



International Heart and Vascular Disease Journal

Journal of the Cardioprogress Foundation



Continuous combined
multicomponent antithrombotic
therapy of patients with coronary
heart disease: the benefits
and risks

Biventricular pacing:
current trends and future
strategies

Features of the hospital
course of myocardial
infarction in patients
with impaired
carbohydrate
metabolism

Report of the European
Congress of Cardiology 2015

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Journal is an official publication of the
Cardioprogress Foundation

Printed in Russia

International Heart and Vascular Disease Journal

Journal of the Cardioprogress Foundation

Volume 3, Number 7, September 2015

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Editor's Welcome

Dear Colleagues!

The seventh issue of the International Journal of Heart and Vascular Diseases presented an editorial, review articles and original articles, and the results of two major congresses.

The editorial is devoted to studying the benefits and risks of the long-term combined multicomponent antithrombotic therapy in patients with coronary artery disease. Meta-analysis of large studies demonstrated that three-component antithrombotic therapy did not reduce overall mortality and the risk of bleeding increased. Individual choice of the drug, based on an assessment of the extent of its effect on platelet aggregation, can be one of the solutions for this problem.

Section 'Review articles' presented the data on efficacy and the prospects for biventricular pacing. Another article is devoted to the benefits of informative and communicative technologies (ICT) for personalized therapy. According to the authors, such an approach can increase the compliance of therapy and patient's satisfaction with quality of medical care.

Section 'Original articles' shows the results of three clinical studies. In particular, the hospital course features of myocardial infarction in patients with diabetes. There is the work, dedicated to the comparative evaluation of the effectiveness of radiofrequency ablation of pulmonary veins in patients with persistent atrial fibrillation, performed in the course of coronary artery bypass grafting, depending on the glomerular filtration rate of the kidneys. A researcher from Azerbaijan demonstrated features of structural-morphometric parameters of the left ventricle in women with chronic heart failure.

The magazine also presents the resume of the European Congress of Cardiology with brief results of international research and the report of the Russian National Congress of Cardiologists.

I invite everyone to cooperate with the magazine; we are waiting to hear from you original articles, literature reviews, discussions, opinions on the issues and recommendations for treatment and prevention.

R.G. Oganov
Chief Editor,
President of the Foundation 'Kardioprogress'

Continuous combined multicomponent antithrombotic therapy of patients with coronary heart disease: the benefits and risks

Mazur N.A.*

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Resume

Meta-analysis of the results, obtained in the long-term controlled studies, showed that treatment with aspirin or clopidogrel compared with placebo reduces significantly the risk of overall mortality, non-fatal myocardial infarction, stroke and vascular death by 25%. Combinatory therapy of aspirin and clopidogrel for patients with acute myocardial infarction did not affect overall mortality, and only the frequency of the combined endpoint decreased by 20% ($p < 0.001$) (non-fatal myocardial infarction, stroke, revascularization of the heart and cardiovascular death). Attempts to evaluate in numerous studies the possibility of increasing the effectiveness of long-term anti-thrombotic therapy in patients after acute coronary syndrome, by increasing the dose of antiaggregant or simply uncontrolled increase in the number of antithrombotic drugs — two antiaggregants in combination with one of the new oral anticoagulants, — showed no significant improvement in the treatment results. Because the frequency of the primary endpoint — overall mortality — did not change. Some reduction in the combined endpoint — a secondary point on its value — accompanied by a significant increase in the risk of bleeding, which is associated with an increased risk of death. The same results were obtained in the study PEGASUS (Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin) in patients with documented chronic coronary heart disease (CHD) (myocardial infarction). The finding data suggests that the uncontrolled increase in the dose of drugs and combinations thereof has no effect on overall mortality. One of the new trends in finding a solution to increase the therapy efficacy, without increasing the risk of bleeding, may be an individual choice of the drug, based on an assessment of the extent of its effect on platelet aggregation. Today, many studies have shown an interconnection between high residual platelet reactivity and mortality of patients with CHD. Based on these data, there have been proposed target levels of the platelet reactivity reducing by therapy with aspirin and clopidogrel, which allow the selection of an effective drug for each patient. This article devoted to the study of this issue.

Key words

Atherotrombosis, antithrombotic therapy, platelet aggregation, antiaggregants

In studies for the prevention of the atherothrombotic etiology diseases, despite the increase of gastrointestinal bleeding in 1–2 times, the presence of benefits of aspirin therapy is proven, which is demonstrated by a significant reduction in overall mortality [1]. The latest index makes it possible to assess the effectiveness of drug therapy or other interventions adequately. All other endpoints are of secondary importance for the patient, especially the so-called combined endpoints.

In addition to aspirin in low doses, up to 100 mg/day, another group of antiaggregants is also used for the prevention of these diseases — inhibitors of P2U12 platelet receptors (clopidogrel, tikagrelol, prasugrel). The results of the data meta-analysis from long-term controlled studies, compared with placebo, have shown that treatment with aspirin or clopidogrel reduces the risk of overall mortality, cardiovascular death and the risk of non-fatal myocardial infarction, stroke by 25%. When analyzed separately, the greatest risk reduction was observed against myocardial infarction — 1/3, stroke — 1/4, and death — only 1/6 [2]. A moderate reduction in the risk of diseases, which caused by atherothrombosis, is associated in particular with the presence of high residual platelet reactivity in many patients during antiplatelet therapy. To improve its effectiveness, attempts were made to use higher doses of aspirin and clopidogrel (up to 1500 mg and 150 mg respectively). The results showed that during prolonged antiplatelet therapy, higher doses only increase the risk of bleeding. In order to improve the efficiency of antiplatelet therapy, a combination of two antiplatelet agents is used, as well as attempts to accede one of the new oral anticoagulants to them.

A positive result of the first study, using the combination of aspirin and clopidogrel in patients with acute myocardial infarction, was defined only by evaluating the combined endpoint, which included nonfatal myocardial infarction, stroke, revascularization of the heart and cardiovascular death, the frequency of which turned out to be 20% lower ($p < 0.001$) [3]. Later on, there have been many studies, which included patients with acute coronary syndrome (ACS), patients with implanted stents in the coronary arteries, for which a double or multi-component antithrombotic therapy was carried out, the results of which were evaluated using meta-analysis. As the main criterion of benefit, the independent authors used indicator of overall mortality. Other indicators — secondary for the patient com-

bined points, on which there were based the findings of the authors who conducted the study, were compared with the risk of serious complications, particularly the risk of major bleeding that required to fill the loss of blood, or have caused death or disability of the patient. In one of the first meta-analyses of data, obtained from > 35 thousand patients [4], there was no difference in overall mortality ($p = 0.6$) with a group of patients, who received a single antiplatelet (aspirin or clopidogrel). However, there was a significant (by 1.5–3 times) increase in the number of major bleeding ($p < 0.001$) and a small (only by 9%) reduction in the number of large cardiovascular events — myocardial infarction, stroke. In another meta-analysis [5], obtained in the treatment of ACS patients ($n = 31\,286$) using dual antiplatelet therapy in combination with one of the new oral anticoagulants (antagonists of Xa factor, inhibitor of thrombin receptors), reduction in total mortality were also absent. The benefits of moderate decrease in risk of stent thrombosis is not higher than the risk of major bleeding. The number of major bleeding increased high significantly ($p < 0.001$) in the triple antiplatelet therapy compared to the control group.

The results of the meta-analysis were confirmed in another meta-analysis [6], which included data obtained at 25 643 patients with ACS on a three component antithrombotic therapy — a combination of two antiplatelet agents and one antagonist of factor Xa or inhibitor of thrombin receptors, in comparison with the results of treatment with two antiaggregants. Triple antithrombotic therapy, compared with standard dual antiplatelet therapy, had no effect on overall mortality ($p = 0.86$), although the frequency of reinfarction decreased slightly ($p = 0.02$). However, the number of major bleeding increased dramatically, in 3 times, particularly intracranial ($p < 0.001$). This indicates that the damage from the triple antithrombotic therapy outweigh the benefits.

We analyzed data collected from 30,866 patients with ACS, for whom to a dual antiplatelet therapy we joined one of the new oral anticoagulants (apixaban, rivaroxaban, direksaban, dabigatran), but only after 7–14 days from the onset of disease. In all studies, such therapy was accompanied by some reduction in the incidence only of the combined endpoint, but increased risk of major bleeding significantly (in 2 or more times) [7].

Thus, the attempts to increase the effectiveness of long-term antithrombotic therapy in patients with ACS, by increasing the dose of antiplatelet or simply

uncontrolled increase in the number of antithrombotic drugs, have not provided significant improvement in the results of treatment, and in particular the frequency of the primary endpoint — overall mortality. Some reduction in the combined endpoint (secondary point of its value) was accompanied by a significant increase in the risk of bleeding. Therefore, the results of the data meta-analysis, which was carried out by independent experts, point on the expediency of finding other ways to improve the long-term treatment of patients with different forms of coronary heart disease (CHD) with the help of antithrombotic drugs.

One of possible options in finding a solution to increase the therapy efficacy without increasing the risk of bleeding may be an individual choice of the drug, based on the extent assessment of its effect on platelet aggregation, particularly among patients with CHD who are in stable condition, including endured ACS. Today, many studies have shown an interconnection between high residual platelet reactivity (RPR), on the therapy, and mortality of patients with CHD [8–10]. Based on these data, target levels of reducing a platelet reactivity have been proposed, while on therapy with aspirin, clopidogrel [11]. Comparative evaluation of information content of methods for determining the aggregation platelet reactivity [12] showed that among the 5 studied methods only 3 methods are optical aggregometry; VerifyNow, Platelet works provided an opportunity to identify patients with high risk of endpoints. When using optical aggregometry, effective decrease of platelet reactivity level was suggested as < 46%, and when using the VerifyNow — less than 208 units. Platelet aggregation during the treatment, which was higher than mentioned parameters, is defined as the high RPR, which indicates a lack of effectiveness of the antiplatelet. The incidence of high RPR in the data analysis, obtained in many studies including > 12 thousand patients under the supervision, differed sharply — from 6% to 79%.

Therefore to assess the possibility of individual choice of the drug, in this study, platelet aggregation reactivity was evaluated in the same patients on different preparations, with a help of laser optical aggregometry and determining the content of the thromboxane B2 in urine [13]. Reduction of metabolite of thromboxane A2 in urine, when determining antiaggregation activity of aspirin, indicates an inhibition of the synthesis of endogenous inducer of platelet aggregation in patient's blood, which further confirmed the results obtained by optical aggregometry.

To assess the reproducibility of results obtained using both methods, for patients in a control period, platelet aggregation was determined twice at an interval of 1 week, without altering the therapy. The differences in these indicators were inaccurate, that allowed to consider the used methods as useful for assessing the results of therapy during dynamic monitoring of patients. Comparative evaluation of two dosage forms of aspirin (resorbable in the mouth and absorbed in the intestine) demonstrated greater efficacy of the drug, resorbable in the mouth. The difference of obtained data is probably explained due to less influence on platelet aggregation by aspirin metabolites, which formed during the first passage of blood through the liver after its absorption in the intestine; which was manifested especially clearly in determining the concentration of thromboxane B2 in the urine. Comparative evaluation of antiplatelet activity of trombo ASS and clopidogrel showed that the enteric form of aspirin affects the platelet aggregation less. The target level of its reduction was achieved during taking trombo ASS only for 28% of patients, while on therapy with clopidogrel — for 63% of patients. Average value of RPR, in this group of patients, was also significantly reduced by treatment with clopidogrel (43%) compared with aspirin (56%). The presence of high RPR on the aspirin therapy indicates that its enteric form is not sufficiently effective for the majority of patients (72%). For many of these patients, clopidogrel therapy provide a reducing of platelet aggregation reactivity to the target level. Among all patients only for 12% of them on clopidogrel and aspirin therapy, the achieving of the target RPR level was not indicated, i.e. there was a resistance to the action of studied antiplatelet.

In March 2015, the results of study PEGASUS-TIMI 54 were published (Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin), in which 21,162 patients were taken under the supervision, taking an aspirin in 1–3 years after suffering myocardial infarction [14].

All patients were divided into 3 groups: a) in the first group tikagrelol was attached to aspirin therapy at a dose of 90 mg 2 times a day; b) in the second group — tikagrelol was 60 mg also 2 times a day; c) in the third group patients received a placebo with aspirin. The median duration of observation was 33 months. The results of therapy: all-cause mortality on tikagrelol therapy did not differ from mortality in group on placebo therapy (in combination with aspi-

rin). In the first group 326 patients died (5.15%), in the second group — 289 patients died (4.69%), in the third group — also 326 patients died (15.16%), differences are unreliable ($p = 0.14$). Similar with studies involving patients with ACS, in this study, a decrease in the risk of combined endpoint was also noted: cardiovascular death, myocardial infarction and stroke. The absence of reducing overall mortality on the tikagrelol therapy, with decreasing cardiovascular mortality, is probably due to available significant increase (at > 2 times) in the number of major bleeding on dual antiplatelet therapy. It is known that among the survivors with this complication, mortality increases significantly.

Thus, the high RPR is recorded in 72% and 37% of patients with chronic CHD, on monotherapy with the enteric aspirin form or clopidogrel respectively. The oral form (absorption in the mouth) of normal aspirin is favorably than enteric form, taking into account not only its pharmacy-economic evaluation. Disaggregation activity of clopidogrel is significantly higher than the aspirin enteric form activity. Patients, in whom aspirin or clopidogrel monotherapy does not provide reducing RPR to the target level, had resistance to the antiplatelet action. Therefore, for these patients prolonged antiplatelet therapy may be carried out using new oral anticoagulants, in particular by means of rivaroxaban. This recommendation is based on data, obtained in the study ATLAS-2 TIMI 51 (Acute Coronary Syndrome Thrombolysis in Myocardial Infarction) [15], in which the efficacy and safety of double and triple antithrombotic therapy were also compared in patients with ACS ($n = 15\,526$).

To the standard therapy with aspirin and clopidogrel, 2.5 mg of rivaroxaban or 5 mg of placebo was added 2 times a day. The incidence of the combined endpoint decreased on triple antithrombotic therapy. However, overall mortality decreased at the expense of cardiovascular only on rivaroxaban therapy at a dose 2.5 mg — 2.9% and 4.5% respectively ($p = 0.002$). At the same time, the incidence of major bleeding increased > 3 times, including intracranial bleeding, especially at a dose 5 mg of rivaroxaban ($p < 0.001$). The reduction of overall mortality in patients, who were on the rivaroxaban therapy at a small dose, may be a justification for the use of this dose for patients with resistance to antiplatelet action; which of course requires a confirmation in additional studies.

Efficacy and safety of the long-term combined multicomponent antithrombotic therapy are not so obvious for all patients without the current control;

because it is useful in some patients, and it harms in approximately the same number of patients.

Conflict of interest: The author states the absence of potential conflict of interest, requiring a disclosure in this article.

References

1. Antithrombotic Trialists (ATT) Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009;373:1849–60.
2. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002,12;324 (7329):71–86.
3. CLARITY-TIMI 28 Investigators. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST elevation. *NEJM* 2005;352:1179–89.
4. Zhou Y-H, Wei X, Lu J, et al. Effects of combined aspirin and clopidogrel therapy on cardiovascular outcomes: a systematic review and meta-analysis. *www.plosone.org*. 2012, 7,2, e31642.
5. Komócsi A, Vorobcsuk A, Kehl D, Aradi D. Use of new-generation oral anticoagulant agents in patients receiving antiplatelet therapy after an acute coronary syndrome: systematic review and meta-analysis of randomized controlled trials. *Arch Intern Med*. 2012 Sep 24;1–911.
6. Obonska K, Navarese E P, Lansky A et al Low-dose of oral factor Xa inhibitors in patients with a recent acute coronary syndrome: A systematic review and meta-analysis of randomized trials. *Atherosclerosis* 2013, 229, 2, 482–90.
7. Oldgren J, Wallentin L, John H, Alexander JH, et al. New oral anticoagulants in addition to single or dual antiplatelet therapy after an acute coronary syndrome: a systematic review and meta-analysis. *Eur Heart J* 2013;34:1670–80.
8. Sofi F, Marcucci R, Gori AM, et al. Residual platelet reactivity on aspirin therapy and recurrent cardiovascular events — a meta-analysis. *Int J Cardiology* 2008;128 (2):166–71.
9. Parodi G, Marcucci R, Valenti R, et al. High Residual Platelet Reactivity After Clopidogrel Loading and Long term Cardiovascular Events Among Patients With Acute Coronary Syndromes Undergoing PCI. *JAMA* 2011; 306:1215–23.
10. Price MJ, Angiolillo DJ, Teirstein PS, et al. Platelet Reactivity and Cardiovascular Outcomes After Percutaneous Coronary Intervention. A Time-dependent Analysis of the Gauging Responsiveness With VerifyNow P2Y12 Assay: Impact on Thrombosis and Safety (GRAVITAS) Trial. *Circulation* 2011; 124:1132–7.
11. Bonello L, Tantry US, Marcucci R, et al. Consensus and future directions on the definition of high on-treatment platelet reactivity to adenosine diphosphate. *JACC* 2010; 56:919–33.

12. Breet N J, van Werkum J W, Bouman H J, et al. Comparison of Platelet Function Tests in Predicting Clinical Outcome in Patients Undergoing Coronary Stent Implantation. *JAMA* 2010;303 (8):754–62.
13. Mazur NA, Lomonosova AA, Zolozova EA, et al. Possibility correction of high residual platelets reactivity on the antiplatelet treatment. *Russian Cardiological Journal* 2012; 4 (96): 74–8.
14. Bonaca MP, Bhatt DL, Cohen M, et al. Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. *PEGASUS-TIMI 54*. *N Engl J Med* 2015; 372:1791–800.
15. Mega JL, Braunwald E, Murphy SA, et al. Rivaroxaban in patients stabilized after a ST-segment elevation myocardial infarction: results from the ATLAS ACS-2-TIMI-51 trial. *JACC* 2013 May 7;61(18):1853–9.

