity that correlates with age. The second study showed that men with stress at work have the highest stress level, which determines the focus of preventive programs. The third original article came from Egypt and is dedicated to the effects of angiotensin receptor-neprilysin inhibitor on exercise capacity in patients with heart failure with reduced ejection fraction. Author concludes that the studied combination can be included into complex chronic heart failure treatment.

The "Review article" section presents the analysis of mechanical dyssynchrony of myocardium assessed with speckle tracking echocardiography. Authors analyzed forty-three scientific publications available in the PubMed search system from 2001 to 2019 years. Interventricular dyssynchrony is more common in patients with left bundle branch block. Intraventricular dyssynchrony is associated with the change of LV segments stimulation sequence.

Traditional "Case report" section includes a report from Uzbekistan that may be of special interest to practicing cardiologists. Authors describe rarely used and effective method of ablating accessory pathway. The patient was 12 years-old girl with Wolf-Parkinson-White syndrome. There was no effect after radiofrequency ablation near the tricuspid annulus then tachycardia was eliminated from the non-coronary cusp. Complains such as palpitations and weakness disappeared after the procedure. This method of ablation is used when the ablation through the tricuspid annulus failed.

We invite everybody to collaborate with the journal. We are waiting for your original papers, review articles, discussions, and opinions about problems, treatment and prophylaxis recommendations.

Rafael G. Oganov
Editor-in-Chief
President of the "Cardioprogress" Foundation

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LEADING ARTICLE

Pathophysiological aspects and therapeutic effects of permanent cardiac pacing

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Abstract. This review article presents a critical analysis of recent clinical trials dedicated to the assessment of pathophysiological mechanisms of modern pacemakers (PM) cardiohemodynamic effects. It has been shown that even the use of "physiological" cardiac pacing modes does not always lead to adequate electromechanical conjugation and maximum restoration of the heart; therefore, not all successful heart rhythm and conduction disturbances corrections with PM implantation are associated with life quality and long-term prognosis improvement. The article highlights various therapeutic effects of cardiac pacing and its pathophysiological mechanisms in various groups of patients with implantable PM. The analysis will determine the course of future clinical studies in order to improve the effectiveness of this method.

Key words: pacemaker, cardiac pacing, cardiohemodynamics, cardiac resynchronization therapy.

Conflict of interests: none declared.

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Introduction

Cardiac pacing was developed over half a century ago and introduced into practice as one of the most effective methods of arrhythmias and conduction impairments treatment that significantly changed the lives of the patients [1–3]. Abound 700.000 pacemakers (PM) per year are implanted worldwide [4]. The progress in PM development contributed to the expansion of its use not only in patients with classical electrocardiographic indications, but also due to its therapeutic effects of various pacing modes [5–8].

Large randomized clinical trials confirmed that optimizing of PM's cardiohemodynamic effects improved life quality and survival of the patients [9–12]. However, despite successful attempts to improve the quality of PMs, it has not been possible to compensate electrophysiological and mechanical functions of the heart yet [13, 14]. It should be noted that PMs and cardioverter defibrillators are implanted into the right ventricle in the majority of cases as well as biventricular pacing in patients with chronic heart failure (CHF) [15– 17]. Therefore, the study of cardiohemodynamic and therapeutic effects of permanent cardiac pacing and its effect on the long-term prognosis in patients with implantable antiarrhythmic devices remains important.

Pathophysiological mechanisms of cardiohemodynamic impairments during various cardiac pacing modes.

It should be noted that cardiohemodynamic effects and long-term prognosis of permanent ventricular pacing differ significantly in different categories of patients, that is associated not only with patient-dependent factors, but also with various pathophysiological effects of right ventricular pacing [13, 18–20]. This indicates that the choice of the PM type, the stimulated chamber of the heart and the PM mode should strictly correspond to heart rhythm disturbances and functional needs of the patient [5–7, 21]. The concept of the "physiological" cardiac pacing includes not only atrioventricular (AV) synchronization and adaptation of artificial rhythm frequency to functional status of the patient, but also optimizing ventricular systolic and diastolic electromechanical functions [1, 22, 23].

The role of chronotropic incompetence of implanted pacemaker and possibilities of hemodynamic effect optimization.

Frequency-adaptive pacemakers are the solution of this problem and are widely used in single and dual chamber pacing [3, 6]. It has been shown that patients with VVIR stimulation had 20-30% higher exercise tolerance compared with patients with VVI stimulation [2, 14]. Moreover, patients with VVIR and DDI stimulation after surgery due to AV blockade did not differ by the frequency of myocardial infarction, stroke, atrial fibrillation, and heart failure [12]. This means that frequency-adaptive pacemakers have more effective hemodynamic support of physical activity compared with a dual chamber atrioventricular fixed-rate pacing even with single-chamber ventricular pacing [1, 6, 7].

Moreover, hemodynamic effectiveness of various cardiac pacing modes depends on the severity of systolic and/or diastolic ventricular dysfunction. This is essential in patients with a fixed-rate cardiac pacing and left ventricular (LV) dysfunction [10, 20, 24]. The study of chronic inotropic regulation of the contractile function of the heart optimization in patients with AAI and VVI stimulation using the frequency of electric impulses ranged from 40 to 100 imp/min with a discrete value of 5 imp/min revealed 2 types of cardiohemodynamic parameters response [25]. Type I included significant increase in stroke and cardiac indices (SI, CI) as pacing frequency decreased from the baseline (60-65 imp / min) to 50 imp / min (average 56 ± 5 imp / min). On the contrary, type II included systolic indices improvement with increased pacing frequency above the baseline to 75-90 imp / min (78 ± 6 imp / min), mainly due to SI increase.

It is also remarkable that type I responce was observed mostly in patients with preserved systolic function and AAI stimulation, and type II was – in patients with more severe CHF and VVI stimulation. Thus, type I cardiohemodynamic response indicates an inadequately frequent cardiac pacing that leads to "pacemaker syndrome", and type II indicates not only the presence of myocardial insufficiency, but also "chronotropic incompetence" with a baseline pacing frequency — 60-65 imp/min.

Maintenance of sinus atrial rhythm and hemodynamic role of atrial systole in patients with ventricular pacing.

A comparative study of cardiohemodynamics in patients with VVI stimulation, especially with fixed-rate pacing, revealed significant differences depending on the spontaneous atrial rhythm [12]. Hemodynamic role of atrial rhythm was assessed in the following groups of patients with VVI stimulation: 1st group — spontaneous sinus atrial rhythm with sinus node normal chronotropic function; 2nd group – sick sinus syndrome with severe bradycardia; 3rd group - persistent atrial fibrillation; 4th group - pacemaker retrograde atrial depolarization. It was revealed that patients from groups I and II had significantly higher ($p < 0.05$) ejection fraction (EF) of LV, stroke index (SI), CI and maximum anteroposterior myocardial fiber shortening compared with groups III and IV. Systolic blood pressure (BP) levels were significantly lower during pacemaker retrograde atrial depolarization compared with 1st and 2nd groups- 17.2 and 14.9%, respectively.

It has been shown that patients with atrial fibrillation and atrial sinus rhythm have LV systolic function deterioration during VVI stimulation because of ventricles diastolic filling dysfunction due to incomplete emptying of the atria and AV dissociation [1, 13, 15]. Pacemaker retrograde atrial depolarization causes pathological sequence of excitation and contraction of atria and ventricles that leads to AV valvular blood regurgitation, decreased cardiac output and systolic blood pressure [18, 26].

The role of pacemaker lead position on the parameters of cardiohemodynamics.

The results of clinical studies on the optimal stimulating electrode ventricle position in order to ensure the maximum hemodynamic effect differ significantly. Punjabi H.A. et al. (2014) study showed that the incidence of tricuspid regurgitation (TR) during two-year follow-up was 21% in patients with septal right ventricular position versus 68% apical right ventricular position ($p = 0.07$) [27]. In other study [26] the development of moderate and severe TR in patients with apical and septal electrode right ventricular positions was observed in 4.8% and 10.5% of cases, respectively, and in 8.3% of patients with left ventricular position. This means that implantation of the electrode in the LV does not decrease the frequency of TR compared to right ventricular implantation [24, 28].

It has been established that septal right ventricular electrode position causes narrow QRS complexes [16, 29]. This is associated with shorter period of ventricular activation due to better myocardial contractility and hemodynamic parameters. In addition, septal electrode position did not cause complications, such as electrode dislocation, pericardial perforation, pericarditis development and muscles contractions [19].

Important hemodynamic and prognostic value of pacemaker electrode position has been demonstrated in patients with cardiac resynchronization therapy (CRT). Dong Y.-X, et al. (2012) compared hemodynamic and clinical outcomes of CRT depending on left ventricular electrode position in patients with DDDR and DDD stimulation modes [28]. It has been shown that patients with anterior and posterolateral electrode positions had higher LV EF, and lower LV local contractility violation index and pulmonary artery systolic pressure compared with posterior and anterior electrode positions. During over 4 years of follow-up, functional class of CHF and mitral regurgitation decreased, and cumulative survival rate was 72% versus 48% ($p = 0.003$).

It is also remarkable that transvenous cardiac pacing made the apical position of the right ventricle more preferable due to easy electrode placement, contact stability, cardiac pacing reliability and electrode design [7, 14]. Guidelines on cardiac pacing and cardiac resynchronization therapy (2013) of the European Society of Cardiology and the European Heart Rhythm Association (ESC / EHRA) emphasize that implantation of the electrode in the right ventricular outflow tract and in the trunk of the His bundle is associated with high LV EF, especially in patients with baseline EF less than 45%, compared with apical position [6]. However, the results of the studies on exercise tolerance, the dynamics of heart failure functional class, quality of life and survival are still not conclusive.

The features of interventricular septum (IVS) movement in patients with ventricular pacing and its effect on cardiohemodynamics.

It has been shown that patients with apical right ventricular electrode position more frequently have pathological IVS movement compared with patients with septal electrode position [18, 20, 30]. This association is confirmed by abnormal IVS movement in patients with intermittent pacing and artificially stimulated ventricular complexes [18].

Sarvari S.I. et al. (2017) revealed abnormal movements ("flash") of IVS forward or backward from the ultrasonic probe in 77% of 74 patients with a fixed right ventricular pacing from the apical position [30]. At the same time, LVEF was lower and LV end systolic volume was higher compared with patients without abnormal LV movement. Moreover, patients with LV dysfunction had higher amplitude of abnormal IVS movement (5 ± 1 mm vs 2 ± 1 mm; $p < 0.001$) and lower amplitude of IVS systolic excursion (4 ± 1 mm vs 8 ± 2 mm; $p < 001$) compared with patients with normal LV function. It has been shown that the duration of artificial ventricular complex over 150 ms and the amplitude of septal "flush" over 3.5 mm with sensitivity and specificity predict the risk of LV dysfunction.

Patients with right ventricular pacing from the apical position had decreased IVS thickness during diastole after 12 and 24 months compared with preoperative values 15.3% (p=0.05) and 21.6% (p=0.008) on average, respectively [20]. Moreover, the IVS thickness to LV posterior wall thickness ratio during diastole also increased and was 12 months after — 1.22±0.03 (p<0.05), and 24 months after — 1.34±0.06. The frequency of detection and the severity of isolated IVS hypertrophy directly correlated with cumulative duration of right ventricular pacing.

The effect of the cumulative duration of ventricular pacing on cardiohemodynamics and prognosis

It has been established that the cumulative duration of the right ventricular pacing affects the long-term prognosis, primarily due to its negative cardiohemodynamic effects [13, 15, 20]. The duration of the right ventricular pacing depends on the ratio of the frequency of spontaneous and artificial heart rhythms and, therefore, the determination of the hemodynamically optimal low frequency of the artificial rhythm will contribute to the improvement of cardiovascular prognosis. It is also remarkable that the cumulative duration of ventricular pacing, that adversely affects cardiovascular prognosis, varies widely due to various cardiohemodynamic advantages and disadvantages of different pacing modes [18].