Biventricular pacing: current trends and future strategies

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Summary

Biventricular pacing has become an accepted therapeutic modality for medically refractory congestive heart failure (CHF). This new pacing strategy also known as cardiac resynchronization therapy (CRT) synchronizes ventricular contraction, which consequently results in improved pumping efficiency, enhanced left ventricular (LV) filling, and reduction in the severity of the mitral regurgitation. Biventricular pacing has substantially altered the natural course of ventricular failure, exerting its physiological impact through favorable ventricular remodeling, with a reduction in LV volumes and improvement in ejection fraction (EF). Despite this success of CRT and the recent expansion of its role in the treatment of patients with CHF, there remain many inherent limitations to the technology and its delivery. A significant minority of patients (about 30%) continue to remain non-responsive to this pacing strategy. This review will highlight biventricular pacing in its present form, will elaborate on strategies to enhance response to CRT, and outline future trends and synergies towards maximizing the potential benefit of CRT.

Key words

Heart failure, cardiac resynchronization therapy

Introduction

Biventricular pacing has become an accepted therapeutic modality for patients with medically refractory congestive heart failure (CHF). This new strategy of stimulation also known as intimate resynchronization therapy (CRT), synchronizes ventricular contraction

which consistently results in improvement of pumping efficiency, to filling left ventricular (LV) and to reduction of a degree of mitral regurgitation. Biventricular stimulation has essentially changed natural course of ventricular failure, showing the physiological influence by means of favorable ventricular remodeling, with

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reduction of volumes of LV and improvement in ejection fraction (Φ_B) [1]. This in turn, results in long-term clinical improvement, such as to the improved quality of a life, reduction of quantity of hospitalization concerning the improvement of heart failure (HF) and to reduction of total mortality [2, 3]. Standard indications for biventricular pacing which originally included patients with severe HF and signs of systolic dysfunction ($EF \leq 35\%$), with violations of intraventricular conduction and symptoms of HF (III and IV functional classes (EF) according NYHA classification), now tends to expansions for inclusion of patients with moderate symptoms of EF — I and II EF according NYHA) [4, 5].

Despite of success of CRT and expansion of its role in treatment of patients with CHF, there are many inherent restrictions of use of this technology still. A significant number of patients (~ 30%) continue to remain “non-responders” to such strategy of stimulation [1, 2, 6]. The present review will open to clinical physicians biventricular stimulation in its current form, will specify the strategy of increase in response on CRT, and will depict in general the future tendencies and joint actions of doctors to increase in potential benefit from CRT.

Physiology of CRT

Electric sequence of heart activation and CRT.

Electric sequence of heart activation is the important, determining factor of the coordinated cardiac contraction and relaxation and full cardiac function. Frustration in electric activation of heart, such as left bundle branch block (LBBB) in most cases can cause the asynchronous and detained reduction of lateral wall of LV, thus, reducing mechanical energy efficiency of the heart resulting in HF.

It is important to note, that intraventricular conduction disorders may lead directly to HF or can again exist as an integral part of the process of cardiac remodeling which complicate coincidence of severe cardiomyopathies. Ventricular Remodeling by HF is progressing process, which includes the degenerate and irreversible changes occur in the tissue, cellular and subcellular levels [7]. The described changes include: cardiomyocyte hypertrophy, regional changes in protein expression, necrosis, inflammation, fibrotic lesion of the conduction system of the ventricles, as a result is broken formation and dissemination of the pulse [8, 9]. Besides disturbances in the conduction system and the degree of asynchrony can be result of significant influence on a myocardium, because of presence of

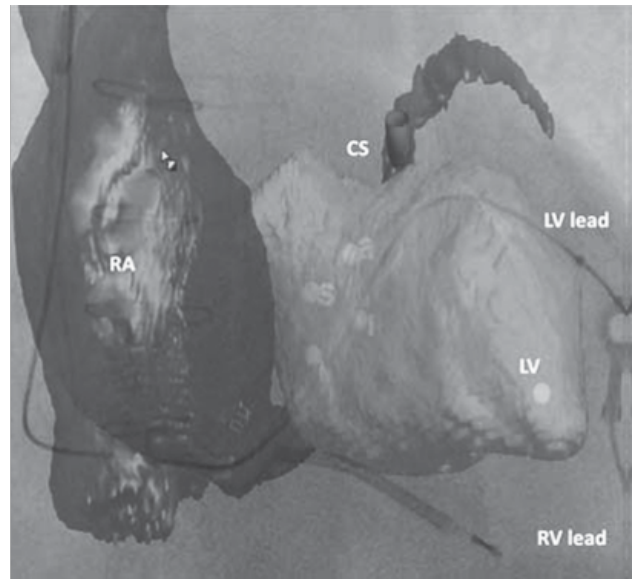


Fig. 1. United image (computed tomography + fluoroscopy).

Note: The figure shows the calculated integrated image of the heart, tomography plus fluoroscopy. Coronary sinus (CS), left ventricle (LV), right atrium (RA); right ventricular electrode (RV lead), left ventricular electrode (LV lead). Truong, et al. [36].

scarring, fibrosis, and an ischemia, which aggravate the nature of intraventricular conduction.

During the CRT, the stimulation of the right ventricle (RV) and left ventricular (LV) (figure 1), produce two wave front ventricular that which begin in LV and RV, raising its side, and heading in opposite directions toward each other. Advantage of CRT is in effective merger of the two wave fronts of depolarization; synchronizing walls of LV. Full synchronous electric activation of LV can be achieved further by change of time of distribution of stimulating pulses on atrioventricular and interventricular conduction system of the heart parts [10, 11].

Mechanical dyssynchrony

Inexactness of QRS complex, which has been written down with the help of surface ECG to predict the answer on CRT, due to the complexity and the different levels of electrical and mechanical dyssynchrony in heart damage. Dyssynchrony can exist at various levels, and can be atrial, atrioventricular, interventricular, intraventricular, and intramural (figure 2) [10]. The majority of researches have emphasized the importance of intraventricular dyssynchrony, as a primary factor promoting progressing of HF, and as predictor of response on CRT. Echocardiographic (ECG) research methods have filled this gap of knowledge by better understanding of the anatomical and functional aspects of cardiac pathology substrate of HF. M — mode, two-dimensional ECG, three-dimensional

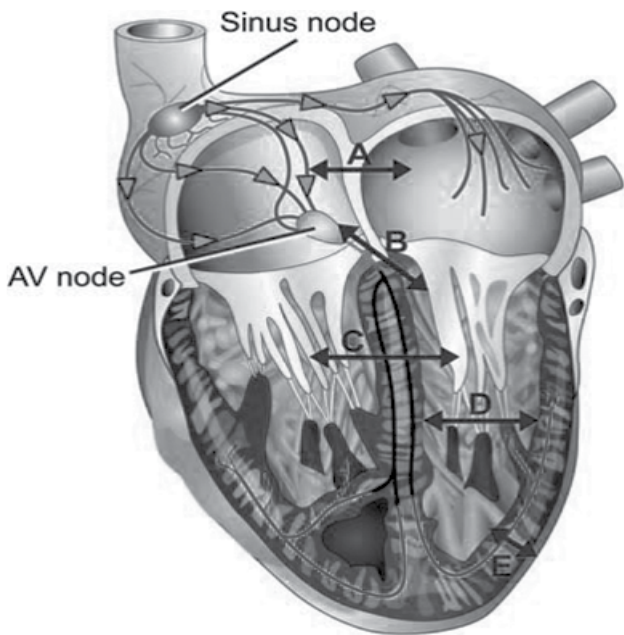


Fig. 2. Levels of mechanical dyssynchrony.

Note: The figure shows the levels of dyssynchrony in heart: (A) interatrial, (B) atrioventricular, (C) interventricular, (D) intraventricular and (E) intramural.

ECG and Tissue Doppler Visualization (TDV) provide the best understanding of a level of an initial parameter of dyssynchrony, sharp responses and symptoms favorable remodeling in response to CRT.

TDV facilitates measurement of dyssynchrony, estimating a direction and travel speed wall infarction in different segments of the LV [11]. The difference of speed of time of rise up to maximal in various segments can be appreciated, and many single-site researches have shown good attributes of the answer on CRT. However, with TDV, passive movement of a myocardium cannot be distinguished between active reductions that take place at an estimation of the patient with ischemic cardiomyopathy, which can have segments with myocardial scar changes. Besides that, TDV still remains prevailing two-dimensional (2D) ECG technology, and demands high frequency of the staff, and it limits the sanction and quality of the image.

Despite of promising results in small works when two multicenter prospective researches were carried out, ECG methods unconvincing predicted the answer on CRT. Researches PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) [12] and [13] were multicenter, developed for an estimation of efficiency of parameters of dyssynchrony in definition of the answer on CRT; in researches [13] — by the patients with nar-

row complexes of QRS. Research PROSPECT was not randomized, prospective, observant research, which involved 426 patients who underwent implantation of the device according to the selection criteria. Before implantation the patients were investigated for dyssynchrony by different methods, for an estimation of intra- and interventricular dyssynchrony by using of the M-mode and TDV. The 6-month's final points including the incorporated clinical report have been analyzed: Death rate from all reasons, hospitalization concerning worsening of HF, a class on NYHA, the general inspection of the patient, and 15%-s' reduction of the end-systolic volume of the left ventricle (LV CSR) in comparison with an initial condition. Despite of training on a workplace on purchase of skills of standard diagnostics and results of three main laboratory blind studies, there was not any ECG parameter of reaction on CRT.

Research [13] randomized, multicenter research executed for an estimation of parameters suitability of dyssynchrony in the forecast of the answer on CRT by the patients with narrow complexes of QRS. 250 patients with HF III or IV FC on NYHA, EF \leq 35% and duration QRS <130 msec were randomized on groups with CRT and without CRT. Dyssynchrony has been determined with help of M — mode of ECG and TDV parameters. For 6 months of research these two groups had no distinctions in final points as a result of increase in peak consumption of oxygen, at least, on 1.0 ml / kg of weight in body / minutes. While these two researches have not defined parameters dyssynchrony to predict CRT, that is distinct from the big number of smaller researches which to some extent have shown some optimism concerning advantage of CRT. It, probably, occurred because of differences in study design, weak and doubtful final points, methods, which have been used for reception of results as well as variability and bad standardization. Now it is known that Research (EchoCRT) is in a stage of realization, for studying the above mentioned problems by patients with narrow complexes QRS [14].

Newer echocardiographic techniques using speckle tracking for measurement of a beam spectrum develop as good parameters of studying predictors of response to CRT. Until now, the method speckle tracking has been checked up only in randomized, small research [15]. For tracking speckle-tracking use, advantage of interference in a beam of ultrasound, which creates small color defects of the digital image on two-dimensional, an echo to images (figure 3).

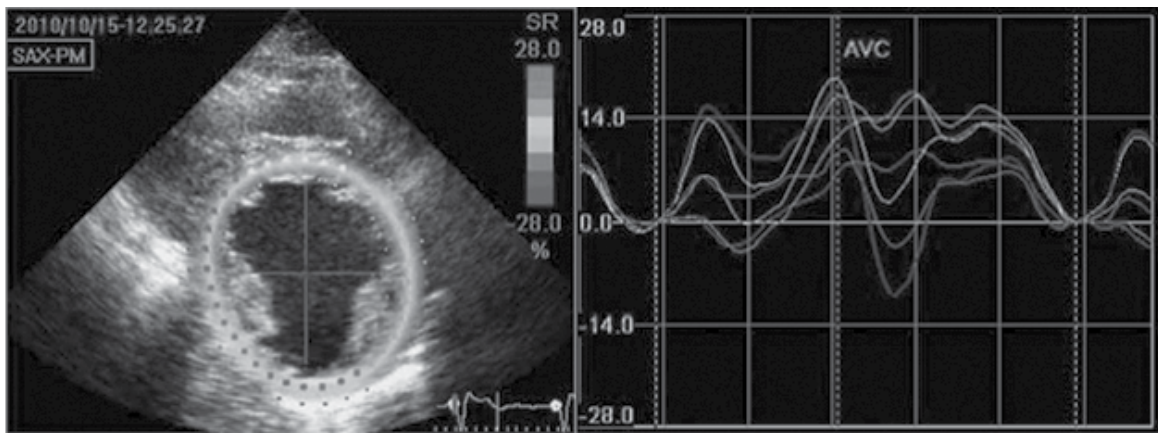


Fig. 3. Tracking speckle-tracking strain imaging.

Note: the left panel shows the two-dimensional images; the right panel shows the curve of segmental strain in time for the left ventricle.

Other methods, such as magnetic resonance tomography (MRT) and computer tomography (CT) of heart offer an opportunity of association of measurements of dyssynchrony for presence of the scars in the myocardium, and studying the anatomy of the coronary veins for implantation of left ventricular electrode. Small researches have shown promising results. Unfortunately, still there is not present big multicenter researches, which have estimated the above-stated technologies of diagnostics.

Researches devoted CRT

Heavy HF

Some thousand patients with heavy HF III and IV FC (NYHA) have been investigated in randomized, controllable, clinical researches with indisputable proofs of that CRT improve the clinical forecast of illness. Below it will be briefly discussed 4 researches in which patients with HF from moderate up to a heavy degree have been included, with obvious behavioral problems (wide complex QRS ≥ 120 ms) and low EF LV ($\leq 35\%$) which have helped to strengthen role of CRT at such population of patients.

Research MUSTIC (Multisite Stimulation in Cardiomyopathies) is one of the first among researches in which studied influence of CRT by 67 patients with heavy HF, normal sinus rhythm and duration of QRS > 150 ms. It was blind, randomized, controlled, crossover study, comparing clinical reaction of patients for the period inactive CRT of stimulation with active CRT stimulation 3 months during each period. By patients who have finished both phases of research, atrio-biventricular stimulation has considerably improved exercise tolerance, quality of a life and has reduced quantity of hospitalization con-

cerning HF [16]. A multicenter, randomized, clinical research MIRACLE (Multicenter InSync Randomized Clinical Evaluation) randomized 453 patients with HF III and IV FC (NYHA) to CRT with optimum pharmacological treatment against only one optimum pharmacological therapy [1]. Other criteria of inclusion were EF LV $\leq 35\%$ and duration QRS ≥ 130 ms. Significant improvement of symptomatic — FC HF (NYHA) both quality of a life, and the functional status — 6 minutes a distance of walking is marked. These improvements were accompanied by increase of ventricular remodeling and reduction of risk by 40% of the incorporated final points, such as death, quantity of hospitalization concerning heavy HF by patients with CRT. Other sign research was influence of CRT on morbidity and mortality in HF — CARE-HF (Cardiac Resynchronization in Heart Failure) in which 813 patients participated. They had III and IV FC HF (NYHA) and have shown advantage of CRT of optimal medical therapy [3]. It is revealed 37% reduction of relative risk in final points, such as hospitalization concerning cardiovascular event, general death rate. It is interesting, that criteria of inclusion for this research were a little more strict: besides EF LV $< 35\%$, it was necessary, that the patients had wider complexes QRS ≥ 150 ms or QRS 120–149 ms with additional presence of mechanical dyssynchrony, determined with help of ECG. Research COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) in comparison of medical therapy, stimulation and defibrillation by patients with HF was the biggest trial, executed with participation of patients with HF [2]. In total 1520 patients with III and IV FC HF NYHA, EF LV $< 35\%$, and QRS > 120 ms were randomized on groups with optimum medical therapy (OMT), biventricular stimulation (CRT-P) +OMT and biventricular

stimulation with defibrillator (CRT-D) + OMT. Patients with CRT-E and CRT-D have shown significant reduction of number of hospitalization concerning worsening of CH with additional reduction of death rate at CRT-D. However in research it was impossible to compare CRT-E with CRT-D, thus, there was open an important question concerning a choice of an adequate kind of the device.

Easy and moderate HF

Early research works, such as 'Intimate resynchronization therapy for treatment of HF by patients with ventricular disturbances in behavior and malignant ventricular tachyarrhythmia (CONTAK-CD) and «Effects of cardiac resynchronization on disease progression by patients with diastolic dysfunction of LV» (MIRACLE ICD-II), with a study of CARE-HF, have shown, that CRT can be effective in group of patients with less heavy HF [17–19]. Proofs of favorable remodeling of LV marked the opposite in both researches by patients with symptoms of HF II FC (NYHA). These results further have been checked up in researches REVERSE-HF (REsynchronization reVerses Remodeling in Systolic left ventricular dysfunction) [5], MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) [4] and RAFT (Resynchronization/Defibrillation for Ambulatory Heart Failure Trial) [20].

610 patients with EF LV <40%, duration of complex QRS \geq 120 ms, I and II FC HF (NYHA), randomized to CRT+ or CRT- participated in research REVERSE-HF. In this research, it was presented differences in duration of the remote supervision between patients in Europe and Northern America, which were observed within 2 years and one year accordingly. A primary final point in this research was the percent of patients, which worsened a clinical total point (which included the quantity of hospitalization concerning deterioration HF, transition in other group of research or deterioration FC (NYHA) points on quality of a life). Preliminary set secondary final point there were changes in EDV LV. During 12 months of research, there was no significant distinction in primary final points: a parity of patients with the worsened result though significant reduction of EDV LV- was observed at CRT+. During 24 months in the European cohort, 19% at CRT + vs 34% at CRT- there was the deterioration of total clinical reaction ($p=0,01$). Amazing reduction of EDV LV was observed in CRT+ — 27.5 + 31,8 ml / m² vs 2.7 + 25.8 ml / m² at CRT-.