It has been shown that patients with VVIR stimulation with cumulative duration of right ventricular pacing over 40% of the time have significantly increased frequency of admissions due to heart failure decompensation compared with patients with cumulative duration less than 40% [11]. Moreover, the survival of patients with sick sinus syndrome and AAI and VVI stimulation did not differ significantly if the cumulative duration of isolated ventricular pacing was less than 40% of the time. Therefore, it is recommended to use DDDR stimulation especially in patients with permanent pacing.

The DAVID study (Dual Chamber and VVI Implantable Defibrillator) showed that patients with implanted cardioverter defibrillator due to LV systolic dysfunction with DDDR mode with base frequency of 70 impulses / min compared with VVI stimulation with frequency of 40 impulses / min had more frequent admissions and/or increased heart failure mortality [6]. Thus, despite AV synchronization maintenance during DDDR stimulation, the cumulative duration of ventricular pacing over 40% contributes to the deterioration of long-term prognosis.

However, Nielsen J.C. et al. (2011) study showed an upward trend in admission frequency due to heart failure decompensation during DDDR stimulation in patients with cumulative ventricular pacing over 80% of the time [31]. Thus, the cumulative duration of ventricular pacing is an independent predictor of adverse cardiovascular events.

Therapeutic effects of implantable pacemakers and its optimization by reprogramming pacing parameters

Controlled frequency-dependent hypotensive effect of cardiac pacing

Patients with implantable PMs usually refer to elderly population and often have arterial hypertension (AH) with very high cardiovascular risk, they require an adequate blood pressure correction [7]. It is also known that the development of complete AV blockade is often accompanied by isolated systolic hypertension, that significantly decreases after pacemaker implantation, sometimes up to "pacemaker syndrome" [13, 32, 33].

Mechanisms of cardiac pacing frequency-dependent hypotensive effect can include various physiological factors involved in the regulation of systemic blood pressure. They mainly include chrono-inotropic relations, for example, frequency-dependent changes of myocardial contractility (Frank-Starling law). In addition, there is a direct correlation between LV contractility and the level of aortic systolic blood pressure (Anrep effect). Baroreflex and humoral mechanisms for blood pressure lowering take place especially in patients with VVI-stimulation, that is associated with increased right atrium pressure and increased atrial natriuretic peptide secretion, that has vasoactive effect [34].

Over the last years, DDD type PMs with an algorithm providing hypertension control were widely used for the treatment of isolated systolic hypertension [9, 22]. The algorithm includes an alteration of 8-13 imposed QRS complexes series with shortened AV interval (20-80 ms) and 1-3 subsequent complexes with extended AV interval (100–180 ms). Neuzil P. et al. (2017) revealed systolic blood pressure decrease in patients with DDD stimulation with short AV interval, due to preload and SI decrease [33]. In this case, systolic BP decreased from 165 ± 10 mmHg to 157 ± 14 mmHg 3 months after and to 142 ± 14 mmHg 6 months after PM implantation. As a result, the number of antihypertensive medications decreases. However, Do D.H. et al. (2017), noted that the use of short AV intervals during DDD stimulation can lead to the development of heart failure, "pacemaker syndrome" and atrial fibrillation, as well as sympathetic hyperactivity [9].

Manisty C.H. et al. (2012) studied the causes of hypotensive effect in patients with biventricular stimulation by programming AV interval in the range from 40 to 120 ms [20]. The SI was determined using doppler echocardiography and blood pressure — using digital photoplethysmography. They showed that the shortening of the AV interval causes immediate increase of blood pressure and SI, however, blood pressure, unlike SI, reduces after a few seconds. According to the authors, blood pressure decreases due to compensatory vasodilation, not due to SI decrease.

To evaluate the frequency-dependent hypotensive effect, we reprogrammed the pulse frequency from 50 to 90 impulses/min with a discrete value of 5 impulses/min in patients with isolated systolic hypertension [32]. The duration of cardiac pacing at each stage of the rhythm frequency was 2–3 days. As the frequency of artificial rhythm increased, systolic blood pressure decreased in patients with AAI and VVI stimulation. At a frequency of 80 impulses/ min, systolic blood pressure decreased from 13.1 to 21.5% and 17.6% ($p < 0.01$) on average, diastolic blood pressure did not change significantly. The results might indicate the chronotropic "incompetence" of the artificial heart rhythm at a base pulse frequency of 60 impulses / min. The antihypertensive effect can be explained by SI decrease that ranged from 11.8 to 18.3% and was 14.5% ($p < 0.05$) on average, and total peripheral vascular resistance had tendency to increase within normal limits.

Frequency-dependent antianginal effect of cardiac pacing

It is known, that the majority of patients with implantable pacemakers suffer from coronary artery disease and had myocardial infarction and/or coronary artery revascularization [35, 36]. Therefore, the optimization of coronary flow reserve by choosing the optimal pacing mode has great prognostic value. Stress echocardiography is often used in order to assess coronary flow reserve in patients with implantable PMs and consists of programmed increase of the artificial rhythm frequency and the study of local LV contractility impairment [37]. Plonska-Gosciniak E. et al. (2008) showed high sensitivity (91%) and specificity (75%), as well as positive and negative predictive value (81% and 88%, respectively) of stress echocardiography in the diagnosis of hemodynamically significant coronary stenosis (more than 50%) in patients with AAI / DDD and VVI stimulation including patients taking beta-blockers [38]. At the same time, positive stress test was observed in 60% of all cases. The local LV contractility impairment index with positive stress test in patients with AAI / DDD stimulation significantly increased from 1.32 to 1.49 and in patients with VVI stimulation from 1.36 to 1.65.

It is also remarkable that frequency-dependent pacing in patients with high coronary flow reserve and implantable PMs is justified on the one hand, and on the other hand, there is a possibility of sensor-controlled tachycardia development [39]. Therefore, modern PMs with DDDR mode have multisensor system that is used to avoid false pacing responses such as unmotivated frequent artificial rhythm [5, 6]. It is also recommended to switch from DDDR mode to VVI mode or to program lower and upper limits of pacing frequency to simulate effective beta-adrenoblockage (for example, 50 and 100 imp/min, respectively).

Moreover, technical AV delay in patients with DDD/ DDDR stimulation, should be selected in order not compromise the hemodynamic benefit of atrial systole by extended AV interval on one hand, and, on the other hand, AV delay should not be short making it difficult to relax and fill the LV, and aggravate coronary perfusion [23, 31]. In this case, PMs with an algorithm that provides frequency-controlled AV delay can be used.

Ibrahim M. et al. (2013) showed that the implantation of DDD PM in patients with complete AV block can cause destabilization of coronary heart disease, that manifests as increased number of angina attacks [40]. This can be explained by 2–3 times increase of the initial heart rate frequency as a result of P-managed ventricular pacing. Authors propose to limit the upper-frequency of DDD / DDDR pacing in patients with angina pectoris and myocardial infarction.

It is also remarkable that PM implantation not only affects the parameters of cardiohemodynamics, but also increases the activity of plasma and tissue coagulation factors and suppresses endothelium vasomotor function that can aggravate cardiovascular prognosis [34].

Bifocal atrial ventricular pacing for the treatment of patients with hypertrophic obstructive cardiomyopathy (HOCM)

Over the last years, sequential atrial ventricular pacing with shortened AV delay has been an alternative to surgical treatment in patients with HOCM [8]. The change in the sequence of excitation and ventricle contraction leads to subaortic gradient decrease (up to 25%) due to regional IVS contractility decrease and, as a result, the extension of LV outflow tract. The delay of the anterior cusp of the mitral valve systolic movement and its amplitude decrease also contributes to it. It is very important to select the shortest AV delay, that ensures premature depolarization of the heart apex, and does not lead to cardiohemodynamics impairment- cardiac output and blood pressure decrease.

Randomized placebo-controlled studies confirm the decrease of systolic pressure gradient in the LV outflow tract, and show an improvement of symptoms and life quality in patients with HOCM [41]. However, it was not possible to detect significant effect of DDD / DDDR stimulation on the course of the disease, the frequency of sudden cardiac death, and physical activity. They also noted diastolic dysfunction aggravation and end-diastolic pressure in the LV increase.

Therefore, the European Society of Cardiology guidelines for the diagnosis and treatment of HCM recommend to use DDD stimulation with shortened AV delay for the treatment of patients with systolic LV pressure gradient over 50 mmHg, refractory to drug therapy, who are not candidates for surgical correction and alcohol septal ablation.

Thus, the variety of cardiac pacing modes used in clinical practice, on the one hand, provide the need for technical and methodological electrocardiotherapy improvement and, on the other hand, stimulate further large and observational clinical studies in order to study the physiological interaction between heart and pacemaker and expand the spectrum of the use of this method.

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Obesity and hypercholesterolemia in open urban population (simultaneous epidemiological study)

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Objective. *To study the prevalence of obesity and hypercholesterinemia in men of working age of open urban population in Tyumen.*

Materials and methods. *According to the results of simultaneous epidemiological study, we established the levels and prevalence of excessive body mass, abdominal obesity and hypercholesterinemia based on the representative sample of men of working age of moderately urbanized Siberian city (Tyumen).*

Results. *Body mass index, waist circumference and total cholesterol characteristics in population are shifted to the right within the normal distribution, which determines the high prevalence of overweight, abdominal obesity and total cholesterol in the open male population of moderately urbanized Siberian city.*

The prevalence of overweight in the male population aged 25–64 years standardized by age in Tyumen was 26%, the prevalence of abdominal obesity was 42.6%, and the prevalence of hypercholesterolemia was 42.7%. Men aged 25–64 years of open population of moderately urbanized Siberian city had increased overweight at the age of 35–44 years, hypercholesterolemia — 35–44 and 45–54 years, abdominal obesity — increased in three youngest age categories.

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Conclusion. *Thus, the results of obtained prevalence of obesity and hypercholesterinemia in various age groups of Tyumen are extremely unfavorable and should be used for primary preventive cardiovascular diseases programs in men of working age of Tyumen and other moderately urbanized Siberian cities.*

Key words: *epidemiological study, open population, men, body mass index, waist circumference, obesity, hypercholesterolemia.*

Introduction

Nowadays, the role of hypercholesterolemia (HC) in the development of chronic noncommunicable diseases, including coronary heart disease, has been proven. The level of lipids in the blood depends on age, gender, external and internal environment factors, for example, nutrition, physical activity, hormonal status and other factors. A number of studies have shown direct correlation between body weight and all-cause mortality. However, the analysis of forty cohort studies by A. Romero-Corral A. et al. showed the correlation between cardiovascular mortality and obesity with a body mass index over 35 kg/m^2, while obesity did not correlate with mortality rate [1].

Abdominal (central) type of obesity with the predominant fat deposition in the abdominal region is the most dangerous. The central, abdominal or visceral type of obesity, when white fat is predominantly located in the mesentery and omentum, is a predictor of diabetes mellitus (T2DM) development of cardiovascular disease (CVD) compared with other obesity types with another fat location and brown fat involvement [2]. Vague first described the concept of the leading role of visceral obesity in the development of impaired glucose tolerance, T2DM and atherosclerosis. Subsequently, the number of epidemiological studies demonstrated the association between visceral obesity, insulin resistance and hyperinsulinemia [3, 4, 5, 6].

Men more often have central ("android") type of obesity with relative body weight that is considered coronary heart disease (CHD) risk factor among men [7]. The results of Paris prospective study on the analyzing various metabolic syndrome (MS) components contribution to sudden death showed that only the presence of abdominal obesity is accompanied by significant risk increase, comparable to the syndrome itself [8].

The objective was to study the prevalence of obesity and hypercholesterinemia in men of working age of open urban population in Tyumen.