Research MADIT-CRT included 1820 patients from > 110 centers in Europe and Northern America. By surveyed it should be EF LV <30% and duration QRS > 130 ms and FC I or II HF (NYHA). Patients were randomized on groups of patients with implantable cardioverter-defibrillators (ICDs) and with CRT-D devices. Almost by 2/3 patients in research MADIT-CRT was QRS > 150 ms and 80% of patients had II FC HF NYHA. Essential distinctions were observed by 17,2% of patients in group SRT-D vs 25,3% of patients in group IKD on the tested incorporated final points of death and quantity of hospitalization concerning weighting of HF ($p < 0,001$). The opposite remodeling it was studied for tracking an outcome of illness with reduction of EDV LV by 57 ml in group SRT-D vs 18 ml in group IKD ($p < 0,001$). 41%-s' reduction of risk of hospitalization concerning HF in group MADIT-CRT vs 53%-s' reductions of time of the first hospitalization concerning deterioration HF in research REVERSE has been revealed. It is interesting, that by women the smaller quantity of hospitalization concerning weighting HF and general death rate with improved by the opposite remodeling of LV was observed in comparison with sick men [21].

Recently executed research RAFT included 1798 patients with II and III FC HF during the 40-month's period. Primary results by quantity of death and/or hospitalization in connection with deterioration of HF are marked by 33,2% of patients in group SRT-D vs 40,3% in group IKD. At stratification on weight HF it has been revealed reduction by 27% of relative risk in primary final points in group of patients with II FC HF has been revealed. Despite of advantage of CRT, substantial growth of a level of early adverse events it has been marked in this group. It is interesting, that CRT rendered independent useful influence both on mortality and on quantity of hospitalization concerning deterioration of HF in group of patients with II FC HF NYHA [20]. It is remarkable, that in all three above mentioned researches, strengthened reaction on bi-ventricular stimulation was observed at patients with wider QRS (> 150 ms) and by those patients by whom it was observed morphology QRS on type LBBBG.

Maximal increase in reaction on SRT

Despite of these obvious advantages, there are some unresolved questions, and most actual of them is that up to 1/3 patients do not answer and do not receive effective advantage from SRT. Because of high prevalence, disease and death rate by CHF and high cost of treatment it is impossible to underestimate value

of increase of the maximal reaction of all patients on SRT. Selection of the correct patient and understanding of differences between patients can predict distinctions in reaction on SRT, the use of the approaches determined for the patient, for implantation of an electrode in LV, with adequate programming the device and corresponding postoperative observation can raise the efficiency of implantation and the answer on SRT.

Morphology QRS, electric activation and comorbidity

After an establishment of the reason resulted in deterioration function of LV and choice OMT, selection of patients on SRT still depends on presence of wide complex QRS on a superficial electrocardiogram. Duration of complex QRS as “the sacred Grail” used for selection of patients and the forecast of the answer on SRT seems to be the super-simplified attribute. Value of duration of QRS complex decreases in connection with that there are patients with the big duration of complex QRS and minimal mechanical dyssynchrony, while there are patients with narrow complexes QRS and significant mechanical dyssynchrony [22]. The big duration of complex QRS can be an attribute of heavy cardiomyopathy and, in spite of the fact that in cases where the best choice of treatment of SRT, this attribute can not reserve natural current of illness. Other approaches investigating bases “SRT the caused changes” in duration QRS on an electrocardiogram, morphology QRS, were not able to predict structure of electric activation of ventricles, but can have some ability to predict response on SRT [23, 24].

Work [10] allows to assume, that it can be the significant difference of the clinical answer by the patients with LBBBG and without LBBBG. As a rule, by LBBBG the sequence of electric activation is distributed aside tops with a delay of distribution in lateral and poster-lateral parts of LV. As the delay of distribution of electric activation is accompanied by a delay of mechanical activation in the same territory, and the choice of a lateral wall for implantation of an electrode in LV is intuitive. Especially even by classical LBBBG when there is a high level of heterogeneity of activation in structures of LV, accompanied with distinction of the functional block. Results of recent works assume, that by patients with morphology QRS on type nonLBBBG, in group of patients with uncertain infringements of intraventricular conduction there is more the worse result, while by the patients

with the right bundle branch block Gis (RBBBG) the results are the worst [25–27]. Patients with RBBBG, probably, do not answer on SRT, the same as the patients with LBBBG, so as by these patients there is no dyssynchrony of LV, suitable for SRT [28]. In addition, patients with RBBBG usually have the accompanying dysfunction of RV, the increased pressure in pulmonary arteries, and more expressed infringements of carrying out. In spite of the fact that only the quarter of patients with RBBBG can have infringements of passage of LV, comparable with LBBBG, almost 50% from them have some delay, which is possible for correcting by SRT [29]. The reduced response on SRT in group of patients without LBBBG can be explained by insufficient changes in a technique of implantation of an electrode, despite of the changed features of front wave of depolarization. By the patients with RBBBG is doubtful, whether really the leading part of an electrode in LV is necessarily to synchronize heart or adequately designed pulse of stimulation from electrode RV can correspond to synchronization.

Except of duration, QRS there are other clinical characteristics, which can influence on ventricular remodeling and an outcome of illness. It is important to recognize, that presence of RV dysfunction, pulmonary hypertension, rumen severe myocardial damage and a marked increase in heart can influence the clinical answer on SRT [30, 31]. In addition coexisting accompanying pathologies, such as a terminal stage of renal failure, an anemia, severe coronary artery disease, etc. can influence the answer at SRT [32]. Though the majority of researches has shown, that patients with ischemic and with not ischemic cardiomyopathies receive the profit from SRT, the tendency of reception of good reaction on SRT was observed in not ischemic group of patients [4, 33, 34].

Reception of images for increase in patient — specific approaches

Reception of the image is an integral part of treatment with use of SRT. Visualization is necessary at all three stages of treatment, i.e. before procedure (for selection and planning of implantation), during procedure (implantation of the device) and after procedure (supervision and optimization). Unfortunately, any unique technique of visualization cannot guarantee performance of all these three aspects of treatment. As the majority of methods of visualization gives the additional information relative cardiac structure (fluoroscopy, CT of coronary venous anatomy) and functions (ECG for mechanical dyssynchrony), the combi-

nation of some from these technologies can help to facilitate a choice of the patient and planning of procedure [35]. Preprocedural estimation of mechanical dyssynchrony, and intraprocedural integration with venous cartography can be useful strategy, but still there is a necessity of improvement in order it will be more practical, reliable and checked up in the future. Conceptually intended stimulation sounds very attractive because the data from small retrospective researches have shown, that stimulation in a place of maximal dyssynchrony and avoiding of the scar area can lead to the best results. Though ECG would be seemed natural suitable for use during procedure to demonstrate the most backward segments, for carrying out LV electrode, is forces heavy and technically causing a pressure technique.

Not combined methods of visualization, such as CT and MRT have an ability to give the information, thus eliminating the requirement for methods of the integrated image [36]. Multidetector CT can provide with the important information on anatomy of coronary veins, contractile function of LV and mechanical dyssynchrony, just as integrated information concerning the relation of a venous branch with a segment of dyssynchrony and/or scar [18, 33]. MRT is strenuously studied its ability to calculate more precisely dyssynchrony, and to improve selection of patients [37]. Now, efforts on application of MRT also are focused in development of new methods to characterize architecture and ultrastructure myocardial fibers, as well as the three-dimensional image of a pressure of a myocardium. MRT, however, remains the urgent offer by this category of patients taking place in bad condition, many of which already have earlier implanted devices.

Strategy of stimulation: whether can we achieve the greater success?

Biventricular stimulation improves synchronism of reduction of LV through stimulation late activated its areas. A usual method of implantation of LV electrode is trans-venous, as a result with accommodation it in one of branches of veins of coronary sine (CS). As soon as vascular access will be achieved, the stimulating electrode canceled by directing introducer and moves ahead through it to branches of CS of the second or third order. Still there are contradictions concerning the best location of an electrode and a choice between optimum anatomic position. The question on place criteria of implantation, or in a segment with maximal mechanical dyssynchrony, or area of the

maximal electric delay, is still discussed. The current tendencies continue to remain simplified and specify, that LV electrode will be placed in optimum according anatomy place of stimulation (usually determined as lateral and poster-lateral wall of LV) [38]. However insufficiently favorable clinical answer by almost 1/3 patients receiving CRT, offers restrictions in this approach to a choice of place of stimulation. Complex interaction between unpredictable character of activation of LV, frequently a casual choice of a final place of stimulation (dictated by presence of suitable venous branch), and the changes caused by stimulation of RV in electric and mechanical structure of activation LV could be a potential explanation of high percent of the patients who are not answering on CRT (even by patients with anatomically optimal position of LV electrode). It is little known about segmentary influence of localization of LV electrode within the limits of the elected substrata. Recently finished work has shown, that apical implantation of LV electrode is connected with the worse results of CRT; preferable arrangement of LV electrode at the basis / on the average segments of the ventricle, can improve results [39]. These results have been recently proved in the analysis of research MADIT-CRT [40].

Small retrospective researches have shown, that stimulation of a place of maximal dyssynchrony can strengthen the reverse remodeling and, hence, improve the forecast of illness. In all these researches, an estimation of the relation an electrode / segment was a retrospective assumption without true integration of image [41]. This approach is limited now to features of anatomy of veins. As CRT is the form of electric therapy for synchronization of chaotic electric activation of heart, is meaningful to try to designate the purpose of implantation of LV electrode the area of the maximal electric delay [38]. Some invasive and non-invasive methods of visualization have been offered for definition of the area of LV with the latest electric activation. In spite of the fact that three-dimensional contactless endocardial LV charting it provides the exact characteristic of sequence of electric activation of LV remains impractical for its performance during implantation of LV electrode. The more practical strategy is intraprocedural use of intracardiac electrogramme, measurement of an electric delay on LV electrode for individual implantation of LV electrode. The electric delay is calculated as a difference of time between the beginning of complex QRS on a superficial electrocardiogram and detectable signal of maximum delays on LV electrode. This

delay is corrected with beginning of QRS (registered simultaneously with LV), expressing it as percent from initial duration of QRS [42]. Stimulation of heart in zones with the big electric delay on LV electrode has been connected with improved sharp hemodynamic answer and an outcome of illness. Good venous angiogram is the important part of procedure of implantation as the detailed venous map helps to outline various accessible variants. Improving technologies (smaller on the size and multipolar electrodes) will allow the doctor who is carrying out implantation to choose specific "not cicatrized" zones in an optimum anatomic place of position or within the limits of segments with a significant electric mechanical delay. Recent efforts on electric mapping of venous system for definition of presence of zones of cicatricial changes and a degree of an electric delay can be executed by use of new electro-anatomic methods of visualization.

Though location of RV stimulating electrode, always goes down to the status of an electrode of the second order, it is remarkable, that it can influence the front of a wave depolarization of LV and, hence, on resynchronization. The previous work has shown, that changes of RV electrode can change the sequence of activation of LV the same as also mechanics of LV [43]. There are data that the relation RV/LV can influence an outcome of illness in its turn. However, based on existence of the various reasons of a substratum of dyssynchrony, localizations LV electrode, sizes of LV and it is probable, that presence or absence of scar, homogeneous position of RV electrode is improbable, and, that the identical effect will take place. Actually, there is a big requirement of definition of individual approaches for each patient which should be estimated prospectively.

Taking into account restrictions usual trans-venous way of implantation, have been offered some alternative approaches of implantation. There is some potential at newer endocardial and epicardial approaches that can change the field of play [44, 45]. Biventricular endocardial stimulation has yielded promising results with high clinical and improved hemodynamic parameters of LV in comparison with epicardial biventricular stimulation [46]. Endocardial stimulation can provide more physiological electric activation when electric activation begins in endocardium and is distributed to epicardium [47]. Some methods have been offered, namely: transaortic, transeptal through interatrial or interventricular partitions and transapikalny. Transeptal approach-

es through subclavian vein can lay a way, which will combine endocardial implantation of LV electrode with usual implantation of the device. Researches of last time informed, that individually based approach with regular testing has shown many places of optimum implantation of LV electrode which strongly differed from usual installation of an electrode through CS, to stimulation of a lateral wall and methods of implantation under control of ECG. Research has shown, that when it is necessary to optimize a site of an electrode, there is a significant difference between various patients [42]. This research has presented certificates that the best place of stimulation of LV is not only specific to each patient, but also that it is difficult to determine beforehand given place. However, some questions concerning a problem of safety, such as thromboembolism or an infection of endocardial electrode demanding extraction, it is necessary to discuss [48]. Last preliminary work also has shown, that bench ventricular excitation using two separate LV electrodes, placed in coronary venous system, can improve clinical and ECG results [49]. The further researches, however, have confirmed the superiority and safety of any multiplace or endocardial stimulations over conventional methods.

By 8–10% of the patients carrying implantation of biventricular pacemaker, implantation of LV electrode is not possible for the various reasons: impossibility of cannulation CS, absence of the suitable venous branches, insufficient stability of an electrode, stimulation of phrenic nerve, etc. Surgical epicardial implantation of LV electrode is a method of a choice by these patients. Some surgical methods have been offered for epicardial implantation of LV electrode, which include such methods as front or side mini thoracotomy, VATS technique and robotic systems of implantation [44]. Especially it is developed the modern conservative percutaneous directions with a technique of implantation of an electrode under xiphoid process. The most important questions of this approach should be still addressed to strategy of fixing of an electrode, and mechanisms of implantation in order that the epicardial electrode casually has not damaged vessels of a coronary arterial channel.

Postimplant supervision: strengthening of opportunities of the patient, the doctor and the device

The modern condition of supervision of the patient after implantation of the device falls short in several areas, in particular: optimization of AV and VV inter-

vals, discussion of the diagnostic information of the implanted device, use of these data for stratification of risk of the patient, optimization of medicinal therapy and, that is even more important, early definition and treatment of patients non-responders.

There are interesting data, which suggest, that adjustment and optimization of AV interval can lead to increase of hemodynamic efficiency, however, there is an insufficient information on influence of this optimization on character of electric activation. The maximal improvement of systolic functions of LV is reached by short, AV interval, which allows the full capture of ventricles by two fronts of a wave of excitation caused by stimulation [50]. Exact value of this AV delay which improves synchronism, is a variable, being specific to each patient.

Recently it has been shown [32], that essential percent of not answering on biventricular stimulation can actually benefit from optimization AV of an interval. Whether AV optimization is necessary for each patient during implantation of the device, it is disputably, though it seems evident, that patients will require optimization of these intervals because of a significant degree of distinctions of position of atrial, RV and LV electrodes, and because of significant distinctions between patients on a principal cause of disease, and because of presence of cicatricial changes of myocardium. Till now the final conclusion is still absent, even that in researches FREEDOM and SMART-AV it has been assumed that "brilliant" parameters of adjustment can work only well [51, 52]. In both researches there were significant restrictions in their design, the group has been appreciated, the decision on performance of research has been preliminary accepted, and force of research has been calculated.

One more factor, which influences on activation of ventricle during time of biventricular stimulations, is the delay of time of interventricular (VV) activation. Modern devices SRT have an opportunity of programming of VV interval of the stimulation, allowing simultaneous or consecutive stimulation LV-RV with a various degree of preexcitation of LV or RV. These adjustments together with adjustments of AV interval can make set of examples of ventricular repolarization, offering by the patients with intraventricular conduction disturbances with intact AV conduct, the certain degree of the control of three fronts of the activation going from BBBG and from RV and LV of electrodes. Though at the majority of patients, simultaneous RV-LV stimulation results in good hemodynamic results,

preexcitation of LV before RV, apparently, further optimizes synchronism, and increases systolic function of LV by the patients [53]. It is necessary to note, that others randomized researches have not shown significant clinical effect from programming an interval of VV delay [54, 55].

Devices SRT write down and provide with the detailed information about activity of the patient, frequency of intimate reductions, independent electric activity, transthoracic resistance and the nearest future events, they also provide with the hemodynamic data in real time [56, 57]. Occurrence of remote monitoring of implanted devices has enabled automatic transfer of the outpatient information in real time concerning frequency of intimate reductions, physical activity, the beginning of development of interstitial pulmonary edema (measurement transthoracic resistance), etc. through the Internet. Continuation of work on improvement of technology of a sensor control has allowed transfer through a global network of such important parameters, as arterial pressure, weight, saturation of blood by oxygen, etc. The control of these patients and their devices over the Internet provides an opportunity for various adjacent experts to transfer the data of the patient, and provide more personalized form of treatment. The Strategies based on the control by the sensors will continue to grow and will be addition for simplification of stratification of risk, will allow predicting early risk of acute decompensation, will allow to automate therapeutic interventions, and will improve outcomes of illness.

The multidisciplinary approach in treatment and supervision of these patients, apparently, becomes a new direction in the future. More often, patients not answering on therapy usually pay to themselves attention by aggravation of HF or by increase in quantity of hospitalization; one of the purposes of the integrated multidisciplinary approach is the early revealing of a problem with Preventive medication regimen modification or parameters of adjustment of the device, for the prevention of acute decompensated disease. Teamwork of experts of all disciplines (electrophysiology, HF and experts on visualization) can facilitate adequate selection of patients with SRT, optimization of SRT device and careful titration of medicamentous therapy in postimplantation period. Despite of understanding, that the multidisciplinary model would provide improvement of the control over the patient, influence of such integrated services should be still appreciated in the future.