Materials and methods

Population-based screening was performed on unorganized population using selective method. Representative sample was formed from adult (25–64 years old) male population of the Central Administrative District of Tyumen city, stratified by age, who were selected using computer program with random number tables based on the electoral lists. Initially, the information was verified with the Tyumen Regional Address Office. The sample included 1000 people — 250 of each age group (25–34, 35–44, 45–54, 55–64 years), the response amounted to 85.0 %.

The study was conducted according to the standards of Good Clinical Practice and Helsinki Declaration principles. Study protocol was approved by the Ethics Committee. All participants signed up written informed consent.

Overweight was determined using traditional Quetelet index II or body mass index (BMI), calculated by the formula: weight (kg) / height^2 (m^2). People with BMI ⩾ 30.0 were considered overweight or obese. For the analysis of abdominal obesity (AO), we used metabolic syndrome criteria IDF (2005) — waist circumference (WC) ⩾ 94 cm for men of European race. The level of total cholesterol (TC) ⩾200 mg/dl (5.17 mmol/l) was considered as hypercholesterinemia (HC).

Statistical analysis was done using IBM SPSS 21.0 Statistics software and Microsoft Excel spreadsheets.

We checked the correspondence of results distribution in each experiment to normal distribution by analyzing standardized asymmetry and excess indicators, that should range from –2.0 to +2.0, and using Pearson criterion and Kolmogorov–Smirnov test. The distribution of quantitative indicators was estimated using percentiles. The analysis was performed separately by age categories 25–34, 35–44, 45–54, 55–64 years, and for general population — 25–64 years. The differences in the dynamics were estimated using paired t-test and analysis of variance on repeated measures. The value of $p < 0.05$ was considered statistically significant. Categorical variables results are presented as percentage (in percent) by four decades of life: 25–34, 35–44, 45–54, and 55–64 years. The comparative analysis with other epidemiological studies data was done by indicators standardization using direct method of standardization. When processing the data in order to standardize the indicators, the age structure from 25 to 64 years was used. Statistical significance of differences between groups was assessed using Chi-square Pearson test with Bonferroni correction.

Results

The analysis showed normal distribution of body mass index in men aged 25–64 years. The pattern of BMI distribution was confirmed by test results (p>0.05). BMI distribution extreme deciles were 22.5 and 34.0. The standardized mean BMI in the open male population aged 25–64 was 26.9 (table 1).

Table 1. **Body mass index in open urban male population aged 25–64 years**

Age, years	BMI						
	M	m	Percentile, %				
			10	25	50	75	90
25–34	25.2	±4.1	20.2	22.4	25.2	28.6	31.5
35–44	27.4***	±4.5	22.9	24.9	27.4	30.9	34.4
45–54	27.5	±4.4	23.1	25.1	27.5	31.1	34.8
55–64	27.9	±4.4	24.1	25.2	27.9	31.2	34.8
25–64	27.2	±4.4	22.5	24.4	21.2	30.5	34.0
ASV	26.9						

Comment: Significance of differences between two subsequent age groups is signed up with (*): *** p <0.001; ASV — age-standardized variable.

Statistically significant increase of mean BMI was observed only in men aged 35–44 years, then the indicator remained stable. Data on percentile distribution of BMI in all male age groups repeated the dynamics of mean values (table 1).

The analysis showed normal distribution of waist circumflex (WC) in men aged 25–64 years. The pattern of WC distribution was confirmed by test results (p> 0.05). WC distribution extreme deciles were 80 and 107 cm. The standardized indicators of WC percentile distribution were 80.4–105.4 cm. Age-standardized mean WC in 25–64 years male population was 92.0 cm.

Mean WC values directly correlated with age. The data on percentile WC male distribution in all age groups had the same dynamics as mean values. Mean waist circumference significantly increased with age, increasing by 1.1 times each analyzed age period (table 2). Waist circumference significantly correlated with abdominal (central) type of obesity increase in each subsequent age group.

The distribution of TC parameters was close to normal that was confirmed by the results of normality test (p> 0.05). 10 % and 90 % cut-off points for TC distribution in open male population aged 25–64 years were 4.0 and 6.5 mmol/L, respectively.

Table 2. **The levels of abdominal obesity — waist circumflex in open urban male population aged 25–64 years, cm**

Age, years	WC						
	M	m	Percentile, %				
			10	25	50	75	90
25–34	87.1	±9.9	74	79	87	93	100
35–44	92.5***	±9.7	80	86	92	99	106
45–54	95.4**	±9.2	85	89	94	102	108
55–64	97.2*	±9.2	88	91	97	104	112
25–64	93.4	±10.1	80	86	93	101	107
ASV	92.0						

Comment: Significance of differences between two subsequent age groups is signed up with (*): * p <0.05; ** p <0.01; *** p <0.001; ASV — age-standardized variable.

Mean total cholesterol among men aged 25–64 in Tyumen was 5.0 mmol/l (standardized indicator). The growth rate of this indicator was not the same in men of different age; the level of TC in the population increased by 1.1 times during all analyzed age period. Thus, average level of TC increased significantly with age from the third to fourth and from fourth to fifth decades of life, with lower rates in 25–34 and 35–44-years age categories (4.6 and 5.0 mmol/l, respectively) compared with general population indicator — 25–64 years (5.1 mmol/l). The values of 90 % cut-off points of TC distribution also had unidirectional age dynamics: the indicator tended to increase during all age range, significantly increasing from the third to the fourth and then from fourth to fifth decades of life (table 3).

Table 3. **The level of total cholesterol in open urban male population aged 25–64 years, mmol/l**

Age, years	TC						
	M	m	Percentile, %				
			10	25	50	75	90
25–34	4,6	±0,9	3,4	4,0	4,6	5,3	5,9
35–44	5,0***	±0,8	4,0	4,5	5,0	5,6	6,1
45–54	5,3***	±0,9	4,1	4,7	5,3	6,1	6,7
55–64	5,5	±0,9	4,4	4,9	5,5	6,2	6,7
25–64	5,1	±0,9	4,0	4,6	5,1	5,9	6,5
ASV	5,0						

Comment: Significance of differences between two subsequent age groups is signed up with (*): *** p <0.001; ASV — age-standardized variable.

Thus, population characteristics of body mass index, waist circumference, and total cholesterol in open male population of Tyumen city aged 25–64 years were shifted to the right within the normal distribution, which determined the high prevalence of BMI, AO, HC.

Overweight prevalence was 66.4 % in open male population and significantly increased in third and fourth decades of life (51.4 % — 73.7 %, p<0.001). The prevalence of general population BMI had significant

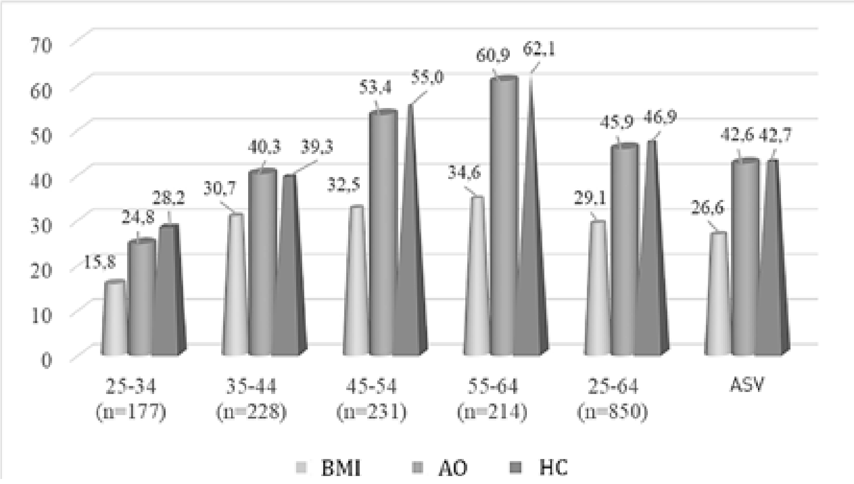

Figure 1. The prevalence of overweight, abdominal obesity, hypercholesterinemia in open urban population of moderately urbanized Siberian city.

differences compared with younger age category — 25–34 years (Figure 1).

Age-standardized prevalence of abdominal obesity rate in the 25–64 years old male population in Tyumen was 42.6%. An analysis AO prevalence results showed consistent age trend in three age categories. Thus, the indicator increased significantly with age, from the youngest age category, to the fifth decade of life (24.8% — 40.3% — 53.4%, p<0.01, respectively, in age groups 25–34, 35–44, 45–54 years), and increased during studied age period 25–64 years by 2.5 times (figure 1).

High prevalence of HC in open population was established in men aged 25–64 years in 42.7% of cases. The indicator increased significantly with age from third to fourth and from fourth to fifth decades of life (28.2% — 39.3%, p <0.05; 39.3% — 55.0%, p<0.001, respectively in age groups 35–44 and 45–54 years). Statistically significant differences in HC by general population indicator were observed in all age categories (figure 1).

Discussion

The results obtained in the open population of moderately urbanized Siberian city showed high average levels of body mass index in men of working age and high prevalence of HC and AO, with a significant increase of all indicators at young age. Unfavorable profile of somatic risk factors in population during simultaneous epidemiological study seems reasonable due to previously obtained data on representative sample of Tyumen men.

Basic epidemiological study in Tyumen has been conducted since the mid-90s. During the period from 1996 to 1997 we obtained data on the high prevalence of CVD risk factors among 25–64-year-old population. The results analysis showed that current situation in Tyumen was caused primarily by atherogenic nutrition, mainly among men of working age, that is associated with conventional behavioral and non-conventional CVD risk factors — chronic social stress factors, low public awareness of CVD risk factors, high prevalence of older people with low health self-esteem, who doubt preventive health measures and healthy lifestyle [9, 10, 11, 12, 13, 14].

According to this study, the prevalence of abdominal obesity in men aged 25–64 years according to different criteria of MS was 42.6%, that is almost the same as the prevalence of HC in population and was significantly higher than the frequency of obesity despite its localization. At the same time, taking into account the data on percentile distribution of BMI in the population, the prevalence of overweight in men of working age was very high and was aggravated by statistically significant increase at young age.

According to high prevalence of AO in the open population and the results of previous studies on the prevalence of MS in Tyumen population, men with abdominal obesity living in moderately urban Siberian city mostly have classic version of MS prevalence with high incidence of hyperglycemia and less often with low lipoproteins fractions, including TC, that has the worst prognosis for severe cardiovascular system diseases [9].

Conclusion

Thus, the results of obtained prevalence of obesity and hypercholesterinemia in various age groups of Tyumen are extremely unfavorable and should be used for primary preventive cardiovascular diseases programs in men of working age of Tyumen and other moderately urbanized Siberian cities. Preventive measures include the formation of model for public health regulating in working population, that involves the activities of the population itself, public institutions, and regional legislative and executive authorities with interaction between local governments departments [15].

Findings

1. Body mass index, waist circumference and total cholesterol characteristics in population are shifted to the right within the normal distribution, which determines the high prevalence of overweight, abdominal obesity and total cholesterol in the open male population of moderately urbanized Siberian city.

2. Age-standardized prevalence of BMI in the male population aged 25–64 years in Tyumen was 26%, the prevalence of AO — 42.6%, the prevalence of HC — 42.7%.

3. BMI prevalence increased in 35–44 years age category, HC — in 35–44 and 45–54 years, AO formed consistent age trend in three younger age categories in men aged 25–64 years in open population in moderately urbanized Siberian city.

Conflict of Interest: None declared.

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ORIGINAL ARTICLES

Effects of angiotensin receptor-neprilysin inhibitor on exercise capacity in patients with heart failure with reduced ejection fraction

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Abstract. *Angiotensin receptor-neprilysin inhibitor (sacubitril/valsartan) is well known to be superior over angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blockers (ARBs) in terms of reducing cardiovascular mortality in heart failure with reduced ejection fraction (HFrEF). However the impact of sacubitril/valsartan therapy on exercise capacity versus ACEI/ARBs for such patients is less tested.*

Methods. *This non randomized observational study enrolled 100 patients with HFrEF. All participants underwent two sets of cardiopulmonary exercise tests (CPET) at baseline and after 6 months of non interrupted sacubitril/valsartan therapy in addition to optimal anti failure medications. Bridging from ACEI/ARBs to ARNI was done at baseline according to guidelines.*

Results. *After 6 months, patients received sacubitril/valsartan had significant improvement in LVEF from 26 ± 5 to 29.6 ± 8%, peak oxygen consumption (VO_2) improved from 14.6 ± 4 to 17.3 ± 5.2 mL/kg/min, oxygen pulse increased from 11.6 ± 4 to 13.6 ± 5 mL/kg/min and $\Delta VO_2/\Delta Work$ increased from 9.1 ± 2.5 to 10.2 ± 1.6 mL/min/watt (p = 0.0001 for all). Conclusion: Sacubitril/valsartan therapy improved exercise tolerance, peak oxygen consumption and LVEF up to 6 months of follow-up.*

Keywords: *heart failure; sacubitril/valsartan; cardiopulmonary exercise test.*

Conflict of interests: none declared.

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Introduction

The **PARADIGM-HF** (Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) trial revealed that sacubitril/valsartan markedly decreased cardiovascular and al-cause mortality in patients with HFrEF compared with the angiotensin-converting enzyme inhibitor (ACEI) enalapril (1). Conversely, only few small trials assessed the improvement in exercise tolerance after initiation of sacubitril/valsartan in patients with HFrEF [2]. Recently in 2019, Palau et al conducted a pilot study demonstrated an increase in peak oxygen consumption (VO_2) after initiation of sacubitril/valsartan, but it was limited by a very short-term follow-up only 1 month with a very limited sample size [3].

Cardiopulmonary exercise test (CPET) is an accurate tool in assessing functional capacity in HFrEF and providing different parameters as peak O_2 consumption (VO_2), oxygen pulse and accelerated rate of O_2 consumption per watt of work ($\Delta VO_2/\Delta Work$) (4). The aim of current study is to evaluate the effects of sacubitril/valsartan therapy on different CPET parameters in a larger sample size and for a longer follow-up period.

Methodology

Study Design and inclusion criteria

A non randomized observational study was conducted at cardiology departments of both Benha university hospital and Benha insurance hospital from February to August 2019. This study included 100 patients with HFrEF with low EF (<35%). Sacubitril/valsartan twice daily was administered for all patients with minimum tolerated dose. Bridging from ACEI/ARBs to sacubitril/valsartan was done at baseline according to guideline recommendations. Patients received sacubitril/valsartan according to recent strategy of national insurance in Egypt. All patients were provided informed consent for participation in this study.

Inclusion criteria:

- Symptomatic heart failure (NYHA) class II–IV, in spite of optimal medical therapy;
- LVEF less than 35%, as measured using 2D echocardiography;
- Previous treatment with maximum tolerated dose of ACEI/ARBs for at least 4 months.

Exclusion criteria:

- Recent hospitalization for HF within 2 months.
- Recent myocardial revascularization within 3 months.
- Concomitant cardiac resynchronization therapy during study follow-up or within 6 months.
- Systolic arterial blood pressure <100 mmHg.
- Estimated glomerular filtration rate <30 mL/min/1.73 m^2 or serum K+ level >5.4 mEq/L.
- Physical inability to perform CPET.

Cardiopulmonary exercise test

Baseline CPET was performed before starting administration of sacubitril/valsartan. Another follow up CPET was performed after 6 months.

All CPETs were performed on a cycle ergo-meter with standard ramp protocol.

Routine warm up was done with a starting work load equal 10 watts with very gradual titration (10 watts every 60 s). Analysis of expiratory oxygen (O_2), carbon dioxide (CO_2), and expired volumes was performed. Twelve lead ECG, pulse oximeter and heart rate monitoring were used during the test. Study end point was limiting dyspnea or fatigue [5].

Switch from aerobic to anaerobic metabolism (anaerobic threshold) was measured using the V-slope analysis and confirmed using ventilatory equivalents and end-tidal pressures of gases (O_2 and CO_2).The relationship between minute ventilation and carbon dioxide production (VE/VCO2 slope) was also used as a measure of ventilatory efficiency. Percent predicted VO_2 represents the achieved peak VO_2 adjusted for age, weight, and height and expressed as a percentage using the equations by Wasserman and Hansen [6].

Statistical Analyses:

P-value <0.05 was considered statistically significant. CPET baseline and follow-up parameters were compared using Mann-Whitney U test for continuous variables and Fisher exact test for categorical variables, respectively.

Results:

Among study population, mean age was 59.8 ± 3 years. Female gender represents 15% of population. According to NYHA classification of HFrEF , Majority of patients were on class II and III (60% and 38%) while only 2 patients (2%) were on class IV. Mean left ventricular ejection fraction (LVEF) was 26 ± 5%. Mean SBP and DBP were 116±13 and 72±2 mmHg respectively. The starting dose of sacubitril/valsartan was (49/51 mg) in 31% of patients while the majority of patients started with lower doses of sacubitril/valsartan (24/26 mg) (69%) (Table 1).

Table 1. **Baseline demographic data**

Baseline demographic data	
Age, year, mean ± SD	59.8± 3
Female sex, no. (%)	15 (15%)
SBP, mmHg, mean ± SD	116 ± 13
DBP, mmHg, mean ± SD	72 ± 2
Heart rate, beats/min, mean ± SD	66 ± 12
Hypertension, no. (%)	52 (52%)
Diabetes, no. (%)	33 (33%)
eGFR, mL/min/1.73 m^2, mean ± SD	67.5 ± 24.1
LVEF (%), mean ± SD	26 ± 5
NYHA functional class II, no. (%)	60 (60%)
NYHA functional class III, no. (%)	38 (38%)
NYHA functional class IV, no. (%)	2 (2%)
Starting dose of sacubitril/valsartan 24/26 mg	69 patients
Starting dose of sacubitril/valsartan 49/51 mg	31 patients

Cardiopulmonary exercise test and LVEF

The results of CPET showed a significant increase in peak O2 consumption (VO_2) from 14.6 ± 4 to 17.3 ± 5 mL/kg/min ($p< 0.0001$).We observed a significant increase in percent predicted VO_2 (10.9%) 53.8 ± 14.1 to 64.7 ± 17.8 ($p < 0.0001$), and a significant increase in O2 pulse from 11.5 ± 3.0 to 13.4 ± 4.3 ml/beat ($p < 0.0007$). We observed a significant increase in $\Delta VO_2/\Delta$Work slope from 9.2 ± 1.5 to 10.1 ± 1.8 mL/min/watt ($p = 0.0001$) with increase in peak ventilation from 48.7 ± 12.7 to 59.3 ± 18.9 L/min ($p < 0.0001$). This improvement in ventilatory response approved with marked reduction in VE/VCO_2 slope from 34.1 ± 6.3 to 31.7 ± 6.1 ($p= 0.005$). All CPET results are shown in table 2.

At follow-up, systolic blood pressure significantly decreased from 116 ± 13 to109 ± 1 mmHg ($p < 0.0001$) and this was none limiting for sacubitril/valsartan continuation in any patient. Mean LVEF increased from 26 ± 5 to 29.7 ± 7% ($p < 0.0001$) and left ventricular end-systolic volume decreased from 152 ± 53 to 146 ± 62 mL ($p = 0.002$).

CPET and LVEF results stratified by maximum tolerated dose of sacubitril/valsartan

Forty one patients tolerated maximum higher doses of sacubitril/valsartan from 49/51 to 97/103 mg twice daily (group 1). 59 patients tolerated maximum lower doses from 24/26 to 49/51 mg twice daily (group 2).

At follow up, Group 1 had a statistically significant increase in peak VO_2 (15.43 ± 2.2 vs12.34± 2.5 mL/kg/min in group 2; $p = 0.0008$). Group 1 had a significant increase in LVEF 31.2 ± 2% vs 28.1 ± 3% in group 2 ($p <0.001$) with non significant decrease in SBP 115 ± 53 vs116 ± 1 mmHg for group 2 ($p = 0.07$) (Figure 1).

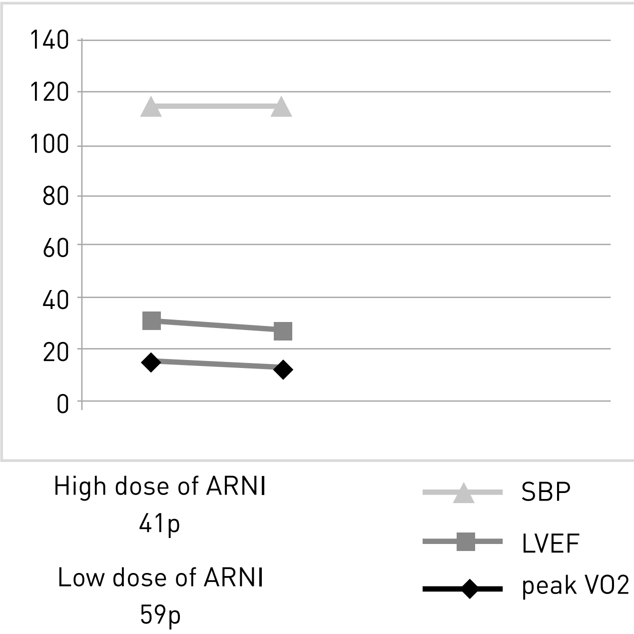

Figure 1. CPET results, LVEF and blood pressure response stratified by maximum tolerated dose of sacubitril/valsartan

Table 2. **Cardiopulmonary exercise test parameters at baseline and after 6 months.**

CPET parameters	Baseline	After 6 months	p value
Peak VO2, mL/kg/min, mean ± SD	14.6 ± 4	17.3 ± 5	<0.0001
Predicted peak VO_2, %, mean ± SD	53.8 ± 14.1	64.7 ± 17.8	<0.0001
O2 pulse (ml/beat)	11.5± 3.0	13.4 ± 4.3	0.0007
Peak RER, mean ± SD	1.12 ± 0.09	1.13 ± 0.09	0.45
Watt (Peak), mean ± SD	70 ± 22	88 ± 29	<0.0001
$\Delta VO_2/\Delta$work, mL/min/watt, mean ± SD	9.2 ± 1.5	10.1 ± 1.8	0.0001
Peak ventilation, L/min, mean ± SD	48.7 ± 12.7	59.3 ± 18.9	<0.0001
Peak tidal volume, L, mean ± SD	1.57 ± 0.43	1.75 ± 0.53	0.009
Peak Respiratory rate, b/m, mean ± SD	30.5 ± 6.7	33.3 ± 7.2	0.006
VE/VCO_2 slope, mean ± SD	34.1 ± 6.3	31.7 ± 6.1	0.005

Discussion

Traditionally, the main indication for cardiopulmonary exercise testing (CPET) in heart failure (HF) was for the selection of candidates to heart transplantation. Recently, CPET is used for risk stratification and evaluation of management strategies [5]. CPET is a valuable tool to guide clinical decision-making and to derive prognostic information in HF patients.(7) In the **PARADIGM-HF** trial, sacubitril/valsartan reduced the risk of death and hospitalization for patients with HFrEF, as compared to enalapril; however, little is known on how sacubitril/valsartan influences cardiopulmonary function [1]. Only few studies showed an improvement in exercise tolerance after initiation of sacubitril/valsartan in patients with HFrEF [2].

In the study of Palau et al, the authors showed an improvement in peak VO_2 in HFrEF patients after sacubitril/valsartan initiation, mostly at low doses. The study was limited by a very short-term follow-up only 1 month with a very limited sample size only 33 patients [3].