Conclusion

Now biventricular stimulation is recognized as safe and effective therapeutic strategy for treatment of patients with refractory to medicamentous therapy 3CH. Implanted SRT devices through synchronized stimulation of RV and LV can improve contractility of the sick heart and thus change natural current of illness. Though biventricular stimulation rendered the big influence on treatment of patients with HF, its full potential is not realized yet. For the following some years, understanding of mechanical ventricular dyssynchrony for the reasons resulted in it and the answer on SRT depending on a place of stimulation will be improved. Wider opportunity of application of innovative forms of stimulation ventricular (s) by the patients with HF will be presented at narrow and wide complexes QRS. The big uniformity in definition of the answer on SRT both early definition and treatment not answering on SRT of the patients will improve its applicability and, hence, profitability.

Conflict of interest: None declared

References

- Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;346:1845–53.
- Bristow MR, Saxon LA, Boehmer J, et al. Comparison of Medical Therapy P, Defibrillation in Heart Failure I. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure [see comment]. *N Engl J Med* 2004;350:2140–50.
- Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;352:1539–49.
- Moss AJ, Hall WJ, Cannom DS, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. *N Engl J Med* 2009;361:1329–38.
- Linde C, Abraham WT, Gold MR, et al. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. *JACC* 2008;52:1834–43.
- Nelson GS, Berger RD, Fetis BJ, et al. Left ventricular or biventricular pacing improves cardiac function at diminished energy cost in patients with dilated cardiomyopathy and left bundle-branch block. *Circulation* 2000;102:3053–9.
- Chakir K, Daya SK, Tunin RS, et al. Reversal of global apoptosis and regional stress kinase activation by cardiac resynchronization. *Circulation* 2008;117:1369–77.
- Spragg DD, Leclercq C, Loghmani M, et al. Regional alterations in protein expression in the dyssynchronous failing heart. *Circulation* 2003;108:929–32.
- Chakir K, Daya SK, Aiba T, et al. Mechanisms of enhanced beta-adrenergic reserve from cardiac resynchronization therapy. *Circulation* 2009;119:1231–40.
- Auricchio A, Fantoni C, Regoli F, et al. Characterization of left ventricular activation in patients with heart failure and left bundle-branch block. *Circulation* 2004;109:1133–9.
- Bax JJ, Ansalone G, Breithardt OA, et al. Echocardiographic evaluation of cardiac resynchronization therapy: ready for routine clinical use? A critical appraisal. *JACC* 2004;44:1–9.
- Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. *Circulation* 2008;117:2608–16.
- Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. *N Engl J Med* 2007;357:2461–71.
- Holzmeister J, Hurlimann D, Steffel J, Ruschitzka F. Cardiac resynchronization therapy in patients with a narrow QRS. *Curr Heart Fail Rep* 2009;6:49–56.
- Delgado V, Ypenburg C, van Bommel RJ, et al. Assessment of left ventricular dyssynchrony by speckle tracking strain imaging comparison between longitudinal, circumferential, and radial strain in cardiac resynchronization therapy. *JACC* 2008;51:1944–52.
- Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001;344:873–80.
- Abraham WT, Young JB, Leon AR, et al. Effects of cardiac resynchronization on disease progression in patients with left ventricular systolic dysfunction, an indication for an implantable cardioverter-defibrillator, and mildly symptomatic chronic heart failure. *Circulation* 2004;110:2864–8.
- Lozano I, Bocchiardo M, Achtelek M, et al. Impact of biventricular pacing on mortality in a randomized crossover study of patients with heart failure and ventricular arrhythmias. *Pacing Clin Electrophysiol* 2000;23:1711–2.
- Cleland JG, Freemantle N, Daubert JC, et al. Long-term effect of cardiac resynchronization in patients reporting mild symptoms of heart failure: a report from the CARE-HF study. *Heart* 2008;94:278–83.
- Tang AS, Wells GA, Talajic M, et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. *N Engl J Med* 2010;363:2385–95.
- Arshad A, Moss AJ, Foster E, et al. Cardiac resynchronization therapy is more effective in women than in men: the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) trial. *JACC* 2011;57:813–20.
- Yu CM, Chan YS, Zhang Q, et al. Benefits of cardiac resynchronization therapy for heart failure patients with narrow QRS complexes and coexisting systolic asynchrony by echocardiography. *JACC* 2006;48:2251–7.
- Lecoq G, Leclercq C, Leray E, et al. Clinical and electrocardiographic predictors of a positive response to cardiac resyn-

- chronization therapy in advanced heart failure. *Eur Heart J* 2005;26:1094–100.
24. Heist EK, Taub C, Fan D, et al. Usefulness of a novel 'response score' to predict hemodynamic and clinical outcome from cardiac resynchronization therapy. *Am J Cardiol* 2006;97:1732–6.
 25. Wokhlu A, Rea RF, Asirvatham SJ, et al. Upgrade and de novo cardiac resynchronization therapy: impact of paced or intrinsic QRS morphology on outcomes and survival. *Heart Rhythm* 2009;6:1439–47.
 26. Bilchick KC, Dimaano V, Wu KC, et al. Cardiac magnetic resonance assessment of dyssynchrony and myocardial scar predicts function class improvement following cardiac resynchronization therapy. *JACC Cardiovasc Imaging* 2008;1:561–8.
 27. Zareba W, Klein H, Cygankiewicz I, et al. Effectiveness of cardiac resynchronization therapy by QRS morphology in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT). *Circulation* 2011;123:1061–72.
 28. Egoavil CA, Ho RT, Greenspon AJ, Pavri BB. Cardiac resynchronization therapy in patients with right bundle branch block: analysis of pooled data from the MIRACLE and Contak CD trials. *Heart Rhythm* 2005;2:611–5.
 29. Fantoni C, Kawabata M, Massaro R, et al. Right and left ventricular activation sequence in patients with heart failure and right bundle branch block: a detailed analysis using three-dimensional non-fluoroscopic electroanatomic mapping system. *J Cardiovasc Electrophysiol* 2005;16:112–9.
 30. Stern J, Heist EK, Murray L, et al. Elevated estimated pulmonary artery systolic pressure is associated with an adverse clinical outcome in patients receiving cardiac resynchronization therapy. *Pacing Clin Electrophysiol* 2007;30:603–7.
 31. Bleeker GB, Schalij MJ, Van Der Wall EE, Bax JJ. Postero-lateral scar tissue resulting in non-response to cardiac resynchronization therapy. *J Cardiovasc Electrophysiol* 2006;17:899–901.
 32. Mullens W, Grimm RA, Verga T, et al. Insights from a cardiac resynchronization optimization clinic as part of a heart failure disease management program. *JACC* 2009;53:765–73.
 33. Molhoek SG, Bax JJ, van Erven L, et al. Comparison of benefits from cardiac resynchronization therapy in patients with ischemic cardiomyopathy versus idiopathic dilated cardiomyopathy. *Am J Cardiol* 2004;93:860–3.
 34. Barsheshet A, Goldenberg I, Moss AJ, et al. Response to preventive cardiac resynchronization therapy in patients with ischaemic and nonischaemic cardiomyopathy in MADIT-CRT. *Eur Heart J* 2011;32:1622–30.
 35. Tournoux FB, Manzke R, Chan RC, et al. Integrating functional and anatomical information to facilitate cardiac resynchronization therapy. *Pacing Clin Electrophysiol* 2007;30:1021–2.
 36. Truong QA, Hoffmann U, Singh JP. Potential uses of computed tomography for management of heart failure patients with dyssynchrony. *Crit Pathw Cardiol* 2008;7:185–90.
 37. Helm RH, Leclercq C, Faris OP, et al. Cardiac dyssynchrony analysis using circumferential versus longitudinal strain: implications for assessing cardiac resynchronization. *Circulation* 2005;111:2760–7.
 38. Gras D, Cebon JP, Brunel P, et al. Optimal stimulation of the left ventricle. *J Cardiovasc Electrophysiol* 2002;13:S57–S62.
 39. Merchant FM, Heist EK, McCarty D, et al. Impact of segmental left ventricle lead position on cardiac resynchronization therapy outcomes. *Heart Rhythm* 2010;7:639–44.
 40. Singh JP, Klein H, Huang DT, et al. Left ventricular lead position and clinical outcome in the MADIT-CRT. *Circulation* 2011;123:1159–66.
 41. Murphy RT, Sigurdsson G, Mulamalla S, et al. Tissue synchronization imaging and optimal left ventricular pacing site in cardiac resynchronization therapy. *Am J Cardiol* 2006;97:1615–21.
 42. Singh JP, Fan D, Heist EK, et al. Left ventricular lead electrical delay predicts response to cardiac resynchronization therapy. *Heart Rhythm* 2006;3:1285–92.
 43. Singh JP, Heist EK, Ruskin JN, Harthorne JW. Dialing-in' cardiac resynchronization therapy: overcoming constraints of the coronary venous anatomy. *J Interv Card Electrophysiol* 2006;17:51–8.
 44. Kamath GS, Balaram S, Choi A, et al. Long-term outcome of leads and patients following robotic epicardial left ventricular lead placement for cardiac resynchronization therapy. *PACE* 2011;34:235–40.
 45. Patwala A, Woods P, Clements R, et al. A prospective longitudinal evaluation of the benefits of epicardial lead placement for cardiac resynchronization therapy. *Europace* 2009;11:1323–9.
 46. Derval N, Steendijk P, Gula LJ, et al. Optimizing hemodynamics in heart failure patients by systematic screening of left ventricular pacing sites: the lateral left ventricular wall and the coronary sinus are rarely the best sites. *JACC* 2010;55:566–75.
 47. Rademakers LM, van Kerckhoven R, van Deursen CJ, et al. Myocardial infarction does not preclude electrical and hemodynamic benefits of cardiac resynchronization therapy in dyssynchronous canine hearts. *Circ Arrhythm Electrophysiol* 2010;3:361–8.
 48. Singh JP, Abraham WT. Enhancing the response to cardiac resynchronization therapy: is it time to individualize the left ventricular pacing site? *JACC* 2010;55:576–8.
 49. Leclercq C, Gadler F, Kranig W, et al. A randomized comparison of triple-site versus dual-site ventricular stimulation in patients with congestive heart failure. *JACC* 2008;51:1455–62.
 50. Gras D, Gupta MS, Boulogne E, et al. Optimization of AV and VV delays in the real-world CRT patient population: an international survey on current clinical practice. *Pacing Clin Electrophysiol* 2009;32 (Suppl. 1): S236–9.
 51. Ellenbogen KA, Gold MR, Meyer TE, et al. Primary results from the SmartDelay determined AV optimization: a comparison to other AV delay methods used in cardiac resynchroniza-

- tion therapy (SMART-AV) trial: a randomized trial comparing empirical, echocardiography-guided, and algorithmic atrio-ventricular delay programming in cardiac resynchronization therapy. *Circulation* 2010; 122:2660–8.
52. Abraham WT, Gras D, Yu CM, et al. Rationale and design of a randomized clinical trial to assess the safety and efficacy of frequent optimization of cardiac resynchronization therapy: the Frequent Optimization Study Using the QuickOpt Method (FREEDOM) trial. *Am Heart J* 2010; 159:944–8.
 53. Leon AR, Abraham WT, Brozena S, et al. Cardiac resynchronization with sequential biventricular pacing for the treatment of moderate-to-severe heart failure. *JACC* 2005;46:2298–304.
 54. Boriani G, Biffi M, Muller CP, et al. A prospective randomized evaluation of VV delay optimization in CRT-D recipients: echocardiographic observations from the RHYTHM II ICD study. *Pacing Clin Electrophysiol* 2009; 32 (Suppl. 1): S120–5.
 55. Rao RK, Kumar UN, Schafer J, et al. Reduced ventricular volumes and improved systolic function with cardiac resynchronization therapy: a randomized trial comparing simultaneous biventricular pacing, sequential biventricular pacing, and left ventricular pacing. *Circulation* 2007; 115:2136–44.
 56. Singh JP, Rosenthal LS, Hranitzky PM, et al. Device diagnostics and long-term clinical outcome in patients receiving cardiac resynchronization therapy. *Europace* 2009;11:1647–53.
 57. Troughton RW, Ritzema J, Eigler NL, et al. Direct left atrial pressure monitoring in severe heart failure: long-term sensor performance. *J Cardiovasc Transl Res* 2010; 4:3–13.

Informative and communicative technologies as a basis for personalized therapies

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Summary

Review of literature is devoted to issues of importance in informative and communicative technologies as part of modern health care development. Some of the important areas of informative and communicative technologies application are presented in practical public health: remote monitoring of key vital functions of the organism, telemedicine consultation, control and security of home rehabilitation, primary and secondary disease prevention and early disease diagnostics support, preventive telemedicine monitoring, the support system of medical decisions. Convincing data on higher "clinical efficiency" and effectiveness of the service, effective protection of public health in young and elderly patients, social and economic benefits, improved life quality, reducing number of hospitalizations and complications, adverse outcomes due to using informative and communicative technologies in medicine, is presented. Significant increase of therapy compliance, increase of public awareness in the present pathology for the purpose of active disease management, as well as patients' satisfaction in quality of health care through personalized communications with doctors are justified.

Key words

Informative and communicative technologies (ICT), patients' deciding, compliance, therapeutic training.

Introduction

There is no doubt that informative and communicative technologies (ICT) in medicine are a useful tool for improving the quality and efficiency of health care, both at the global and local levels. Not being an alternative to traditional forms of treatment and rehabilitation, information telemedicine systems are ICT, enhancing the effectiveness of conventional treatment.

The use of ICT in daily practice requires training of medical personnel, literacy of doctors and patients in the field of some service, organization of the health care structure and its management. Some researchers suggest, that “clinical productivity” of services and performance are achieved not by the introduction of the telemedicine technologies, but by an adequate interpretation of the results of their use and acceptance of medical and organizational solutions for achieving the main objectives of health care [1–8].

In the implementation of tasks using ICT, one of the fundamental roles is taken by active participation, awareness and literacy of patients in self-management of health, joint decision-making responsibility of the patient and the doctor for chronic diseases [2]. A number of scientific studies shown, that low literacy in health issues associated with inequitable access to health care, which results in an increase in the frequency of hospitalization, mortality, deterioration in quality of life (Figure 1) [2].

There is strong evidence of a more effective protection of public health in the application of additional opportunities in the form of ICT [2–5], with an emphasis on active participation of the patient in accomplishing the task. The positive experience of the clinical use of ICT worldwide put the medicine to a new level, successfully helping to reduce the number

of hospitalizations, complications, adverse outcomes, as well as socio-economic benefits, improving the quality of life [4]. It is proved that increase in the efficiency of preventive, curative and rehabilitative measures is achieved through dynamic monitoring of patients in a real-time, control and emergency correction of the key parameters of vital functions of the human body, preventive measures to ensure the safety of home rehabilitation. The account of features of the disease can improve significantly the efficiency and safety of the decisions [2, 4, 9–12]. It is noteworthy that the increase in the availability of medical care for patients with disabilities, as well as overcoming the spatial and temporal barriers between health workers and people living in remote regions lead to clinical and socio-economic benefits for patients [1–6, 13].

A number of large clinical trials [4, 6, 9, 13, 14] shown the data on the effectiveness of clinical use in all medicine branches of such ICT as the remote monitoring of key vital signs (blood pressure, heart rate, blood glucose, etc.), telemedicine consultations, monitoring of the home rehabilitation, a support system of medical solutions. Thus, various aspects of the individual approach to patients developed increasingly, which should be based more on the study of regularities rather than intuition or experience of the doctor. Approach to remote telemonitoring has unlimited possibilities and is often implemented in implantable devices — pacemakers and implantable cardioverter defibrillator, providing data on the functioning of the implanted system, as well as extensive information on the patient’s state [1, 10, 15, 16].

Statistics show that by 2020, senior citizens will make up 25% of the world’s population [17], i.e. it pays attention to the issue of “aging”. As soon as

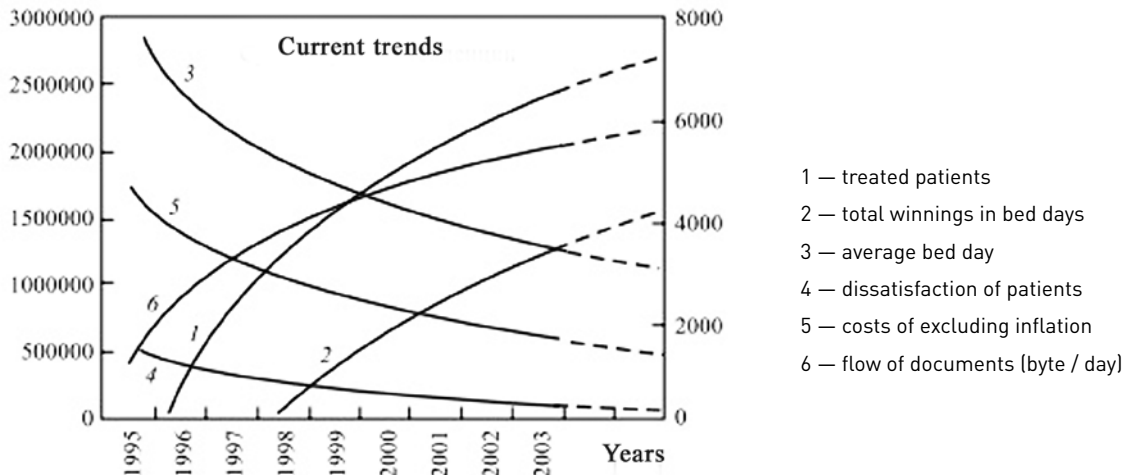
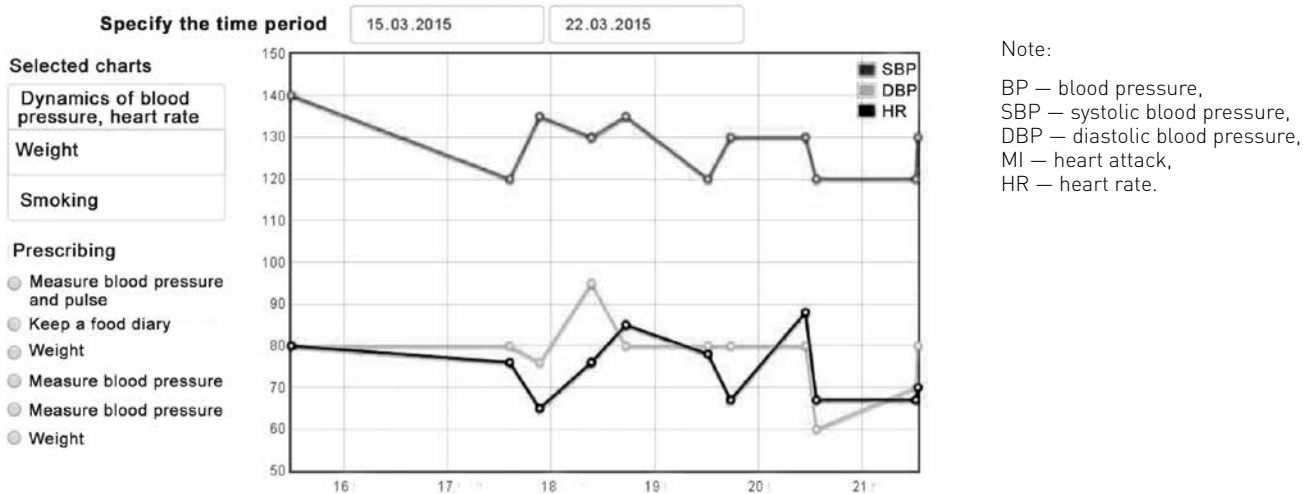


Figure 1. Trends in the use of health ICT [2].