In current study, we targeted a larger population (100 patients) and a longer follow-up (6 months) with advanced methodology included higher dosages of sacubitril/valsartan up to 97/103 mg twice daily in 41% of study population. We observed a marked improvement in all CPET parameters with sacubitril/valsartan mainly obtained from an improvement in peak VO_2 (14.6 ± 4 to 17.3 ± 5 mL/kg/min which should be secondary to the improvement of cardiac performance (Table 2). Similar to our results, Vitale G et al. observed an improvement in peak VO_2 (+17% versus baseline) and VE/VCO_2 slope (–7% versus baseline) at follow-up, they conclude in their observational trial that administration of sacubitril/valsartan was associated with a significative improvement in exercise tolerance, peak oxygen consumption, and ventilatory efficiency at 6.2 months follow-up [7].

The prognostic value of CPET in HF with reduced ejection fraction (HFrEF), especially if combined with other key clinical parameters, has been the subject of recent papers.(5) Swank et al. reported in a previous study that for every 6% increase in peak VO_2 there is an 8% reduction in cardiovascular mortality or HF hospitalization ($p < 0.001$).(8) Arena et al. reported worse 1-year event-free survival from cardiac mortality (83.1% vs. 99.2%; $p<0.0001$) and worse 1-year event-free survival from cardiac hospitalization (50.6% vs. 84.6%; $p < 0.0001$) in patients with VE/VCO_2 slope ⩾34. (9)

A **PARADIGM-HF** post-hoc analysis by **Vardeny et al**. demonstrates that lower doses of sacubitril/valsartan confer a similar treatment benefit over enalapril; however, patients taking low doses were associated with a higher risk of the primary events [10].

In current study, patients taking higher doses had better improvement of CPET parameters as compared to patients taking lower doses. Among 41 patients who received sacubitril/valsartan with doses ranged from 49/51 to 97/103 mg, peak VO_2 increased up to15.43 ± 2.2 vs only 12.34± 2.5 mL/kg/min in 59 patients who received a lower doses ranged from 24/26 to 49/51 mg ($p = 0.0008$). In association, LVEF increased in patients who received higher doses 31.2 ± 2% vs 28.1 ± 3% ($p <0.001$) with non significant decrease in SBP 115 ± 53 vs116 ± 1 mmHg ($p = 0.07$) (Figure 1).

Study Limitations

An important limitation of current study is the small sample size; nonetheless, to our knowledge, No other work represents larger sample size of HFrEF patients followed by CPET parameters. This was an observational trial with no control group. Finally, only 2 patients with NYHA class IV were included and the majority of study population had NYHA class II, III on optimized medical therapy.

Further studies are necessary to better clarify underlying mechanisms of this functional improvement.

Conclusions

Sacubitril/valsartan therapy in patients with HFrEF associated with a significant improvement in exercise tolerance up to 6 months follow-up. Higher doses equal better improvement in both exercise tolerance and LVEF.

Conflicts of Interest: The authors declare no conflict of interest.

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ORIGINAL ARTICLES

Stress at work and attitude to health in open urban male population: prevalence and associations

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Objective. *To study association between the prevalence of certain stress parameters at workplace and attitude to medical care in men aged 25–64 years of open urban population in Tumen.*

Materials and methods. *The representative sample of 1000 people was taken from the electoral lists of men aged 25–64 years (the response amounted to 85.0 %.) Stress at work and attitude to medical care were determined using the WHO MONICA psychosocial questionnaire "Knowledge and attitude towards their health".*

Results. *By studying the awareness and attitude to medical care, we can determine the level of participation in preventive programs, the initial preventive examination, and adherence to certain practical recommendations. Elderly patients have decreased positive health self-esteem. Over the last 12 months the fourth part of the Tyumen male population has changed their workplace (the third part in 25–34 years age group), 34.0 % of Tyumen*

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men increased workload, 44.7% increased responsibility at work. Load and responsibility increase were noted mainly among young people.

High-risk groups, including people who changed specialty and workload in the workplace over the past 12 months, were associated with low health self-esteem. People with negative attitude to work did not differ significantly by low and high health self-esteem.

Conclusion. *The results of obtained in this study conducted in unorganized population of Tyumen may be used as the scientific basis for organizing complex socially oriented preventive programs in other moderately urbanized Siberian cities with the main focus on the needs of risk groups — men who underwent stress at workplace.*

Key words: *stress at work, open urban population, men, health self-esteem.*

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Stress at work is one of the most significant social problems in Russia and developing countries [1]. Psychosocial risk factors can be divided into two main categories: chronic stress factors (social factors) and emotional stress factors (psychological factors). Chronic stress factors including family status, stress at work and at home, low social support, low socioeconomic status (education, profession) [2]. Russian and foreign studies have shown that during socioeconomic reforms, the requirements for all workers became changed: massive job cuts, high requirements for employees, work/leisure imbalance, high professional skills demands and low salary, low safety measures at workplace, etc. All these factors lead to stress at work, and to labor resources decrease (disability, admissions) [3, 4].

Positive attitude to healthcare can be reached by gaining knowledge on healthy lifestyle and possible risk factors. The importance of health self-esteem is growing, since it causes psychological difficulties at work and has negative impact on male population [5, 6, 7].

The analysis of Russian and foreign literature showed number of studies on health self-esteem and various parameters of stress at the work [9, 10].

At the same time, the association between these parameters haven't been studied enough yet and the results obtained the Tyumen city model can serve as the scientific basis for organizing complex socially oriented preventive programs in other moderately urbanized cities.

Objective

To study the association between the prevalence of certain stress parameters at workplace and attitude to medical care in men aged 25–64 years of open urban population in Tumen.

Materials and methods

Epidemiological study was done using strictly standardized epidemiological methods on representative sample of open urban population that was formed from the electoral lists of one of the central administrative districts of Tyumen. The studied group initially included 1000 people each age group by age decades and the response of participating in cardiological screening amounted to 85.0%.

The cardiological screening included questioning of participants using WHO-MONICA psychosocial questionnaire "Knowledge and attitude towards their health". The study analysis included data on chronic social stress parameters (stress at work) and one of objective-subjective health parameter (health self-esteem) [2].

WHO-MONICA psychosocial questionnaire "Knowledge and attitude towards their health" included 33 questions on health self-esteem, attitude to medical care and preventive measures, behavioral risk factors, family stress and stress at workplace, associations between which were statistically significant in Tyumen population.

Statistical analysis was done using IBM SPSS Statistics. Direct standardization method and the structure of 25–64 years Russian Federation urban population (census data) were used in order to standardize indicators by age. Pearson's chi-squared test (X^2) was used to determine the statistical significance of the results between different groups ($p \leq 0.05$).

Results

By studying healthcare awareness, we can determine population attitude to participate in preventive programs, examination and certain practical recommendations.

Table 1 presents the health self-assessment in men of Tyumen population depending on their age group.

Table 1. **Health self-esteem in men of Tyumen depending on age**

Question/attitude	Age group										
	25–34		35–44		45–54		55–64		25–64		◊
	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	%
1. How do you estimate your health											
1.1. Absolutely healthy	6	3.4	5	2.2	4	1.7	5	2.3	20	2.4	2.4
1.2. Good health	34	19.2	32	14.0	22	9.5^{**}	12	5.6^{***}_{**}	100	${}_{**}11.8^{**}$	13.0
1.3. Healthy	92	52.0	111	48.7	85	36.8^{**}_{**}	39	${}^{***}18.2_{***}$	327	38.5^{**}	41.8
1.4. Not completely healthy	43	24.3	73	32.0	107	46.3^{***}_{**}	120	${}^{*}56.1^{***}_{***}$	343	${}_{***}40.4^{***}$	37.4
1.5. Sick	2	1.1	7	3.1	13	5.6^{*}	38	${}^{***}17.8^{***}_{***}$	60	7.1^{**}	5.4

Comment: statistically significant differences between parameters are signed with (*) in the upper right corner of the table cell between 25–34 age group and other age groups; in the lower right corner of the table cell — between 35–44 age group and other groups; in the upper left corner of the table cell — between 45–54 age group and other age groups; in the lower left corner of the table cell — between 55–64 and 25–64 age groups: * p<0,05; ** p<0,01; *** p<0,001; ◊ age-standardized variable.

Table 2. **Stress at work in men aged 25–64 years**

Question/attitude	Age group										
	25–34		35–44		45–54		55–64		25–64		ASV
	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	%
1. Did your specialty change over the last 12 months?											
1.1. Yes	84	47.7	99	43.4	81	35.1	77	36.0	341	40.2	41.2
1.2. No	92	52.3	129	56.6	150	64.9	137	64.0	508	59.8	58.8
2. Did your workload change over the last 12 months?											
2.1. I started doing additional work	72	40.9	87	38.3	74	32.0	35	${}^{***}16.4^{***}_{***}$	268	${}_{***}31.6$	34.0
2.2. It didn't change	71	40.3	98	43.2	130	56.3^{**}_{**}	100	46.7	399	47.0	47.1
2.3. I stopped or started doing less additional work	33	18.8	42	18.5	27	11.7	79	${}^{***}36.9^{***}_{***}$	181	${}_{***}21.3$	19.5
3. Do you like your job?											
3.1. I don't like it at all	1	0.6	1	0.4	0	0.0	4	1.9	6	0.7	0.6
3.2. I don't like it	7	4.0	9	3.9	5	2.2	8	3.7	29	3.4	3.4
3.3. Moderate	60	34.1	77	33.8	86	37.2	70	32.7	293	34.5	34.6
3.4. I like it	86	48.9	121	53.1	114	49.4	109	50.9	430	50.6	50.6
3.5. I really like it	22	12.5	20	8.8	26	11.3	23	10.7	91	10.7	10.8

Comment:.statistically significant differences between parameters are signed with (*) in the upper right corner of the table cell between 25–34 age group and other age groups; in the lower right corner of the table cell — between 35–44 age group and other groups; in the upper left corner of the table cell — between 45–54 age group and other age groups; in the lower left corner of the table cell — between 55–64 and 25–64 age groups:
* p<0,05; ** p<0,01; *** p<0,001; ASV — age-standardized variable.

Thus, 47.4 % of men said that they are "not completely healthy" or "sick". 73.8 % of men aged 55–64 years claimed that they were "not completely healthy" or "sick". The number of "perfectly healthy" men were low in all age groups. The amount of "good health" and "healthy" answers naturally decreased in older age groups. The answer "not completely healthy" in the age categories 25–34 and 35–44 years was much less common in younger age groups compared with older patients. The answer "sick" had similar prevalence (Table 1).