Health card

Message exchange

School for patient

School for patient with MI. Class #1. First aid for a heart attack

School for patient with MI. Class #2. Nutrition for coronary heart disease (CHD)

School for patient with MI. Class #3. Primary prevention of cardiovascular diseases

School for patient with MI. Class #4. Non-pharmacological therapy of arterial hypertension

Figure 2. Primary and secondary disease prevention and early diagnosis

people approach retirement age, they enter a period of life associated with a high risk of costly and life-threatening chronic diseases. In this case, an important component of health monitoring can be a monitoring of physiological parameters of patients, related to the prevention and treatment of diseases; as well as the organization of telemedicine consultations, which contribute to closer contacts between doctors and patients, producing for patients the feeling of “security” under supervision of a physician (patient’s satisfaction from communication with the doctor) and increase of compliance [9, 18, 19].

A recent randomized controlled study, on the use of telemedicine in the individual management of patients, showed improvement in blood glucose control in diabetes elderly in areas, deemed as “not getting enough medical care” in the state of New York (USA) [18]. Considering the high percentage of chronic diseases in this group of patients, in some European countries telemedicine programs of self-service and therapeutic education are often implemented, which

help to raise an awareness of patients about the disease, to develop the necessary skills allowing to manage their diseases long and actively, and to provide a dynamic timely control for the prevention of complications [20–21].

The support to the primary and secondary disease prevention and early diagnosis gets even more relevance (Figure 2) [4, 9]. A high percentage of the prevalence of cardiovascular disease, which flows including covertly among young and middle-aged people, and therefore a high risk of cardiovascular complications, requires a before-symptomatic diagnosis in this age group [12] in the light of the modern medicine positions, defined as predictive, personalized and preventive medicine [22]. This fact requires special approaches to the early diagnosis and correction of the identified risk factors, as well as early forms of disease in these groups of patients. A significant role is given to the use of telemedicine and to the telemedicine preventive monitoring. In the implementation of preventive measures in young patients with

no complaints and not focusing on the state of their health in this context, it is important to give an awareness of the important role of risk factors, understanding the causes of disease, the initial manifestations of the disease. This again shifts the emphasis in favor of literacy and therapeutic education for health and its self-control in young and middle-aged people.

One of the important components of the effectiveness of rehabilitation measures is their continuous monitoring and active participation of the patient. According to foreign literature data, telemedicine technologies contribute to “overcome the barriers to access a cardio-rehabilitation for large range of patients, and can be widely used in the world” [13]. Thus, the physician assumes the possibility of direct control access to comprehensive information on the patient’s condition in an online mode, receives data not only on the parameters of the cardiovascular system, but also on other vital systems potentiating “a syndrome of mutual aggravation”, and if necessary, he can make adjustments to the treatment and rehabilitation programs. Clinical experience, with telemonitoring of the category of high-risk patients in many studies, proved the prospects of development of remote monitoring systems for patients with the help of external devices and sensors of the human vital parameters, as well as increased self-control of patients [1, 19–20].

A significant increase of compliance with the treatment was proved (90%) in patients actively using methods of home self-control [12, 19], reduction in the frequency of hospitalizations [4, 23], reduction in mortality among patients with cardiovascular disease by 20–25%, compared with the traditional technology of medical care (Figure 3) [3, 5, 23, 24]. Positive dy-

namics in the application of telemonitoring systems is also achieved by increasing awareness and literacy with existing disease, the patient’s satisfaction with the quality of medical care, the achievement of patient’s consent to treatment and timely delivery of medical recommendations.

The important role is played by access to health care of groups living in geographically remote areas, rural areas, patients with disabilities, as well as patients of closed or organized groups. An example of the application of telemedicine technologies is widely implemented in the states of Georgia and Texas, where telecommunications are carried out between medical institutions, state prisons and hospices [18, 25].

The use of telemonitoring in psychological rehabilitation is successful for patients, who are in need of psychiatric, psycho-physiological or psychological care [1, 25, 26], by the audiovisual communication of the patient and the doctor. The patient no longer feels lonely and helpless, his psycho-physiological condition is improving, there is self-confidence, resulting in a marked acceleration of physical rehabilitation, improving of life quality [17, 26, 27].

The introduction of telemedicine technologies in pediatrics is topical, which is confirmed in a number of studies by a positive effect on the psychological status of the parents of sick children — the use of telemonitoring systems in pediatrics reduces the level of parents’ anxiety significantly [28]. The project of telemedicine use to support maternal and newborn health at Los Angeles Children’s Hospital and at the National Center for Maternal and Child in Mongolia showed a decrease in infant and maternal mortality and reducing the gap between the level of medical services in urban and rural areas [29].

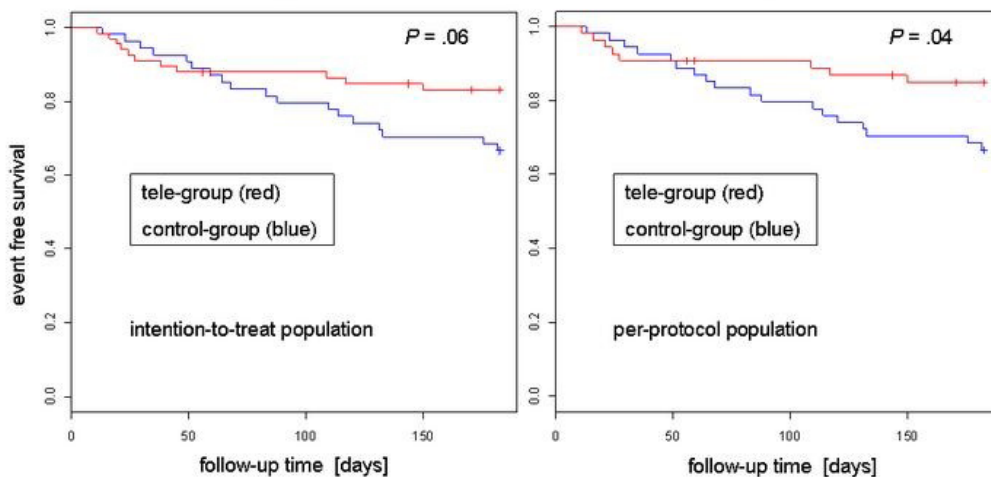


Figure 3. The primary endpoints — reduction in the frequency of hospitalization and mortality when using telemedicine technologies [23]

There are evidences of the effectiveness of telemedicine support for rehabilitation of patients after surgery [4, 7, 8, 17]; rehabilitation and telemedicine services for women before and after a childbirth period [17, 30]; the organization of consulting support for medical care in emergency situations from highly professionals of major medical centers [17, 25]; telemedicine support of the critical conditions medicine [31], as well as military telemedicine [25]. An important role has the information support of the activities in the field of a health care organization, clinical audit [3, 25].

Conclusion

The introduction of ICT with the dynamic monitoring of patients and raise of awareness about the disease in the form of virtual learning are an auxiliary therapeutic agent, which allows the patient to adapt to the disease more quickly, and to acquire the knowledge and skills necessary for the active management of their disease. Remote control of therapeutic, rehabilitative and preventive measures contribute to the growth of patients' satisfaction with medical services, improvement of life quality and cost-effectiveness of health care in all its spheres. The possibility of permanent access and remote monitoring helps to overcome both territorial and psychological barriers between doctor and patient.

Conflict of interest: None declared

References

1. Klark JL. Heart failure 2011: review of selected studies that contributed to the latest developments of clinical cardiology. *Ukrainskij kardiologicheskij zhurnal*. 2012; 2:119–28. Russian.
2. Coulter A, Parsons S, Askham J. Where are the patients in decision-making about their own care? Policy Brief. WHO Regional Office for Europe. Copenhagen: European Observatory on Health Systems and Policies; 2008. 18p.
3. Serdjukov AG, Naberezhnaja IB, Zaharov DA. A sociological study of implementation of telemedicine technologies into practice. *Zamestitel' glavnogo vracha*. 2008; 2:12–20. Russian.
4. Kazakov VN, Vladzimirskij AV, Dorohova ET. Telemedicine is the practice of the general doctor. *Ukrainskij zhurnal telemedicini*. 2005;3(2):124–30. Russian.
5. Engelbrecht R. Telemedicine — a way to better care. *Deutsches Forschungszentrum fur Umwelt und Gesundheit Koch-Metschnikow-Forum, Sektion eHealth*. Berlin, Helmholtz Zentrum Munchen, 2009. <http://zdrav.tomsk.ru/export/sites/ru.tomsk.zdrav/ofic/konferenz/engelbreht.pdf>
6. Hasanov ISh. Medical information systems, and mobile telemonitoring of patients. Publishing of the conference "Information technology in health care", Kazan', June 9, 2011. http://www.kirkazan.ru/@files/upload/Khassanov_2011.pdf. Russian.
7. Lyamina NP, Kotelnikova EV. Computer technology in the organization of rehabilitation in primary care in patients with coronary heart disease. *Zdravoohranenie Rossijskoj Federacii*. 2010; 5:32–5. Russian.
8. Lyamina NP, Kotelnikova EV. Introduction of telemedical technologies in rehabilitation practice of modern health system. *Health care*. 2013;8:106–112.
9. Meystre S. The Current State of Telemonitoring: a Comment on the Literature. *Telemed J E Health*. 2005; 11 (1): 63–69.
10. Hasanov ISh. Telemonitoring of the patients with cardiac diseases as a basis for the development of remote monitoring of patients. *Healthy Nation*. 2011; 3:61–65. Russian.
11. Lyamina NP, Kotelnikova EV, Karpova JeS, Bizjaeva EA. Possibilities of telemedicine technologies in improving the quality of home rehabilitation in patients with cardiovascular disease. *Cardiovascular Therapy and Prevention*. 2014;13(S2): 71. Russian.
12. Lyamina NP, Kotelnikova EV, Nalivaeva AV. The telemedicine system of screening and monitoring of risk factors based on the "cloud" technologies in the prevention of cardiovascular disease. *CardioSomatika*. 2015; S1:61–2. Russian.
13. Martin-Lesende I, Orruño E, Cairo C, et al. Assessment of a primary care-based telemonitoring intervention for home care patients with heart failure and chronic lung disease. The TELBIL study. *BMC Health Services Research*. 2011;11:56–62.
14. Home — The Best Place for Health Care A positioning statement from The Joint Commission on the state of the home care industry. USA: The Joint Commission, 2011. http://www.jointcommission.org/assets/1/18/Home_Care_position_paper_4_5_11.pdf.
15. Lakshmanadoss U, Shah A, Daubert J. Telemonitoring of the Pacemaker. *J Modern Pacemakers — Present and Future*. 2011;129–46.
16. Bourge RC, Abraham WT, Adamson PB, et al. COMPASS-HF Study Group. Randomized controlled trial of an implantable continuous hemodynamic monitor in patients with advanced heart failure: the COMPASS-HF study. *JACC*. 2008; 51:1073–9.
17. Arhipov IV. The elder's life quality problems. The well-being of older people — the problem of the whole society. 2015;2(22): 2–5. Russian.
18. Caring for people with chronic conditions: A health system perspective. Edited by E. Nolte and M. McKee. Berkshire: Open University Press, 2011. 290 p.
19. Woodward J, Eldridge D. Compliance, commitment, consent — it is not in the title. *New medicine of millennium*. 2011; 5:16–9.

20. Patterson V, Swinfen R, Azzo M. Supporting hospital doctors in the Middle East by email telemedicine: something the industrialized world can do to help. *Journal of Medical Internet Research*. 2007;9 (4):e30.
21. Johnston K, Kennedy S, Murdoch I, et al. The cost-effectiveness of technology transfer using telemedicine. *Health Policy and Planning*. 2004; 19 (5): 302–9.
22. Safonicheva OG, Martynchik SA. The objectives of the scientific platform of medical science "Preventive environment": technological solutions. *Uspehi sovremennogo estestvoznaniya*. 2015; 3:102–6. Russian.
23. Scherr D, Kastner P, Kollmann A, et al. Effect of home-based telemonitoring using mobile phone technology on the outcome of heart failure patients after an episode of acute decompensation: randomized controlled trial. *Journal of Medical Internet Research*. 2009; 11 (3):e34.
24. Ingilis C, Clarke R, Mcallister F. Structured telephone support or telemonitoring programs for patients with chronic heart failure. *The Systematic Reviews of Cochrane Database*. 2010. Issue 8. Russian.
25. Venediktov DD, Grigor'ev AI, Kazinov VA, et al. Telemedicine technology in health care in Russia. Review. 2004. http://pathology.narod.ru/new_page_16.htm. Russian.
26. Kruchinin G. Telemedicine in the delivery of mental health care. http://online.zakon.kz/Document/?doc_id=31191877. Russian.
27. Kolesnik AJu. International experience in monitoring health services and evaluating public health. Analytical note. USAID, 2005. Russian.
28. Anjers R, Rutkowski AF. The Telebaby Case. In: *EHealth Care Information Systems: An Introduction for Students and Professionals*. T. Tan eds. John Wiley & Sons, 2005: 27–36.
29. Elizabeth Earl. Children's Hospital Los Angeles, Mongolian hospital to expand partnership on telemedicine. <http://www.beckershospitalreview.com/healthcare-information-technology/children-s-hospital-los-angeles-mongolian-hospital-to-expand-partnership-on-telemedicine.html>.
30. Information technologies in medicine (thematic scientific collection). Ed. by G.S. Lebedeva, O.V. Simakova, Ju.Ju. Muhina. M.: Radiotekhnika. 2010; 152 p. Russian.
31. Vasil'kov VG, Safronov AI. Telecommunication technologies and the development of services of critical care medicine. *Informacionnye tehnologii*. 2000; 6:48–50. Russian.

Features of the hospital course of myocardial infarction in patients with impaired carbohydrate metabolism

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Resume

Objective

To study the influence of concomitant diabetes mellitus (DM) on the course of myocardial infarction with the ST segment elevation (STEMI) and hospital prognosis for patients.

Material and methods

The study included 83 patients with STEMI, admitted in 2014. Patients were analyzed in 2 groups: group I — patients with type 2 diabetes ($n = 38$; average age $58,4 \pm 8,1$ years; male / female — 28/10); and group II — patients with normal carbohydrate metabolism ($n = 45$; average age $59,9 \pm 7,2$ years; male / female — 32/13). We studied the baseline clinical and hemodynamic laboratory parameters of patients, as well as hospital prognosis of MI.

Results

Comparative analysis showed that among patients with diabetes, hypertension occurred significantly more often as the background of the disease, and the middle class of acute heart failure according to the Killip classification was significantly higher at the admission time in patients of the first group. Ventricular arrhythmias of the heart: couplets, group PVCs, unstable paroxysms of ventricular tachycardia were detected in 2.5 times more frequently in patients with STEMI and DM. In addition, patients with diabetes were characterized by relatively severe dilation of the cavity of the left ventricle (LV) and the left atrium, at relatively low values of LV ejection fraction. During the period of hospital treatment in patients with STEMI and the type 2 diabetes, more cases of early post-infarction stenocardia (11 %) and of acute left ventricular aneurysm were recorded (9 %), (both $p > 0.05$), while the prevalence of the hospital mortality cases.

Conclusion

The presence of concomitant diabetes burdens the course of STEMI, manifesting by a pronounced left ventricular dysfunction, a high risk of ventricular arrhythmias and cardiac complications of acute myocardial, associated with a trend to an increase in index of hospital mortality.

Key words

Myocardial infarction, diabetes mellitus, hospital prognosis.

Diabetes mellitus (DM), being common «social» disease, is simultaneously a risk factor for cardiovascular diseases; at the same time, it is a factor burdening their course [1, 2]. Numerous studies prove the effect of diabetes on the prognosis of chronic heart failure, arterial hypertension (AH) and various forms of coronary heart disease (CHD) [3–5]. Thus, according to the assertions of the American Heart Association, patients with diabetes had the risk of myocardial infarction (MI) 2 times higher than patients with normal glycemic status; at the same time, the first group characterized as a lower survival [6]. Sub analysis of the study VALIANT (Valsartan in Acute Myocardial Infarction Trial) showed that in patients with MI and newly diagnosed diabetes, the disease outcomes were significantly worse than in patients without diabetes [7]. By analyzing the results of a retrospective cohort study ($n > 118$ thousand), a 30-day and 1-year mortality in patients with acute MI on a background of diabetes was studied. It shows a significant predominance of incidence of both endpoints in patients, suffering from diabetes, compared to patients without diabetes [8].

However, a number of studies emphasizes the clinical and prognostic significance of the reverse state — namely a hypoglycemia in patients with diabetes and acute myocardial damage. The results of other studies also show the negative impact of severe hypoglycemia on a MI course in patients with diabetes, according to which fatal arrhythmic complications can develop in such patients [9]. Ambiguity in the question of the possible mechanisms of the effect of hyper and hypoglycemia on the course, prognosis of MI, including a short-term one, in diabetic patients supports the interest of researchers to further study this issue.

The purpose of research is to study the influence of concomitant diabetes mellitus (DM) on the course of myocardial infarction with the ST segment elevation (STEMI) and hospital prognosis for patients.

Material and Methods

In the register study, 83 patients with STEMI were included, hospitalized in 2014 to the intensive care

and the cardiology departments of Domodedovo central hospital. Inclusion criteria were a presence of STEMI within a period of 48 hours in patients with diabetes and without it. Exclusion criteria were the duration of STEMI > 48 hours, patients > 75 years old, known cancer pathology.

In addition to the evaluation of clinical status, registration 12-lead ECG, all patients were underwent a transthoracic echocardiography using ultrasonic apparatus IE-33 («Phillips», The Netherlands). On admission to the hospital, blood sampling was carried out for general clinical and biochemical blood tests. Levels of glycated hemoglobin (HbA1c) were measured, using the method of immunoturbidimetric endpoint test with a help of analyzer «Sapphire 400» (Japan). In addition, the concentration of cardio-specific enzymes were determined: Troponin I, MB fraction of creatine phosphokinase (CP-MB).

Patients were analyzed in 2 groups: group I — patients with type 2 diabetes ($n = 38$; average age $58,4 \pm 8,1$ years; male / female — 28/10); and group II — patients with normal carbohydrate metabolism ($n = 45$; average age $59,9 \pm 7,2$ years; male / female — 32/13). Age-gender and clinical-anamnestic characteristics of patients are shown in Table 1.

The diagnosis of type 2 diabetes was established by medical history, as well as on the basis of medical documentation. Newly diagnosed diabetes were diagnosed during the hospital period, based on the repeated determinations of glucose on an empty stomach, HbA1c, as well as the test results on glucose tolerance. Treatment of patients in the hospital was carried out according to the recommendations of the Russian Society of Cardiology (2014).

Statistical processing of data was performed by the application package Statistica, designed for Microsoft Windows. Data are presented as arithmetic means (M) and standard deviation (SD). The significance of differences was determined in accordance with the use of non-parametric Student's t test for normal distribution of feature, non-compliance with the last — the Mann-Whitney. Differences are considered

Table 1. Clinical-anamnestic characteristics of patients with STEMI, included in the study

Sign	I group (with DM, n=38)	II group (without DM, n=45)	<i>p</i> ; χ^2
Average age, years	58.4±8.1	59.9±7.2	0.37
Gender Female, n (%)	10 (26.3)	13 (28.8)	0.9
ИМТ>30, n (%)	14 (36.8)	13 (28.8)	0.59
Burdened by MI heredity, n (%)	8 (21)	6 (13.3)	0.47
AH, n (%)	28 (73.7)	22 (49)	0.03; 4.3
Smoking, n (%)	24 (63.1)	28 (62.2)	0.8
PICS, n (%)	8 (21)	8 (17.8)	0.9
Prior therapy of CHD, n (%)	8 (21)	9 (20)	0.87
Localization of MI: — front, n (%) — back, n (%) — other localizations, n (%)	17 (45) 12 (31) 9 (24)	21 (47) 16 (35) 8 (18)	0.96 0.88 0.17
Class of AHF according to Killip, average.	1.46±0.6	1.23±0.57	0.047; 3.94
Terms of admission / appeal since the development of the first symptoms, hours	24.4±38.4	21.2±34.5	0.69

Note: *p* — accuracy of intergroup differences; BMI — body mass index, PICS — post-infarction cardio-sclerosis.

reliable at values of $p < 0.05$. The accuracy of differences of quality indicators was determined using the criterion χ^2 .

Results of the study

Analysis of initial clinical-anamnestic parameters of patients, admitted to hospital, showed that groups, compared by middle age and gender distribution, were similar (Table 1). In addition, female patients were 26.3% and 28.8% respectively. It was noted that the number of patients with obesity (body mass index — BMI ≥ 30) was 36.8% in I group vs 28.8% in II group; although the differences did not reach statistical significance. Comparative analysis showed, that AH was recorded significantly more often as the background of the disease among patients with diabetes — 74% and 49% respectively; and at the moment of admission, the middle class of acute heart failure (AHF) according to the Killip classification was significantly higher in patients of I group. Hereditary factor traced in medical history a bit more often in patients with type 2 diabetes: 21% of them said that there were cases of MI among the relatives of the first line.

Approximately 1/5 of the patients in each group followed an adequate ambulatory therapy of coronary heart disease (CHD), but among patients with known medical history of CHD, this index did not reach 40%. There is the noteworthy rate of hospitalization and / or treatment of patients since the development of the first symptoms, which was average almost one day — 24.4 ± 38.4 21.2 ± hours and 34.5 hours respectively ($p > 0.05$), in patients of both groups. However, it is need to be noted, that these averages are caused due to individual cases, when patients consulted a doctor

on 2nd-7th day after development of a long intensive anginal attack; while the time of the ambulance call and hospitalization held < 60 minutes. Distribution of patients according to localization of myocardial injury has shown, that in most cases front and front-spread MI was recorded, and in approximately 1/3 of the cases — the bottom / back localization.

When analyzing the clinical and hemodynamic parameters according to their glycemic status, the following results were revealed. Baseline systolic blood pressure (SBP), as an indicator of central hemodynamics in patients with diabetes, were higher by 4.5% than in the comparison group of patients (Table 2). In patients of groups I and II, a permanent form of atrial fibrillation was recorded. At the same time in group II in 2 (4.5%) patients, the STEMI was complicated by the development of paroxysmal tachycardia with narrow QRS complexes. However, ventricular cardiac arrhythmias: couplets, group ventricular premature beats (PVCs), unstable paroxysms of ventricular tachycardia were detected 2.5 times more frequently in patients with STEMI and DM.

Echocardiography was performed by a transthoracic access on 2nd-5th day of hospital treatment. At comparison of terms and localization of MI, the number of patients with post-infarction cardio-sclerosis, diabetic patients were characterized by relatively severe dilation of the cavity both in the left ventricle (LV) and the left atrium (LA), at relatively low values of the ejection fraction (EF) of the LV.

Comparative analysis of laboratory parameters revealed the expected hyperglycemia in patients of group I. In addition, the maximum values of fasting glucose were > 20 mmol / l in some patients. Nevertheless, only 20 (52.6%) patients with type 2 diabetes followed

Table 2. **Clinical-hemodynamic and laboratory parameters in patients with MI, depending on the impaired carbohydrate metabolism**

Sign	I group (with type 2 DM, n=38)	II group (without DM, n=45)	P
SBP, mmHg	138±30.6	132±32.7	0.39
DBP, mmHg	78.8±12.8	80.7±13.2	0.51
HR, beats / min	80.7±14.6	78.9±16.3	0.60
Basic rate — AF, n (%)	1 (2.6%)	2 (4.5%)	0.88
Ventricular arrhythmias of the heart, n (%)	8 (21)	3 (6.7)	0.1
EDS LV, mm	58.6±15.4	55.4±14.3	0.3
EF LV, %	49.6±9.1	52±8.6	0.2
LA, mm	41.2±7.8	40.8±6.3	0.83
Thickness of IVS, mm	11.8±3.2	11±2.4	0.19
Thickness of RWLV, mm	10.1±2.8	10.4±2.4	0.89
Glucose fasting, mmol / l	11.7±3.1	5.6±0.87	0.000
HbA1c, %	8.1±1.23	—	
Urea, mmol / l	8.87±2.5	7.01±2.6	0.03
Creatinine, micmol / l	106.3±23.9	92.6±29.4	0.07
Total cholesterol, mmol / l	6.4±1.3	6.2±1.42	0.94
LDL, mmol / l	3.7±0.91	3.47±1.03	0.98
Triglycerides, mmol / l	2.34±1.29	1.96±1.04	0.14
Troponin I, ng / ml	8.4±10.9	11.7±20.1	0.36
CP-MB, u / l	40.3±42.8	38.8±50.2	0.88

Note: p — the accuracy of intergroup differences; SBP — systolic blood pressure, DBP — diastolic blood pressure, HR — heart rate, EDS LV — end-diastolic size of left ventricular, IVS — interventricular septum, RWLV — the rear wall of the left ventricle, LDL — low-density lipoprotein.

an adequate and regular hypoglycemic therapy before MI. The mean values of HbA1c were higher than the norm by 24.6% in patients of group I. At comparable mean values of total cholesterol in patients with MI, a significant prevalence of cholesterol low-density lipoprotein and triglycerides was revealed in patients with diabetes. Also in patients with type 2 diabetes, plasma concentrations of urea and plasma creatinine are significantly higher than in the comparison group by 25.7% and 11.2% respectively (both $p < 0.05$). In the comparative aspect, levels of cardiac enzymes did not reveal any significant differences.

The next stage of the study was the studying of hospital prognosis of patients with STEMI in connection with the state of carbohydrate metabolism. During the period of hospital treatment, patients with STEMI and type 2 diabetes had an increased incidence of early post-infarction stenocardia (EPS) by 11% ($p > 0.05$) and acute aneurysm of LV by 12% ($p < 0.05$) (Table 3). Moreover, among patients in both groups, by one case of acute cerebrovascular accident was detected in the hospital. In addition, the prevalence of the hospital mortality cases was noted in patients with STEMI and DM, which was almost 2 times higher than in group II. To stabilize the condition and following the next stages of rehabilitation, patients in group I needed 11% more hospital days ($p < 0.05$).

Table 3. **The study of hospital prognosis for patients with STEMI depending on the impaired carbohydrate metabolism**

Sign	I group (with DM, n=38)	II group (without DM, n=45)
Cardiogenic shock, n (%)	3 (7.9)	2 (4.4)
Acute aneurysm LV, n (%)	6 (16)	2 (4.4)*
Early post-infarction stenocardia, n (%)	5 (13.1)	1 (2.2)
Relapse of MI in hospital, n (%)	2 (5.2)	3 (6.6)
AIS, n (%)	1 (2.6)	1 (2.2)
Hospital death, n (%)	6 (16)	4 (8.9)
Gap of LV (anatomic-pathological), n (%)	1 (2.6)	1 (2.2)
The duration of hospitalization, days	18.1±4.1	16.3±3.6*

Note: * — $p < 0.05$, AIS — acute ischemic stroke.

Discussion

The results of studies, on the problem of studying the clinical features of acute coronary conditions when combined with diabetes, show existence of a sufficiently close relationship between the course and the outcome in particular of MI and the level of hyperglycemia, both at the stationary phase and during long-term hospital period [10].

In this study, the initial clinical-anamnestic parameters in patients with and without diabetes did not show significant intergroup differences. However, among patients in group I, concomitant AH prevailed, as well as at the time of admission, they were characterized

by a higher class of AHF according to Killip. According to a meta-analysis of the well-known British 30-year study UKPDS (UK Prospective Diabetes Study), patients with diabetes and asymptomatic MI were characterized by older age and the prevalence of the female gender. It was also specific, that the average BP in a group of patients with MI and diabetes were higher despite the more aggressive antihypertensive therapy, with the prevalence of microvascular complications [11].

In the analysis of the electrocardiogram (ECG) in the vast majority of patients in both groups, a sinus rhythm was recorded as a base. But attention is drawn to the fact that in patients with STEMI and diabetes, episodes of ventricular cardiac arrhythmias of high grade were more common, the frequency of which was > 2.5 times higher than in the comparison group. In previous studies, the effect of hyperglycemia on the electrophysiological processes was proven in patients with heart diseases.

The study [12] showed that increased levels of HbA1c > 8.5% in patients with CHD and type 2 diabetes was accompanied by an increased ventricular arrhythmias, which was reflected in statistically significant differences, in relative indexes and a positive correlation of HbA1c level with the amount of PVCs. The research results of other Russian authors also show, that prolonged hyperglycemia is capable of causing cardiac arrhythmia, particularly recurrent tachyarrhythmia, the development of which is caused by abnormal automaticity [13]. Finnish researchers studied the particular parameters of Holter monitoring in patients with diabetes. Within 3–12 months after the coronary angiography, 1001 patients were examined, of whom 526 patients had diabetes. The heart rate turbulence and the T wave alternation were analyzed as powerful predictors, including fatal arrhythmias in patients with CHD. Significant prevalence of interruptions of these parameters was noted in the group of patients with CHD and diabetes — 58% vs 24% ($p < 0.001$) and LV EF < 50% [14]. On models of transgenic mice using an implantable ECG telemetry, we tried to explain the cause of arrhythmias in the presence of hyperglycemia. The authors argue that the increase in the intracellular concentration of lipids in cardiomyocytes and the overexpression of receptors-activators of the peroxisome proliferation, observed in patients with diabetes and obesity, lead to QT prolongation and associated with it spontaneous ventricular arrhythmias, including a polymorphic ventricular tachycardia and ventricular fibrillation [15].

The parameters analysis of intracardiac hemodynamics in patients with STEMI showed that in the case of type 2 diabetes, the concomitant LV dysfunction was more pronounced. End-diastolic size of LV in patients of group I, exceeding the analogous index by 5.7%, was accompanied by a corresponding decrease in LV EF by 4.6% relatively to the comparison group.

The results of the published study, which included 210 patients with MI, showed that hyperglycemia, occurs in the first 24 hours of the disease, is associated with the development of the LV dysfunction; which is a powerful predictor of the worst long-term prognosis due to the development of AHF. Multivariate analysis showed, that hyperglycemia in the first 24 hours of the disease is an independent risk factor for the LV dysfunction and consequently the development of heart failure and adverse outcome in patients with MI [14]. Global contractility of LV was assessed using magnetic resonance tomography in 4998 patients of 45–84 years old, including those without clinical signs of CHD. 13% of patients had impaired glucose tolerance, 12% had diabetes. A significant correlation between the presence of diabetes and a decreased shortening fraction of LV, subsequently a chronic heart failure developed in 96 cases [16].

Finally, certain differences are revealed in the study of the short-term prognosis of patients with STEMI with and without diabetes. According to the observations, diabetic patients were received with a higher class of AHF. In addition, an acute phase of MI in these patients was often complicated by the development of an acute LV aneurysm, including established post-mortem and the EPIS. Kemerovo researchers describe features of hospital prognosis of patients with MI and carbohydrate metabolism disorders. By the study results with a number of observations > 600, the authors showed the presence of significant differences in the prognosis already at a stationary stage. In patients with diabetes, having STEMI, more cases of EPIS, a stent retrombosis and recurrence of MI were recorded. In addition, negative effect of hyperglycemia on the prognosis of patients was also evident in individuals with impaired glucose tolerance [17]. The study Cooperative Cardiovascular Project (USA) analyzed the prognosis of MI patients with diabetes and without it, depending on the level of blood glucose on admission. In the analysis involving 141 680 patients in the period 1994–1996, the proportion of patients with severe hyperglycemia > 240 mg / dl was 26%.

It was revealed that the mortality rate within 30 days among patients with diabetes and blood glucose

> 240 mg / dl was 24 %, while patients with severe hyperglycemia on admission but without the previously diagnosed diabetes, this index was 39 % ($p < 0.001$) [8]. The relationship between impaired glucose tolerance, diabetes and the development of sudden cardiac death was studied in the study Honolulu Heart Program. They studied the sudden death within 1–24 hours after the onset of acute symptoms. The hazard ratio of death within 24 hours in patients with high normal blood glucose values (151–224 mg / dl) and diabetes, compared with persons without diabetes, was 1.59 and 2.76 respectively ($p < 0.05$). A similar association was revealed in the analysis of sudden death within 1 hour, which the authors associated with a high risk of life-threatening ventricular arrhythmias in these patients, rather than coronary [18]. The values of glycemia at admission was identified as an independent predictor of death in patients with acute coronary syndrome according to the results of the Dutch scientists study. It has been shown that increasing the concentration of blood glucose at 1 mmol / l (with initial values > 9 mmol / l) increases the risk of death by 10%. At the same time, indicators of 30-days mortality among patients with diabetes and without it amounted 16.8 % and 5.2 % respectively [19].

Regarding the mechanisms of negative influence of diabetes on the MI course, we can state the following. The experimental studies have shown the damaging effect of hyperglycemia on endothelial function, the development of collateral circulation and increasing microvascular dysfunction [20]. Acute hyperglycemia can also degrade the coagulation properties of the blood, increasing the tendency to thrombosis [21]. Researchers at the Health Science Center (Oklahoma, USA) showed in a cell culture of umbilical vein, that high concentrations of glucose may be a trigger of apoptosis. Subsequently, they proved their hypothesis at the models of mice with streptozotocinum-induced diabetes [22].

Conclusion

Thus, the presence of concomitant diabetes burden the course of STEMI, manifesting as a pronounced LV dysfunction, as a high risk of ventricular arrhythmias and complications of an acute MI period. Also negative effect of hyperglycemia associated with a trend to an increased index of hospital mortality in patients with STEMI.