The results of the study on stress at the work in the male population of Tyumen are presented in table 2. 41.2 % of men said that their «specialty changed over the last 12 months». The change in specialty did not depend on age. 47.1 % of men did not start doing additional work over the last 12 months, 34 % started doing additional work, 19.5 % stopped or started doing less additional work. Men aged 55–64 years (16.4 %) started doing less additional work compared with other age groups. The most stable work load was determined in the 45–54 years age group and had significant differences compared with younger age groups — 25–34 and 35–44 years (56.3 % — 40.3 %, p <0.01 and 56.3 % — 43.2 %, p <0.01, respectively). Men aged 55–64 years stopped or started doing less additional work more common compared with other age groups and general population (36.9 % — 21.3 %,

Table 3. **How do you estimate your health?**

Question/attitude Abs, %	n=850 Absolutely healthy m=20 abs. m=2.4%		Good health m=100 abs. m=11.8%		Healthy m=327 abs. m=38.5%		Not completely healthy m=343 abs. m=40.4%		Sick m=60 abs. m=7.1%	
	м abs..	м %	м abs.	м %	м abs.	м %	м abs.	м %	м abs.	м %
1. Did your specialty change over the last 12 months?										
1.1. Yes	13	65.0	37	37.0	135	41.3	136	39.7	21	35.0
1.2. No	7	35.0	63	$^{***}63.0$	192	$^{***}58.7$	207	$^{***}60.3$	39	$^{***}65.0$
2. Did your workload change over the last 12 months?										
2.1. I started doing additional work	13	65.0	35	35.0	114	34.9	99	28.9	7	11.7
2.2. It didn't change	7	35.0	51	51.0	152	$^{**}46.5$	167	$^{***}48.7$	24	40.0
2.3. I stopped or started doing less additional work	0	0.0	14	$^{***}14.0^{***}$	61	$^{***}18.7^{***}$	77	22.4^{***}	29	$^{***}48.3$
3. Do you like your job?										
3.1. I don't like it at all	0	0.0	0	0.0	0	0.0	5	1.5	1	1.7
3.2. I don't like it	0	0.0	3	3.0	8	2.5	14	$^{*}4.1$	3	5.0
3.3. Moderate	3	15.0	29	29.0^{***}	116	35.5^{***}	124	$^{***}36.2^{***}$	21	$^{***}35.0^{***}$
3.4. I like it	6	30.0	57	$_{***}57.0^{***}$	163	$_{***}49.8^{***}$	174	$_{***}{}^{***}50.7^{***}$	32	$^{***}53.3^{***}$
3.5. I really like it	11	$_{**}55.0$	11	$_{**}11.0_{***}$	40	$_{***}12.2^{***}{}_{***}$	26	$_{***}{}^{***}7.6_{***}$	3	$_{***}5.0_{***}$

Comment: statistically significant differences are signed with (*) in the upper left corner between 1.1 and 1.2; 2.1 and 2.2, 2.3; 3.1 and 3.2, 3.3, 3.4, 3.5, in the upper right corner between 2.2 and 2.3; 3.2 and 3.3, 3.4, 3.5, in the lower left corner between questions 3.3 and 3.4, 3.5, in the lower left corner between questions 3.4 and 3.5: ** p<0,01; *** p<0,001.

p<0.001). Over 70% of the men of the Tyumen population liked their work by all five categories of answers, and age groups did not differ significantly (Table 2).

Men of open population with stress at work, who changed their specialty over the last 12 months felt less healthy ("not completely healthy" (39.7%—60.3% p<0.001), "sick" (35.0%—65.0% p<0.001)) compared with men without stress at work. Men who felt healthier ("healthy" (41.3%—58.7% p <0.001) and "good health" (37.0%—63.0% p<0.001)) did not change their specialty over the last 12 months.

Men with low health self-esteem ("sick") started doing less additional work over the last 12 months. Thus, men with low health self-esteem, reduced or stopped doing additional work more frequently than started doing additional work (11.7%—48.3% p <0.001).

Men with high health self-esteem ("good health" (35.0%—14.0% p <0.001); "healthy" (34.9%—18.7% p <0.001) more frequently increased workload than reduced or stopped doing additional work.

Men who felt "not completely healthy" did not show significant changes in the work load over the last year.

Men who felt "sick" mostly answered "I like my job" to the question "Do you like your job?" compared with "I don't like my job" (53.3%—5.0% p <0.001) or "I don't like my job at all" (53.3%—1.7% p <0.001).

Men who felt "not completely healthy" more frequently answered "I like my job" compared with "I don't like my job" (50.7%—4.1% p<0.001) and "I don't like my job at all" (50.7%—1.5% p<0.001). This group also had statistically significant differences between men who answered "I really like my job" and "I don't like my job at all" (7.6%—1.5% p<0.001).

Men with high health self-esteem ("healthy") mostly liked (49.8%—2.5% p<0.001) or really liked (12.2%—2.5% p<0.001) their jobs.

Men with "good health" had statistically significant differences between the answers "I like my job" and "I don't like my job" (57.0%—3.0% p<0.001). (Table 3)

Discussion

2016 European recommendations for the prevention of cardiovascular diseases in clinical practice consider stress at work as one of chronic social stress factors in terms of risk factor correction for coronary heart disease (CHD) prevention [11]. The significance of stress at work as CVD risk factor in men was demonstrated in epidemiological studies using the WHO MONICA—PSYCHOSOCIAL algorithm in open populations [12, 2]. The analysis of Tyumen population data showed that men of open population of working age have high level of stress parameters at work in moderately urbanized Siberian city [12, 13]. The results of previous study on medical activity in Tyumen population confirm that attitude to health and its self-esteem have been studied fully. It was revealed that in open population of moderately urbanized Western Siberia city, 42.8% of men aged 25–64 years old consider themselves sick and do not care enough about their health. At the same time, 55.2% of people believe in serious diseases prevention. Positive health self-esteem decreases with age, and self-healthcare increases [5, 6, 7].

Data analysis showed that high-risk groups, including people who changed their specialty and workload over the last 12 months, associated with low health self-esteem.

At the same time, negative attitude to work did not differ significantly between groups with low and high health self-esteem. The results obtained on the association between attitude to work and health self-esteem in population are fair since negative attitude to one's work according to Novosibirsk researcher's data is seen in all population groups, regardless of subjective-objective health parameter [3]. Nevertheless, this parameter is extremely important in cardiovascular risk analysis and prognosis [11, 1].

Data on the association between health self-esteem and stress at work in the male population may be useful for organizing complex scientifically based preventive programs with main focus on high-risk groups among working-age men of moderately urbanized Siberian city. Socially oriented preventive programs such as (advanced training in public health, medical conferences on public health, tests on behavioral risk factors in order to assess professional skills of medical personnel, training doctors and nurses on prevention programs; training social workers on public health and measures for increasing physical activity in population) in working male population should be aimed, first of all, for studying attitude to health and its self-esteem, carried out using a high-risk strategy.

Conclusion

The results obtained in this study conducted in unorganized population of Tyumen may be used as the scientific basis for organizing complex socially oriented preventive programs in other moderately urbanized Siberian cities with the main focus on the needs of risk groups — men with stress at work.

Older age groups have significantly decreased positive health self-esteem in Tyumen population.

Over the last 12 months, the fourth part of Tyumen male population changed their job (at the age of 25–34 years — the third part), 34.0% of Tyumen men increased workload, 44.7% — responsibility at work, load and responsibility mainly increased among young people.

High-risk groups — men who changed specialty and workload over the last 12 months — were associated with low health self-esteem.

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REVIEW ARTICLE

Assessment of mechanical dyssynchrony during patient's selection for cardiac resynchronization therapy by speckle tracking echocardiography

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Abstract. *Myocardial strain is the degree of myocardial segment thickness or length from final diastolic to final systolic value that is assessed using speckle tracking echocardiography (STE). We analyzed forty-three scientific publications available in the PubMed search system from 2001 to 2019 years.*

Interventricular dyssynchrony is more common in patients with left bundle branch block. Early transseptal activation lead to pressure gradient change and septal flash (SF). SF is a presystolic abnormal contraction of interventricular septum basal segments before left ventricular (LV) walls contraction. It is possible to identify SF during all strain types — longitudinal, radial and circumflex.

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Intraventricular dyssynchrony is associated with the change of LV segments stimulation sequence. Strain delay index (SDI) is calculated as the ratio of systolic to maximum strain peak delays. Longitudinal Dyssynchrony Index — maximum difference among final systolic strain peaks of 12 myocardial segments.

Key words: *speckle tracking echocardiography; mechanical dyssynchrony; cardiac resynchronization therapy; congestive heart failure.*

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Myocardial morphology and kinetics

Heart contraction is a complex physiological process due to its anatomical and morphological features. The wall of the left ventricle (LV) has three layers. Middle layer consists of circular muscles. The muscles of subendocardial and subepicardial myocardium are longitudinal, have spiral orientation, and rotate orthogonally (multidirectional): the subendocardial part rotates in clockwise direction (a right-handed helix), and subepicardial part — in counterclockwise direction (a left-handed helix). Global rotation at the basal segments level, papillary muscles and LV apex is the ratio of presented layers rotation and is measured in degrees. The severity strictly decreases from apex to basal segments to middle segments [1,2]. Such architectonics provides homogeneity of cardiac contraction and LV twist and untwist — important cardiac biomechanical processes. This twist is a mutual rotation of LV apex and base and is also measured in degrees. Base usually rotates in clockwise direction, and apex — in counterclockwise [3,4].

Methodology

Speckle Tracking Echocardiography (STE) estimates myocardial strain — the degree of myocardial segment thickness or length from final diastolic to final systolic value (in percent). Its derivative — strain rate shows the speed of shortening or thickening [5]. The method is based on a semi-automatic analysis of the speckle movement — group of points ranging in size from 20 to 40 pixels and form unique acoustic patterns [6]. STE is registered in the mode of a gray-scaled two-dimensional ultrasound image, so it does not depend on the scanning angle. This makes it possible to assess myocardial segments deformation in three directions: longitudinal, circular and radial, that makes it superior to tissue doppler imaging (TDI) [7]. STE also highly correlate with magnetic resonance imaging [8].

On the other hand, there are several potential limitations of this method. Firstly, it strictly depends on the optimal frame rate — 35–70 per minute. Secondly, it requires extremely high quality of two-dimensional ultrasound images in order to visualize blood-endocardial border, epicardial and pericardial cavities. Recording should also be done during breath holding in order to avoid acoustic patterns drift with stable electrocardiographic picture — heart sinus rhythm [7,8].

Normative values

The results of resent studies on the assessment of myocardial deformation using STE, are reflected in modern recommendations. Only Global Longitudinal Strain (GLS) was reliable and reproducible indicator for LV systolic function assessment. Thus, the meta-analysis of 24 studies from 2009 to 2011 (2597 healthy volunteers, average age 47 years, 51 % — men), the average GLS was 19.7 % [9]. According to the JUSTICE study (817 healthy volunteers, average age 36 years, 61 % — men), average GLS value differed for devices companies: 21.3±2.1 % for General Electric; 18.9±2.5 % for Phillips and 19.9±2.4 % for Toshiba [10]. The intra- and inter-research variability was low: 5.2 % and 6.5 %, for General Electric; 5.1 % and 6.2 % for Philips; 6.2 % and 5.4 % for Toshiba, respectively [11]. The HUNT study revealed gender differences in GLS values: 15.9 % for men; 17.4 % for women [12]. It is also remarkable that the severity of GLS decreases with age: 22.2±2.2 % for patients under 20 years; 20.9±1.9 % for patients over 60 years [13].

Therefore, current guidelines published by EACVI / ASE in 2015 propose using the GLS value above 20 % as a normal [14]. The 2011 ASE / EAE recommendations suggested using 18±2 % as the lower limit of the normal value [15].

Average rates of global radial LV deformation in adults were 54.6±12.6 % and 42±7 %, global circular deformation 22.8±2.9% and 23.3±3% according to different studies [10.16]. The severity of circular deformation decreases or remains unchanged, radial — always remains the same [13,16].

The results of studies on the rotation and twisting reveal extremely large interval of average values. It is also remarkable that according to Yi Zhang, the apical rotation increases with age — from 2.19±1.27 ° to 10.34±1.54 °, and basal decreases — from 1.13±0.39 ° to 7.21±2.19 ° [17].

Thus, large variability of values that determine lower limit of deformation, rotation and twisting of the myocardium, shows that each laboratory using the STE method to assess myocardial function need to determine its own normative values.

Chronic heart failure and cardiac resynchronization therapy

Global longitudinal strain (GLS) decreases in all three directions in patients with chronic heart failure (CHF). Moreover, the severity GLS reduction correlates with NYHA functional class (FC) of CHF, that is due to change in myocardial fibers orientation due to cardiac remodeling [18]. Moreover, GLS is a promising indicator for patients with mild systolic dysfunction with preserved LV ejection fraction (EF), and can be useful for patients with unexplained symptoms of heart failure [19]. Some authors claim that 16% of GLS is associated with CHF with preserved LV EF, and 12% with severe systolic dysfunction [20].

Cardiac resynchronization therapy (CRT) improves LV contractility and leads to cardiac reverse remodeling. Numerous randomized clinical trials demonstrated that NYHA FC of CHF, the number of admissions due to CHF progression and CHF and all-cause mortality decreases due to CRT [21].

Nowadays, combination of parameters is used in order to select patients for CRT: FC of CHF, duration of QRS complex, left bundle branch block (LBBB), LV EF. Thus, myocardial electrical dysynchrony is emphasized. But about 30% of patients do not respond to therapy [21].