Conflict of interest: None declared.

References

1. Kolchin Y.N., Karpenko A.I., Bezuglova S.V. Hyperglycemia at patients with type 2 diabetes mellitus in combination with coronary artery disease. *Internal Medicine* 2007;2(2):42–8. Russian.
2. Mamedov M.N. Diabetes and cardiovascular disease. M.: Media press 2012; 173 p. Russian.
3. Caroline SF, Sean C, Paul DS, et al. Cardiovascular Disease Burden Due to Diabetes Mellitus. *The Framingham Heart Study. Circulation.* 2007;115:1544–50.
4. Imamura F, Mukamal KJ, Meigs JB, et al. Risk factors for type 2 diabetes mellitus preceded by β -cell dysfunction, insulin resistance, or both in older adults: the Cardiovascular Health Study. *Am J Epidemiol.* 2013; 177 [12]:1418–29.
5. Mardanov B.U., Mamedov M.N., Akhmedova E.B., Oganov R.G. Issues course and prognosis of cardiovascular disease in patients with diabetes. *Cardiovascular Therapy and Prevention.* 2015; 14(1):83–9. Russian.
6. Buse JB, Ginsberg HN, Bakris GL, et al. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. *Circulation.* 2007;115:114–26.
7. VALIANT study group Newly Diagnosed and Previously Known Diabetes Mellitus and 1-Year Outcomes of Acute Myocardial Infarction: The Valsartan in Acute Myocardial Infarction (VALIANT) Trial. *Circulation.* 2004; 110:1572–8.
8. Berger AK, Breall JA, Gersh BJ, et al. Effect of diabetes mellitus and insulin use on survival after acute myocardial infarction in the elderly (the Cooperative Cardiovascular Project). *Am J Cardiol.* 2001; 87 (3):272–7.
9. Mellbin LG, Malmberg K, Waldenstrom A, et al. Prognostic implications of hypoglycaemic episodes during hospitalisation for myocardial infarction in patients with type 2 diabetes: a report from the DIGAMI 2 trial. *Heart.* 2009; 95:721–7.
10. Prakash D., Kosiborod M., Barrett E. Hyperglycemia and Acute Coronary Syndrome: A Scientific Statement From the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation* 2008; 117:1610–9.
11. Davis TE, Coleman RL, Holman RR, et al. Prognostic Significance of Silent Myocardial Infarction in Newly Diagnosed Type 2 Diabetes Mellitus. *Circulation* 2013; 127:980–7.
12. Strogina L.G., Kornev K.G., Panov E.I. Rhythm disturbances and metabolic control in patients with type 2 diabetes. *Cardiology* 2005; 11:46–9. Russian.
13. Anikin V.V., Savin V.V. The features of manifestations of the arrhythmias at CAD combined with type II diabetes. *Problems of Endocrinology.* 1999; 12:24–7. Russian.
14. Perkiomaki Juha, Olli-Pekka Piira, Samuli Lepojarvi, et al. Arrhythmia Risk Profiles in Patients with Coronary Artery Disease: The Influence of Diabetes. *Circulation* 2012; 126:A11036.

15. Morrow JP, Katchman A, Ni-Huiping Son, et al. Mice With Cardiac Overexpression of Peroxisome Proliferator-Activated Receptor γ Have Impaired Repolarization and Spontaneous Fatal Ventricular Arrhythmias. *Circulation* 2011;124:2812–21.
16. Bertoni AG, Akwo EA, Bleumke DA, et al. Myocardial Contraction Fraction, Diabetes, and Heart Failure: The Multi-Ethnic Study of Atherosclerosis. *Circulation* 2012; 125:AP243.
17. Belenkova Y.A., Karetnikova V.N., Dyachenko A.O., et al. The effectiveness of percutaneous coronary intervention at ST-elevation myocardial infarction patients with impaired glucose tolerance and diabetes. *Cardiology*. 2014; 11 (54):4–10. Russian.
18. Curb JD, Rodriguez BL, Burchfiel CM, et al. Sudden Death, Impaired Glucose Tolerance, and Diabetes in Japanese American Men. *Circulation* 1995;91:2591–5.
19. Lipton JA, Barendse RJ, Van Domburg RT. Hyperglycemia at admission and during hospital stay are independent risk factors for mortality in high risk cardiac patients admitted to an intensive cardiac care unit. *European Heart Journal: Acute Cardiovascular Care* 2013; 2 (4):306–13.
20. Popov D. Endothelial cell dysfunction in hyperglycemia: Phenotypic change, intracellular signaling modification, ultrastructural alteration, and potential clinical outcomes. *Int Jour of Diab Mellitus* 2010; 2:189–95.
21. Lamekes BA, Hermanides J, Devries JH, et al. Hyperglycemia: a prothrombotic factor? *Journal of Thrombosis and Haemostasis* 2010; 8:1663–9.
22. Song P, Wu Y, Xu J, et al. Reactive Nitrogen Species Induced by Hyperglycemia Suppresses Akt Signaling and Triggers Apoptosis by Upregulating Phosphatase PTEN (Phosphatase and Tensin Homologue Deleted on Chromosome 10) in an LKB1-Dependent Manner. *Circulation* 2007; 116:1585–95.

Comparative assessment of the effectiveness of radiofrequency ablation of pulmonary veins by the patients with persistent atrial fibrillation, effected in the course of coronary artery bypass grafting, depending on the renal function

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Abstract

Aim

To determine the effectiveness of radiofrequency ablation (RFA) with concomitant Coronary Artery Bypass Grafting (CABG) by the patients with persistent atrial fibrillation (AF) depending on the glomerular filtration rate (GFR).

Material and methods

403 patients (253 males and 150 females) aged from 50 to 67 (average age: 60.5±6.7 years) with persistent AF were examined. The duration of AF before an operation ranged from 1.5 to 8 years and on average 4.7±1.5 years. The initial figures of GFR accounted for from 59 to 45 ml/min/1.73 m² in 247 patients (the 1st group) and from 89 to 60 ml/min/1.73 m² in 156 patients (the 2nd group).

Results

During inpatient hospital period of CABG it was diagnosed Acute Kidney Injury (AKI) by the 132 patients (53.4 %) in the 1st group and by the 35 patients (22.4 %) in the 2nd group. Early recurrences of AF were revealed by 43.3 % of patients in the 1st group and by 23.7 % of patients in the 2nd group ($p < 0.001$). In the 1st group the diagnosis of early re-

currences of AF was made significantly more frequently among patients with AKI than among patients without it. 12 months after operation late recurrences of AF without antianginal therapy were revealed by 31.3% of patients and among them by 37.8% of patients with AKI in the 1st group; and by 21.2% and 24.2% respectively in the 2nd group. The figures of GFR were higher by patients with effective RFA than by patients with ineffective RFA on average at 37.8% ($p = 0.002$). It was revealed that GFR directly correlates with an effective refractory period of the left atrium ($r = 0.56$; $p < 0.001$) and a frequency threshold for induction of arrhythmia ($r = 0.53$; $p = 0.013$). Elimination of paroxysms of AF after RFA procedure was followed by considerable improvement of morpho-functional and electrophysiological parameters of heart.

Conclusion

It was shown that the presence of renal dysfunction in patients with persistent AF adversely influences on effectiveness of RFA with concomitant CABG and a short- and long-term cardiovascular prognosis.

Key words

Renal dysfunction, coronary artery bypass graft surgery, radiofrequency ablation, atrial fibrillation.

Introduction

It is known that the atrial fibrillation (AF) belongs to the most common types of tachyarrhythmias, adversely influences the cardiovascular forecast, and demands the differentiated approach to therapy depending on types of AF [1, 2]. At present, for tactical control of sinus rhythm by patients with atrial fibrillation medications interventional and surgical techniques are successfully used [1, 3, 4]. Clarification re-entry locations in the mouths of the pulmonary veins responsible for the occurrence of AF in 80–90% of cases and the development of a method for mapping nonflyuroskopik charting created the preconditions for the widespread use of the procedure of isolation of the pulmonary veins and the ganglionic plexus with a view to effective control of sinus rhythm [3, 5]. Along with an intervention method of ablation the arrhythmogenic zones by patients with AF, in recent years it's often used a surgical ablation as simultaneous intervention in time of operation of the Coronary Artery Bypass Grafting (CABG) and/or heart valve replacement [6, 7]. Simultaneous heart operations allow to eliminate the causes of cardiovascular hemodynamic of AF, to influence most effectively on arrhythmogenic substrates, and also to isolate the left atrium as the most frequent source of intracardiac thrombosis and increased risk of cardioembolic stroke [1, 3].

It is shown that efficiency of a radiofrequency ablation (RFA) of mouths of pulmonary veins and plexus ganglion depends on the AF form — paroxysmal, persistent and permanent, frequency rates and ways RFA — surgical, transvenous, mono — and bipolar, etc., severity of cardiac remodeling, comorbidity index, and ranges from 50% to 90% [3, 4, 7, 8]. It is established that the risk of renewal of paroxysms of

AF after the successful medicamentous and electric cardioversion depends on function of kidneys, i.e. on existence of a proteinuria and/or reduction of glomerular filtration rate (GFR) [9–11]. It is revealed that the chronic kidney disease (ChKD) correlates with the increased risk of emergence of AF and the thromboembolic complications [2, 12].

It is also known that existence of ChKD considerably increases risk of emergence of acute kidney injury (AKI) during the early period after heart operation, especially with application of artificial blood circulation [13, 14]. However opinions of experts on influence of AKI by patients with initial kidney dysfunction subjected CABG surgery in combination with RFA are diverged on the remote cardiorenal term. The researches devoted to an assessment of cumulative effect of ChKD and postoperative AKI by the patients with persistent AF subjected CABG in combination with RFA are single [7].

When assessing the prognostic role of ChKD by patients with HR it is necessary to consider dynamics of cardiovascular and kidney changes in the remote period after cardiac interventions in combination with RFA. As a rule, after operation CABG and/or prosthetics of valves of heart most of patients has an improvement the cardiac and renal functions that positively affects the remote forecast and survival [8, 13]. Therefore, the assessment of dysfunction of kidneys by patients with AF before operation, and especially its dynamics after simultaneous heart operations is obviously important for forecasting of efficiency of RFA.

The aim of the study was to compare efficacy of GFR in combination with RFA by patients with persistent AF depending on GFR in the remote period after operation.

Material and methods

The clinical study included 403 patients, 253 men and 150 women aged 50–67 years (mean age — $60,5 \pm 6,7$ years) with persistent AF subjected to operation CABG in combination with RFA of pulmonary veins in the Penza federal center of cardiovascular surgery. By 221 (89.5%) patients during operation it was performed isolation of the left atrial appendage to prevent cardioembolic stroke in case of resumption of recurrent AF.

Prescription AF before operation mad up from 1.5 to 8 years and the average — 4.5 ± 1.6 years (Table 1). Paroxysms of AF recurred from 2 to 7 times a year and generally stopped using antiarrhythmic drugs. The initial sizes of GFR determined by a formula CKD-EPI [15] by 247 patients made up from 59 to 45 ml/min. / 1,73 sq.m (1 group) and by 156 patients — from 89 to 60 ml/min. / 1.73 sq.m (the 2nd group). AKI was diagnosed and classified by creatinine level in blood serum, using criteria of AKIN (Acute Kidney Injury Net-work) [16].

The comparison of the clinical and anamnestic data revealed prevalence of comorbid states in 1 group on comparison with the 2nd group — the postponed myocardial infarction ($p=0.027$) and a stroke ($p=0.025$), chronic heart failure of stagnant type ($p=0.011$), anemia ($p=0.039$) and obesity ($p=0.036$). Besides, in 1 group the frequency of paroxysms of AF ($p=0.003$) and their duration ($p=0.011$) was more, than in the 2nd group.

Criteria for an exception from research were: primary diseases of kidneys; diabetes of 2 types; carrying out a program hemodialysis before operation; sick sinus syndrome and/or atrioventricular block of the II–III degree; valvular heart disease; thyroid disease with violation of hormonal activity.

Doppler echocardiography was carried out on the device Acuson X300 (“Siemens-Acuson”, Germany) at a sinus rhythm. It was determined the final diastolic and final systolic sizes of the left ventricle (FDSL, FSSL), an index of the volume of the left atrium (IVLA), the ejection fraction (EF) of LV, cardiac index (CI) LV, myocardial mass index LV (MMI) and specific peripheral vascular resistance (SPVR). For an assessment of LV diastolic function it was defined indicators of a transmitral diastolic flow: maximum speed of a fast and slow blood supply (V_e , V_a); their ratio (V_e/V_a); isovolumic relaxation time of LV (IVRT), and also it was calculated the Cardiothoracic ratio (CRCR).

Electrophysiological research of heart was conducted by transesophageal electrical stimulation of the left atrium. It was calculated the following indicators: wave dispersion of P (dP); recovery time of sinus node function (RTSNF); corrected DACE (RACE); ef-

Table 1. The clinical characteristic of the examined patients in groups before operation

Options	1group (n=247)	2 group (n=156)
Men, n / %	156 / 63.2	97 / 62.2
Age, years (M±SD)	60.5±6.7	61.6±6.3
Prescription AF years (M±SD)	4.7±1.5	4.3±1.2
The frequency of paroxysmal AF per year (M±SD)	4.49±1.38	3.62±1.16*
Heart rate during AF in minute. AF (M±SD)	130.7±11.5	129.1±10.2
Duration paroxysm AF, hours (M±SD)	6.28±1.76	4.81±1.46*
CHF II–III functional class, n / %	102 / 41.3	44 / 28.2*
Arterial hypertension, n / %	147 / 60.5	83 / 53.2
Myocardial infarction, n / %	106 / 43.6	49 / 31.4*
previous stroke, n / %	35 / 14.2	10 / 6.4*
Anemia (Hb < 110 r/n), n / %	29 / 11.7	8 / 5.1*
GFR ml / min/1,73 m ² (M±SD)	54.3±4.4	72.9±6.1*
abdominal obesity, n / %	103 / 41.7	48 / 30.8*
Chronic obstructive pulmonary disease, n / %	18 / 7.3	18 / 7.3

Note: ur — unreliable ($p>0,05$). CHF — congestive heart failure; HR — heart rate; Hb — hemoglobin.

fective refractory period of the left atrium (ERPLA); frequency threshold of induction of arrhythmia (FTIA). Holter monitoring of the electrocardiogram was carried out by means of Astrocord system (“Meditek”, Russia) for the purpose of identification of violations of a warm rhythm, including asymptomatic and unstable paroxysms of AF (duration < 30 sec.). Tool researches were conducted before, in 6 and 12 months after operation.

Research was carried out according to standards of appropriate clinical practice (Good Clinical Practice) and the principles of the Helsinki Declaration of the World medical association. The protocol of research was approved by Ethical committee of the institute and before inclusion in research patients signed the written informed consent.

Statistical processing of results of research was carried out with application of the Statistic 6.0 program. The normality of distribution of signs was determined by Kolmogorov-Smirnov’s test. Depending on nature of distribution of signs reliability of distinctions was defined by means of parametrical (Student’s t-criterion) and nonparametric methods (Mann-Whitney’s U-criterion). Comparison of frequencies of a binary sign was carried out by definition of nonparametric criterion χ^2 according to Pearson. Conjugacy of the studied parameters determined by method of the one-factorial correlation analysis by Pearson. Data were presented in the form by M±SD. Distinctions were considered reliable at $p < 0.05$.

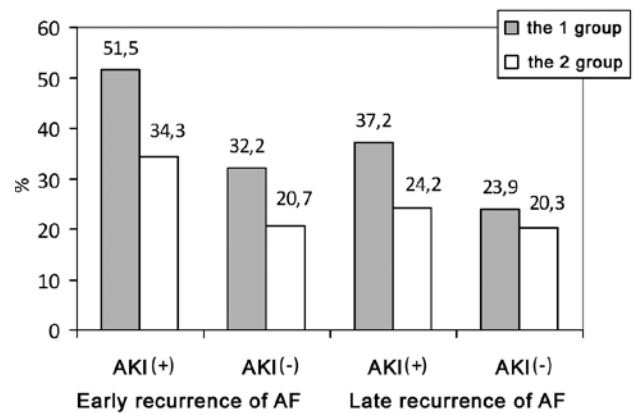
Results

During the hospital period of supervision after operation it was diagnosed AKI for 167 patients, including in the 1 group — by 132 (53.4%) patients and in the 2nd group — by 35 (22.4%) patients. As a result, in each group allocated two subgroups: patients with AKI and without it. It should be noted that in the next 30 days after operation early recurrence of AF in 1 group was revealed by 107 (43.3%) patients and in the 2nd group — by 37 (23.7%) patients, distinction is reliable ($\chi^2=15.16$; $p < 0.001$). Besides, in the 1 group with AKI early recurrence of AF was diagnosed for patients authentically more often ($\chi^2=7.05$; $p=0.008$), than by the patients who don't have AKI (figure 1). Early recurrence of AF by the patients who don't have AKI was authentically more often in 1 group, than in the 2nd group: 33,9% vs 20,7% ($\chi^2=4.59$; $p=0.032$).

The assessment of efficiency of RFA in 12 months after operation has showed that in the 1 group late recurrence of AF without application of antianginal therapy is diagnosed by 71 (31.1%) of the patient and in the 2nd group — by 32 (21.2%) of patients. Thus in the 1 group the number of the patients who transferred AKI was reliable more, than patients without AKI: 37.8% vs 23.9% ($p=0.033$). Besides this, the probability of emergence of late recurrence of AF by patients without AKI authentically didn't differ depending on initial function of kidneys.