A number of studies have shown that the criteria of clinical response to CRT in patients with intraventricular and interventricular mechanical dyssynchrony in combination with the selection criteria used in the national guidelines are superior to existing criteria alone [22].

Mechanical dyssynchrony and speckle tracking echocardiography method

Dyssynchrony is the pathological contraction or relaxation of individual heart chambers or myocardium segments due to electrical conductivity impairment [23]. When assessing mechanical dyssynchrony in patients with heart failure using STE method, it is important to remember that electrical impulses (EI) propagate faster in the longitudinal direction of cardiomyocyte (CM) — 0.50–0.98 m/s than in the transverse — 0.19–0, 26 m/s [24,25]. The coincidence between CM position and EI direction is physiological and is called isotropic conduction. Under certain conditions, the CMs may underwent "functional dissociation", therefore, the speed of EI in the longitudinal direction can decrease [24]. Since the direction and orientation of the myocardial layers changes in patients with CHF, it seems relevant to use the STE method to study myocardial deformation in three directions: longitudinal, circular and radial.

The following types of mechanical dyssynchrony are distinguished: atrioventricular, interventricular and intraventricular. Atrioventricular dyssynchrony is premature left atrium contraction before venous return during LV filling phase and the reduction of LV filling time. Due to the reduction of LV preload, the Frank-Starling mechanism is lower that compromises the stroke volume [26]. However, the STE method is potential assessment method of only the types of mechanical dyssynchrony described below.

Interventricular dyssynchrony: left bundle branch block and septal flush

Interventricular dyssynchrony is seen in patients with EI impairment with block of one of His bundle branches, most often LBBB. The anterolateral segment of the right ventricle is excited earlier due to an electrical impulse propagation through the intact right branch of His bundle. Distribution has the following sequence: interventricular septum (IVS), LV anterior wall, vertically through the anterolateral LV segment, heart apex. Subsequently, excitation changes direction from LV apex downward, — reaches the lateral and posterolateral LV segments close to the mitral annulus (MA) and forms U-shaped conduction pattern [27,28].

Despite obvious conduction impairment, LBBB is a complex heterogeneous disorder at several anatomical levels. The transseptal activation front subsequently propagates along preserved Purkinje fibers or CMs with significantly lower speed compared with specialized cells. The line of functional conduction block is usually parallel to the septum, directed from LV base to its apex in patients with LBBB. Its location can be front, lateral or lower (low septal) [27].

Not only the location of conduction block line, but also the place of EI conduction through IVS and transseptal conduction time are the factors determining QRS complex duration. According to Auricchio A. et al. patients with septal apical EI conduction showed longer transseptal conduction time, and patients with over 40 ms had QRS complex duration significantly higher (197±28 ms and 154±21 ms; p=0.001). Patients with lateral functional block line had lower duration of the QRS complex (156±19 ms and 194±32 ms; p=0.003) and shorter transseptal conduction (18±21 ms and 61±22 ms; p=0.001) [27]. This explains why, in a number of studies, the response to CRT was associated not only with QRS complex duration and its morphology — complete LBBB, but also with mechanical myocardial dyssynchrony.

It is also remarkable that early transseptal activation — less than 20 ms — is accompanied by transeptal pressure gradient change and abnormal presystolic basal IVS segment displacement into LV cavity (pre-ejection septal shortening) before heart walls movement, since there is no LV resistance [29]. Septal shortening stops due to late LV wall contraction and is called septal rebound stretch [30]. This phenomenon was first described in 1982 as septal flash (SF) and can be determined using STE (Figure 1) [31,32]. As a result, posterior papillary muscle can move towards the MA and lead to early systolic mitral regurgitation [26]. Identification of SF is possible during the assessment of all deformation types: longitudinal, radial, circular [32–34]. According to several authors, SF is a consequence of LBBB, and is the best predictor of the response to CRT [32,33]. The START study evaluated circular deformation of six LV myocardial segments at papillary muscles level. The results of the study showed that standard deviation increase of the intervals between the circular deformation peaks in the curves with several peaks (T first-SD of CS> 116 ms) and the beginning of QRS complex is more reliable approach to identify the response to CRT compared with echocardiography (OR 9.83; 95 % CI 3.78–25.6; p<0.001) [32].

Moreover, SF may be associated with expanded response to CPT [35]. Several myocardial deformation models were revealed in patients with SF and varying degree of response to CPT [36].

Intraventricular dyssynchrony

Intraventricular dyssynchrony is associated with the change of LV segments stimulation sequence. Local stretching of uncoordinated segments of the myocardium occurs during isovolumetric contraction. The systole effectiveness decreases, and metabolic needs of contracting part of the myocardium subsequently increase. Asynchronous contraction of the papillary muscles, as well its tightening due to the asynchronous contraction of other LV myocardium segments can lead to excessive tendinous cords tension, displacement and incomplete closure of the mitral valve and regurgitation [37].

Intraventricular myocardial dyssynchrony assessment using STE is based on measuring delays be-

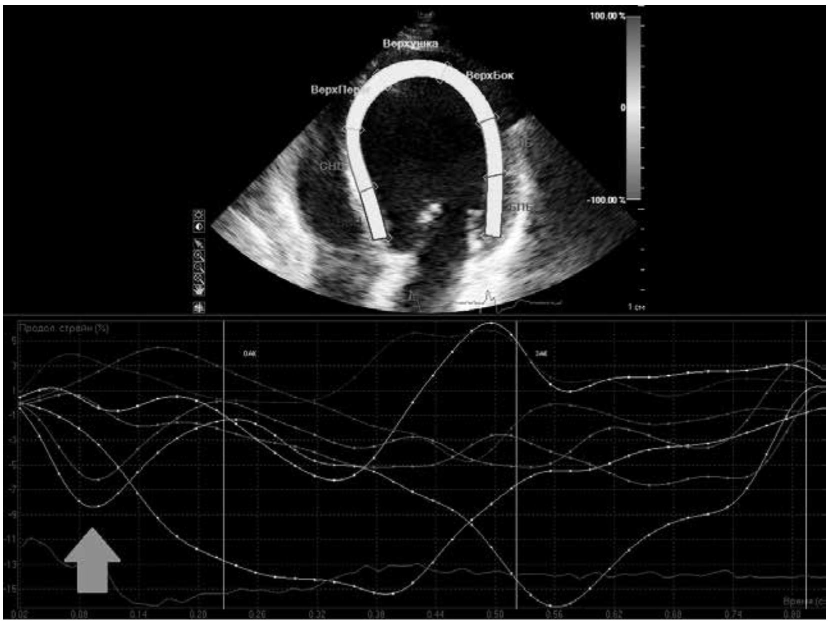

Figure 1. Early presystolic LS peak in basal and middle IVS segments in patient with SF (indicated by an arrow).

tween deformation peaks. Thus, only mechanical dyssynchrony is estimated.

The Strain Delay Index (SDI) — wasted energy of sixteen LV myocardial segments is commonly used. SDI is maximum and final systolic deformation peaks delay ratio [38]. The authors of the MUSIC study demonstrated that longitudinal SDI correlated with reverse LV remodeling (r=0.61; p<0.01) in patients with wide and narrow QRS complexes. SDI over than 25 % predicted the response to CPT with positive and negative predicted 80 and 84 % values, respectively (AUC=0.88; p<0.001) [38].

Researchers also use traditional for two-dimensional echocardiography and simpler in calculation method — the determination of the interval between the deformation peaks of the middle segments of opposite LV walls — the posterior and anterior-septal (opposing wall delay) [39]. Thus, according to STAR study, it was found that pronounced radial deformation dyssynchrony with 130 ms cut-off value of response to CRT with 87 % sensitivity and 67 % specificity (AUC=0.71; p<0.001) [40]. It is important to note that the results of several studies with long observation period showed higher survival rate of patients with initial pronounced radial deformation dysynchrony compared with patients without dysynchrony [39].

The CARDIA study showed that the longitudinal strain estimation is more reproducible compared with radial and circular strains [41]. It was also noted that combined dyssynchrony index of all three strain types has better prognostic value compared with using each parameter separately [42].

Longitudinal Dyssynchrony Index, 12SD-ε is evaluated using STE and TDI and is also remarkable [38, 39]. Standard deviation of the intervals between deformation peaks of 12 myocardial segments (basal and middle LV levels) and the beginning of the QRS complex were determined. 12SD-ε value over 60 ms according to TDI predicts the response to CRT with a 79 % sensitivity and a 92 % specificity (AUC=0.852; p<0.001) [39]. Therefore, complex approach — the use of STE and TDI together — improves the assessment of the global systolic LV function and also increases the ability to predict the response to CRT (table 1) [43].

Table 1. **Predictors of the CRT effectiveness according to STE and TDI**

Parameters	Method	Cut-off value	Strain type
T first-SD, ms	STE	>116	Circular
SDI, %	STE	>25	Longitudinal
Opposing wall delay, ms	STE	>130	Radial
12SD-ε, ms	TDI	>130	Longitudinal

Comment: T first-SD — standard deviation of the intervals between the peaks of circular deformation of curves with several peaks; SDI –Strain Delay Index; 12SD-ε — Longitudinal Dyssynchrony Index; STE — Speckle Tracking Echocardiography; TDI — Tissue Doppler Imaging.

Conclusion

The assessment of interventricular dysynchrony — the search of interventricular septum movement impairments — and intraventricular mechanical dysynchrony in order to predict the response to CRT using the STE method is a promising section of modern ultrasound diagnostics.

Conflict of interests: None declared.

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CASE REPORT

A case of successful ablation of accessory right anterior-septal pathway (parahisian) through the non-coronary cusp: case report

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Background. *Usually, accessory pathways are easy to map and ablate, however, ablation of some APs become challenging. For instance, ablation in parahisian region requires an assess to right atrium.*

Case summary. *In this case, we describe rarely used and effective method of accessory pathway ablation. We present case of a 12 years-old girl with WPW syndrome. Radiofrequency ablation near the tricuspid annulus had no effect, and tachycardia was eliminated through the non-coronary cusp. Complains such as palpitations and weakness disappeared after the procedure.*

Discussion. *Radiofrequency ablation of accessory pathway that is located in the anterior-septal area might be performed through the non-coronary cusp. This method of ablation is used when the ablation through the tricuspid annulus was ineffective.*

Keywords: *supraventricular tachycardia. Accessory pathway. Noncoronary cusp. Radiofrequency ablation. Case report.*

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Introduction

Radiofrequency ablation (RFA) is radical treatment method of accessory pathways (APs) [1–2]. Ablating of accessory pathways through the non-coronary cusp have been presented in several case reports [3–5]. In our report we present patient with right anterior-septal accessory pathway that is eliminated through the non-coronary cusp. Through the anatomical point of view, the procedure was performed successfully due to non-coronary cusp bordering with right anterior-septal area.

Case presentation

12-years-old Uzbek female patient was admitted to hospital with complaints to tachycardia attacks that begin suddenly and stop after intravenous injection of verapamil. Duration of attacks were approximately 15–20 minutes. Physical and laboratory examinations results were normal. 12 lead ECG and echocardiography results did not reveal any pathology. At the hospital the she was diagnosed with supraventricular tachycardia (SVT). ECG results confirmed the diagnosis of SVT (figure1) and electrophysiological study was recommended. After exclusion of all contraindications for the procedure, electrophysiological study of the heart started.

First, the operation area (puncture area) was processed with betadine and alcohol. Further, under local anesthesia of Sol. Novocaini 0.5 % — 40.0 ml according to the Seldinger technique, the right femoral vein was punctured with needle, 2 electrodes were inserted into the heart cavity using an introducer into the cardiac sinus and right ventricular (RV) positions.

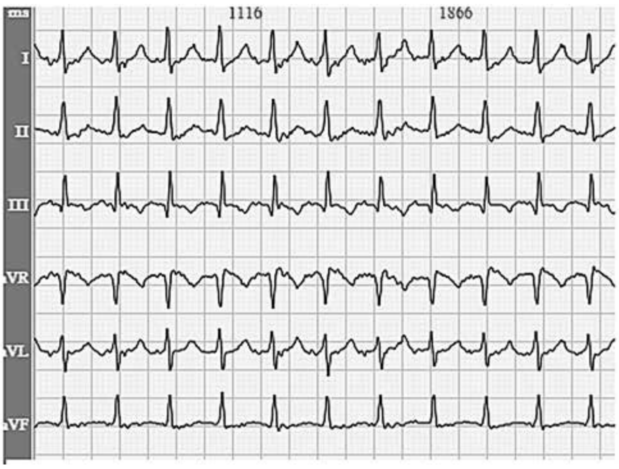

Figure 1. Supraventricular tachycardia

An invasive electrophysiological investigation (EFI) was performed. During the retrograde stimulation an early activation of the atrium in areas CS9–10 was determined, decrement was absent. During antegrade stimulation, a paroxysm of orthodromic tachycardia was induced with a cycle of 270 ms.Wolf-Parkinson-White (WPW) syndrome was verified (figure 2).

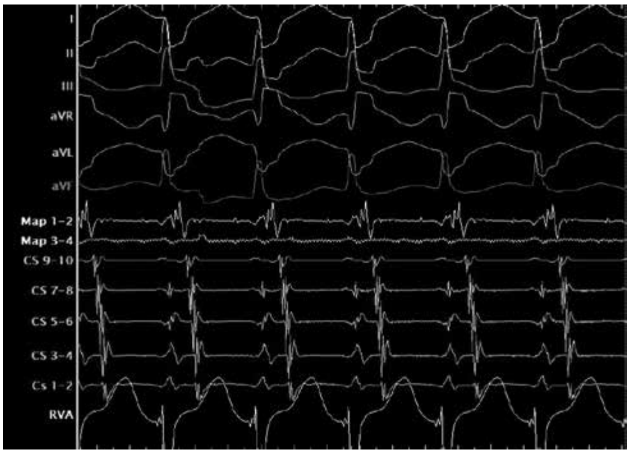

Figure 2. A paroxysm of orthodromic tachycardia, with a cycle of 270 ms. Earliest activation at CS 9-10

Figure 3. Fluoroscopic image of electrodes. LAO 30. Ablating electrode installed in the projection of the AP at the level of the right fibrous ring and diagnostic electrode is in the coronary sinus

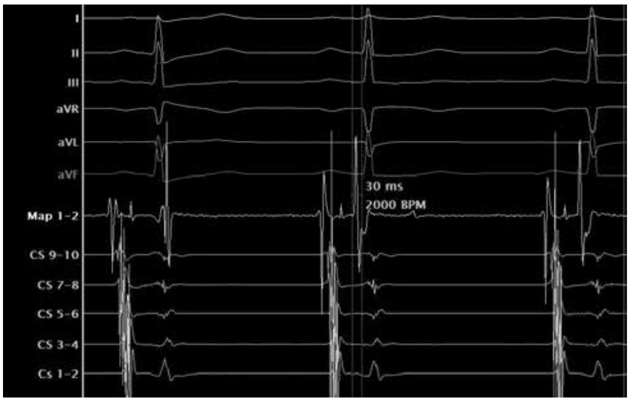

Figure 4. Decreasing H-V interval and P-Q interval. One of the signs of the non-effective ablation of AP

Next step was entering of mapping-ablation electrode in the cavity of the heart. A subsequent mapping revealed parahisian bundle of Kent. Under fluoroscopic and electrophysiological control ablating electrode was installed in the projection of the AP at the level of the fibrous ring of the tricuspid valve (fugure 3). The AP area was ablated with radio frequency (RF) energy (55 C, 40 W), but without any effect (figure 4).

It was decided to continue mapping on the left side. Right femoral artery was punctured, and mapping electrode was inserted into the left ventricular (LV) cavity with the help of the introducer (figure 5). Sol. Heparini 3000 ED was injected. The shortest VA interval was registered in the region of the non-coronary cusp (pre-excitation 30MS). Under fluoroscopic and electrophysiological control ablating electrode was installed in the projection of the AP.

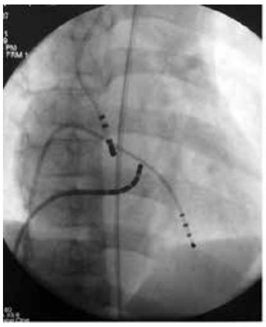

Figure 5. Fluoroscopic image. RAO 30. Ablating electrode is in the LV cavity. First diagnostic electrode is in the CS. Second is in the cavity of RV

The field of AP was ablated with RF energy (50–60 C, 40–45 W). At the 3rd second of impact, the orthodromic tachycardia stopped due to blockade at the level of AP.

Dynamic observation for 30 minutes: transmission of impulses through the AV node was maintained. Control EPS: Atrioventricular conduction — through AV node. Wenkebach point — 190 impulses per min. RRPAV-node= 330 мs/120 per min.

ERP AV-node= 270ms/120 per min. Retrograde conduction — through the AV node.Wenkebach point — 140 imp per minute. RRP AV-Nr=440 ms / 100 per min. ERP AV-Nr=380 ms / 120 per min. Programmed (up to three extrastimuli), frequent, superfrequent (up to 150 per min), ECS tachycardia paroxysms were not induced and VA-dissociation was detected. (figure 6). Electrodes extracted. Pressure bandage was placed at femoral vessels.

Discussion

Nowadays radiofrequency catheter ablation is the most common method of radical treatment of APs and other arrhythmias. Ablating APs that are located near the AV-node is technically difficult. During the ablation of this area with radiofrequency energy, surgeon can damage AV-node that may lead to serious heart rhythm disturbances. That's why there are a lot of modifications, created by professional electrophysiologists. Ablating of the anterior-septal AP through the non-coronary cusp is one of successful modern modifications. There are some advantages

Figure 6. V-A dissociation. One of the signs of AP ablation

of this method. At first, as we said earlier, ablating area is far from AV-node and it helps to work safely. Furthermore, ablating APs that are located on the right anterior-septal area is more effective than treating through right atrium.

However, there are some disadvantages of this method. For instance, for entering non-coronary cusp surgeon have to puncture artery that enhances risk of thrombosis.

Conclusion

Ablation of APs that are located in the right anterior-septal area through the non-coronary cusp is more effective compared with the right atrium.

Conflict of interests: None declared.

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Muromtseva G. A.[1], Kontsevaya A. V.[1], Konstantinov V. V.[1], Artamonova G. V.[2], Galaganova T. M.[3],...

[1] FGBU State research center of preventive medicine of the Ministry of health of Russia, Moscow;

[2] FGBU Research Institute of complex problems of cardiovascular diseases SB RAMS, Kemerovo;

[3] RD VPO North Ossetian state medical Academy, Vladikavkaz;..., Russia.

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10. All manuscripts that have been reviewed and evaluated by an expert in statistics are submitted to the editorial Board, which decides on the publication.

After the decision on the admission of article for publication, the Editorial office inserts the publication of the article in terms of publications. Information about the annual (thematic) plan of publications is placed on the website of the journal.

11. The decision to publish a manuscript is made solely on the basis of its significance, originality, clarity of presentation and compliance of the research topic with the direction of the journal. Reports on studies in which negative results are obtained or the provisions of previously published articles are challenged are considered on General grounds.

12. Original reviews are kept in the Editorial office for 5 years from the date of publication.

13. In case of a decision to refuse to publish an article, its archive copy remains in the electronic system of the editorial Board, but access to it by editors or reviewers is closed.

IX. The manner of publication of manuscripts

1. According to the requirements of the Higher attestation Commission, the journal provides priority for post-graduate and doctoral works, the period of their publication depends on the expected date of protection, which the authors must specify in the primary documents attached to the manuscript.

2. Each issue of the journal is formed by a separate Executive editor appointed by the editor-in-Chief and/or editorial Board. It is the responsibility of the editor-in-charge to select high-quality articles for publication, and he can be guided by both thematic principles and a separate scientific direction.

3. All selected articles are submitted to the scientific editor and proofreader. After creating the layout of the article and editing it, the article will be available to the Author through the site. At this stage, it will be possible to send comments on the text of the article. The author is obliged to send his / her consent to the publication or his / her comments within the established time specified in the cover letter.

4. The editorial office does not send the author's copy by mail or PDF of the article by e-mail, access to the published numbers is open.

Subscription to the printed version is carried out by half a year (through subscription agencies).

X. After the publication in the journal

1. Information on publication is distributed in the following scientific citation databases: Russian science citation index, CYBERLENINKA and others. The article is assigned a DOI index and the full text is publicly available on the journal's website.

2. Information about the publication of the issue is distributed by mailing of The Cardioprogress Foundation and in social networks.

3. We expect the authors of the articles to actively make efforts to bring the results of their research to the public, namely: to have a personal page on the Internet (personal page), to monitor and update your profile ORCID and RecsearcherID, to involve colleagues in their work through social networks.

XI. Revocation or correction of articles

The full text of the journal's policy on Revocation and correction of articles is available in the information section on the website. The editors follow COPE Recommendations issued by the Committee on publishing ethics (COPE) — http://www.publicationethics.org.uk. in cases:

Editors of journals should consider the opinion of the publication, if:

they have clear evidence of the unreliability of the information published, either as a result of conscious actions (for example, falsification of data), or due to good faith errors (for example, errors in calculations or experiments); the findings have been previously published in another publication and there is no proper reference, authorization and justification for re-publication (i.e. duplicate publication).); it is plagiarism; describes unethical research.

Editors of journals should consider the concerns, if:

they received information about the authors ' inappropriate actions, but there is no clear evidence of such behavior; there are arguments that the results of the work are unreliable, and the institution in which the authors work is not going to find out the truth; they believe that the investigation into the alleged violations committed by the authors in connection with the publication has either not been or will not be fair, impartial and convincing; the authors ' violations are being investigated, but the results are not expected soon enough.

Journal editors should consider making amendments if:

a small part of the rest of the high-quality publication is unreliable (especially because of conscientious errors); the list of authors / sponsors contains errors (i.e., it does not contain someone who is worthy to be an author, or a person who does not meet the authorship criteria).

In most cases, a review is not appropriate if:

authorship needs to be changed, but there is no reason to doubt the validity of the findings.

XII. Position E-log backup (if journal is no longer published)

The purpose of backup is to prevent loss of information in case of hardware, software, critical and crisis situations, etc.

Information of the following main categories is subject to backup: — personal information of authors (personal directories on file servers); — pdf of published articles; — information about literary links to the article in the DOI system.

All this information is publicly available in The system of the Russian citation index on the website of the Electronic library www.elibrary.ru

XIII. Journal subscription

Information on subscriptions is available on the journal website in the section "Subscription":

XIV. Journal subscription

The name of the journal in English is International heart and vascular disease journal.

Official sites where information about the journal is placed:

http://www.heart-vdj.com

On the reception of the articles, making decisions about publication, reviews — mmamedov@mail.ru

On organizational issues (working with the site, subscription) — editor.ihvdj@gmail.com

Editorial office:

Room 213, Building 2, Prospect Gostinichny 6, Moscow 127106, Russia

e-mail: editor.ihvdj@gmail.com

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1. The manuscripts are accepted if has not been published or submitted for publication elsewhere.

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Files with a letter of transmittal and General information have been prepared for upload to the site.

3.The cited literature is presented in full, framed by the Rules for the authors and does not contain duplicates. All references are indicated in the text of the article.

4. Text should be typed with an interval of one line spacing, font Times New Roman, 12 pt; to highlight the accents it is recommended to use italics rather than underlining (except Internet links). All images, graphics and tables are placed within the text according to the meaning of the particular part of text (and not at the end of the document).

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