By the end of the supervision period in the 1 group efficiency of RFA without application of AAT made 68.9% and in combination with AAT — 80.7%, in the 2nd group — 79.5% and 90.1%, respectively. Thus, the patients who transferred AKI, had an efficiency of RFA below, than at the patients who didn't have postoperative AKI. Without AAT, patients of the 1 group which transferred AKI had the minimum direct efficiency of RFA and made up 62.2%, and maximum efficiency took place by the patients without dysfunction of kidneys, both before operation, and after it, made up 80.5% ($\chi^2=9.10$; $p=0.003$).

When studying relationships of cause and effect between early and late recurrence of AF after operation distinction in the compared groups has been revealed. It is shown that in the 1 group by the patients with AKI and with early recurrence of AF the probability of preservation of recurrence of AF and in the late period after operation is high: in 51.1% of cases. However patients without AKI have a preservation of recurrence of AF, which arose in the early postoperative period, it was observed by 42.3% of patients. In the 2nd group in the presence



Note: AKI (+) — patients with AKI; AKI (-) — patients without AKI.

Figure 1. Comparison of efficiency of RFA depending on the initial function of kidneys and development of postoperative AKI without application of AAT

of early recurrence of AF by the patients who transferred AKI, arrhythmia paroxysms in 12 months after operation were noted in 37.5% of cases and by the patients without AKI — in 33,3% of cases. It testifies that existence of early recurrence of AF after operation CABG in combination with RFA does not exclude possibility of preservation of a stable sinus rhythm in the remote period.

It should be noted that patients with early recurrence of AF have cardiovascular complications — a perioperative myocardial infarction, an ischemic stroke, a sharp heart and renal failure, etc., took place authentically more often than at preservation of a sinus rhythm. The hospital lethality depending on initial function of kidneys and development of AKI fluctuated from 9.8% to 2.5%.

It should be noted that in 12 months after operation CABG in combination with RFA in the 1 group by 21 (9.2%) of the patient, including by 14 (11.8%) of the patients who transferred AKI progressing of the dysfunction of kidneys preceding operation and in the 2nd group — 3.3% and 6.1%, respectively took place. The stable increase in GFR in 12 months after operation in the 1 group it was observed by 117 (51.3%) of the patients, including by 48 (40.3%) of the patients who transferred AKI and in the 2nd group — 60,9% and 54.6% respectively. As a result, in 12 months after operation from 379 patients by 263 (69.4%) the size of GFR was >60 ml/min. / 1.73 in sq.m and by 116 (30.6%) of the patients it was <60 ml/min. / 1.73 sq.m. It is also shown that efficiency of RFA at size GFR >60 ml/min. / 1.73 sq.m in comparison with GFR <60 ml/min. / 1.73 sq.m are reliable above (figure 2): 74.1% and 57.8% respectively ($p=0.011$). It is revealed that by the patients from successful RFA the size of

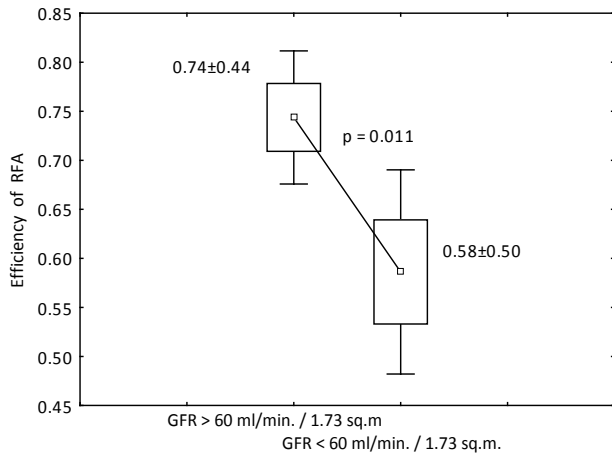


Figure 2. Efficiency Comparison of RFA depending on size of GFR in 12 months after operation

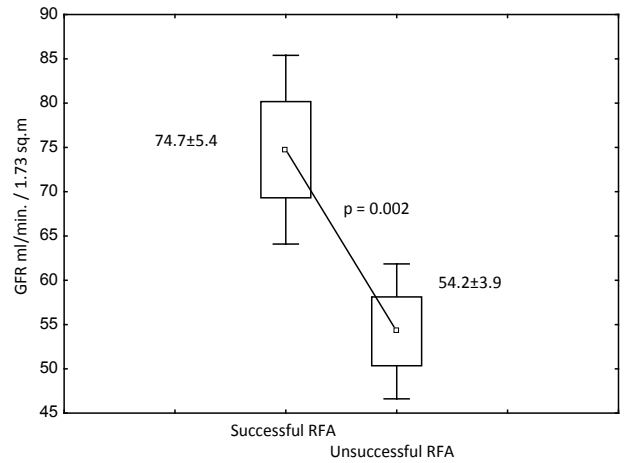


Figure 3. Comparison of Sizes GFR depending on efficiency of RFA

GFR in average for 37.8% ($p = 0.002$) surpasses that by the patients from unsuccessful RFA (figure 3).

By means of the one-factorial correlation analysis the correlations of GFR and electrophysiological indicators of heart testifying that decrease in GFR of kidneys is associated with factors of electric heterogeneity of atrial- violation of diastolic relaxation of ventricles, dilatation of the sizes of atrials, anemia, etc. [1, 17] are revealed. It is shown (figure 4) that size GFR directly correlates with indicators ERPLA ($r = 0.56$; $p < 0.001$) and FThIA ($r = 0.53$; $p = 0.013$).

Comparison initial of the morpho-functional and electrophysiological parameters of heart depending on efficiency of RFA didn't reveal the distinction (table 2). However, 12 months later after operation it is noted that elimination of paroxysms of AF leads to improvement of parameters of cardiohemodynamics, and also to reduction of cardiometric parameters. Thus indicators of systolic function — CI and

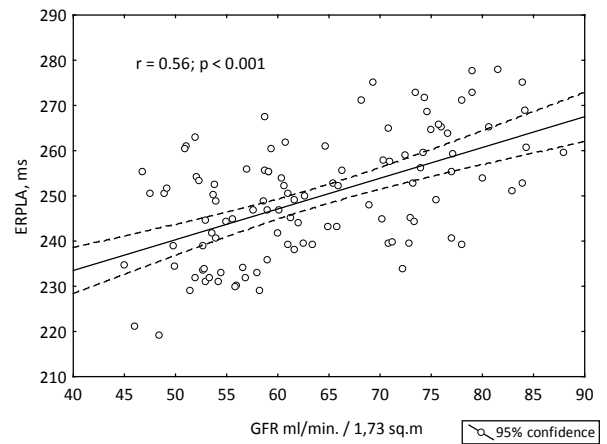


Figure 4. Correlation of Indicators GFR and ERPLA irrespective of initial function of kidneys

EF increased in average by 13.9% ($p=0.008$) and 16.9% ($p=0.026$), respectively, indicators of the diastolic function LV —Ve/Va and IVRT also changed authentically: in average for 32.6% ($p<0.001$) and 9.0%

Table 2. Comparison of dynamics of the morpho-functional and electrophysiological parameters of the heart in 12 months after operation taking into account efficiency of RFA (M±SD)

Indicators	Patients with successful RFA (n = 320)			Patients with unsuccessful RFA (n = 59)		
	Initially,	After operation	p	Initially,	After operation	p
EDSLV, mm	55.4±4.7	51.8±5.1	ur	54.9±4.2	53.0±5.2	ur
VILA, ml/m ²	42.7±3.6	34.5±4.3	0.014	43.2±4.0	38.6±3.2*	0.031
EF LV, %	46.7±4.1	54.6±5.2	0.026	47.1±3.8	50.3±5.0*	ur
CI, l/min/m ²	2.38±0.19	2.71±0.23	0.008	2.35±0.21	2.54±0.26*	0.014
SPVR, conventional units.	55.0±6.4	43.0±5.5	<0.001	54.6±5.9	47.0±6.1	0.011
ILVM, g/m ²	118.3±12.7	108.2±11.6	0.029	117.4±13.2	114.5±12.3	ur
CR, %	44.3±5.0	39.6±4.7	0.032	44.5±5.6	41.7±3.8	ur
Ve / Va	0.86±0.07	1.14±0.13	<0.001	0.85±0.09	1.03±0.12*	0.006
IVRT, ms	101.5±9.7	92.4±10.6	0.011	102.6±9.4	96.5±8.3	ur
KBBΦCY, ms	290.8±22.5	245.1±18.3	ur	318.0±27.6	263.1±30.2	ur
ERPLA, ms	235.2±18.1	276.4±23.9	0.008	241.6±20.3	255.4 ±24.9*	0.031
FThIA, impulse/min	477.0±63.2	822.5±74.3	<0.001	485.1±70.6	608.5±56.0*	0.022
Wave dispersion P, vc	41.8±3.9	35.4±3.5	0.036	42.3±4.5	40.2±4.8	ur

Note: * — distinction of indicators after operation in groups, ur — unreliable ($p<0,05$).

($p=0.011$), respectively. It is important to note that stable preservation of a sinus rhythm, improvement of contractile and pump function of the heart, thanks to successful RFA and a revascularization of a myocardium, promoted reduction of the increased initial sizes of heart — ED_{SLV}, CR, VILA and ILVM. In group of patients with successful RFA indicators ERPLA and FThIA increased in average in 17.5% and in 1.72 times, respectively, and wave dispersion P decreased in average in 15.3% ($p = 0.036$).

In the group of patients with unsuccessful RFA the changes in morphological and functional indicators of heart were also reliable, but are less expressed, than by the patients with successful RFA. Despite preservation of rare paroxysms of AF after RFA and against AAT, the frequency of waves of fibrillation (f waves) and HR during a paroxysm of AF decreased authentically, indicators ERPLA, FThIA and amplitude of waves, contrary, increased. By most of patients with successful RFA it wasn't succeeded to induce AF paroxysms by means of transesophageal electrostimulation, or unstable paroxysms were induced.

It is important to note that existence of dysfunction of kidneys by patients with persistent AF both in an initial state, and after operation CABG in combination with RFA influences risk of development of adverse cardiovascular events, mortality and a further current of an arrhythmic syndrome. It is shown that within the first year of supervision cardiovascular complications after successful RFA arose less than at patients with late recurrence of AF (table 3). Repeat of paroxysms of AF after operation was followed by

Table 3. Comparison of clinical outcomes depending on efficiency of RFA in combination with CABG 12 months later after operation (n/%)

Cardiovascular complications and manipulations	Patients with successful RFA (n = 320)	Patients with unsuccessful RFA (n = 59)
Acute coronary syndrome / myocardial infarction	7 / 2.19	4 / 6.78
Ischemic stroke / transient ischemic attack	4 / 1.25	5 / 8.48*
The manifestation of sick sinus syndrome	6 / 1.88	3 / 5.08
Long persistent / permanent AF	0/0	7 / 11.86*
Pacemaker implantation	7 / 2.19	3 / 5.08
The frequency of hospitalization for cardiac causes (M±SD)	0.46±0.48	1.13±0.52*
Percutaneous coronary interventions	5 / 1.56	4 / 6.78
Thrombosis / embolism	3 / 0.94	2 / 3.39
Cardiovascular mortality	6 / 1.88	5 / 8.48*
Program hemodialysis	0 / 0	4 / 6.78*

Note: * — distinction between groups ($p < 0,05$).

the increased need for implantation of a pacemaker, a program hemodialysis and reception of indirect anticoagulants. Annual mortality after discharge from a hospital in group of the patients with successful RFA was authentically higher ($p=0.019$), than at preservation of recurrence of AF after RFA.

Thus, existence of ChKD with the lowered GFR <60 ml/min. / 1.73 sq.m by the patients with persistent AF subjected to operation of CABG in combination with RFA is associated with low efficiency of RFA procedure in comparison with intact function of kidneys, and also adversely influences cardiovascular and renal forecasts.

Discussion

In recent years in connection with the steady growth of frequency of identification of ChKD in the general population the study of cardiorenal relationship becomes relevant, characterized cardiorenal syndrome and cardiorenal continuum. It is proved that existence of the dysfunction of kidneys, which is shown a proteinuria and/or decrease in GFR increases risk of emergence of AF, reduces efficiency of medicamentous control of a sinus rhythm [10–14, 18]. Results of the conducted research showed that efficiency of the RFA procedure executed during operation of CABG depend not only on an initial functional condition of kidneys, but also more depend on postoperative dynamics of ChKD. It is shown, that at patients with successful RFA the preservation of a stable sinus rhythm promotes increase of cardio hemodynamic effectiveness of CABG, in its turn, improvement of contractile and pump function of the heart by revascularization within optimizes renal hemodynamics and glomerular filtration.

It is important, that postoperative dynamics of morpho-functional heart remodeling correlates with the effectiveness of RFA. Preservation of a stable sinus rhythm in 12 months. after CABG in combination with RFA is associated with regression of left ventricular hypertrophy of LV, improvement of indicators of systolic and diastolic functions of heart and reduction of the sizes of the left ventricular which in total reduce "arrhythmogenic potential" atria. Several authors emphasized the prognostic value of baseline morphological and functional indicators in assessing the effectiveness of the procedure RFA by patients with the AF various forms [2, 6, 7]. It is shown, that initial morpho-functional and electrophysiological risk factors for late recurrence of AF correlate with inefficiency RFA procedure, on the contrary, by pa-

tients with a successful outcome of RFA postoperative values of these parameters play an important role regardless of the dynamics of the initial parameters. It means that, based on initial morphological and functional parameters of the heart one can not conclusively predict the efficacy of RFA, especially, carry out profiling of patients to which this procedure can be refused.

It is also revealed, that effective RFA is followed by reliable shifts of the electrophysiological indicators characterizing electric characterized by an electrical heterogeneity ("arrhythmogenic readiness") of the atria. It is shown, that in the group of patients with lack of late recurrence of AF the reliable increase in presurgical indicators ERPLA and FThIA is noted. Despite of preservation of recurrence of AF after RFA, it's often marked the reduction of expressiveness of clinical and hemodynamics symptomatology of AF that is shown by reliable reduction of frequency and duration of paroxysms of AF, increase in the specific frequency of asymptomatic paroxysmal AF. Therefore, morpho-functional indicators of heart, and the lowered GFR of kidneys before operation of CABG in combination with RFA in comparison with their postoperative values possess less expressed predictive value of efficiency of surgical RFA in the remote period.

It is also noted, that the development of postoperative AKI is followed by increase in frequency of early recurrence of AF, and adversely influences the next cardiovascular forecast irrespective of initial size of GFR. Efficiency of RFA in combination with operation of CABG and the cardiovascular forecast during the remote period is much worse by the patients who transferred AKI and by initial dysfunction of kidneys.

Therefore, absence of full antiarrhythmic effect dictates the need to perform repeated procedures of RFA, including expansions potential the arrhythmogenic sites, which are exposed to ablative effects, and eliminating postincisional supraventricular tachycardia [6, 7].

Thus, the importance of the received results consists in that the predictive value of decrease in GFR <60 ml/min. / 1,73 sq.m both before operation, so after CABG in combination with RFA in the remote period. In this regard holding cardio- and neuroprotective therapy, including use of a program hemodialysis is actual. It is revealed that the improvement of glomerular function of kidneys, thanks to simultaneous operation of CABG and the RFA procedure, promotes improvement of the cardiovascular forecast.

Conclusions

Early recurrence of AF after operation of CABG in combination with RFA appears at initial size of GFR < 60 ml/min. / 1,73 sq.m and in case of development of postoperative AKI, than by the patients with size of GFR > 60 ml/min. / 1,73 sq.m and in the absence of AKI authentically more often.

Efficiency of the single procedure of RFA in combination with CABG and without application of antiarrhythmic therapy, in 12 months after operation by the patients with size of GFR < 60 ml/min. / 1.73 sq.m, made up 68,9%, including by the patients who transferred postoperative AKI, – 62.2% and by patients with size of GFR > 60 ml/min. / 1.73 sq.m — 79.5% and 75.8%, respectively, in a combination with AAT – 80.7 and 90.1%, respectively.

Size of GFR irrespective of dysfunction of kidneys directly correlates with indicators of the effective refractory period of the left ventricle ($r=0.56$; $p < 0.001$) and frequency threshold of induction of AF ($r=0.53$; $p=0.013$). By the patients with successful RFA the size of GFR reliable above in average for 37.8% ($p=0.002$), than by the patients with unsuccessful RFA.

Conflict of interest: None declared.

References

1. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation. The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology. *Eur Heart J*. 2010;31:2369–429.
2. Fomin VV, Kiyakbaev GG. Chronic kidney disease and atrial fibrillation. *Klinicheskaya nefrologiya*. 2010;6:34–8. Russian [Fomin V.V, Kiyakbaev G.G. Chronic kidney disease and atrial fibrillation. *Clinical Nephrology*. 2010;6:34–8].
3. Bokeriya LA, Revishvili ASh. Modern approaches to nonpharmacological treatment of atrial fibrillation. *Vestnik aritologii*. 2006;45:5–18. Russian [Bokeria L.A, Revishvili A.Sh. Modern approaches to pharmacological treatment of atrial fibrillation. *Bulletin of arrhythmology*. 2006;45:5–18].
4. Willems S, Drewitz I, Steven D, et al. Interventional therapy of atrial fibrillation: possibilities and limitations. *Dtsch Med Wochenschr*. 2010;135 (Suppl 2): 48–54.
5. Beukema WP, Sie HT, Misier AR, et al. Predictive factors of sustained sinus rhythm and recurrent atrial fibrillation after a radiofrequency modified Maze procedure. *Eur J Cardiothorac Surg*. 2008;34 (4): 771–5.
6. Veasey RA, Segal OR, Large JK, et al. The efficacy of intraoperative atrial radiofrequency ablation for atrial fibrillation during concomitant cardiac surgery: the Surgical Atrial Fibrillation

- Suppression (SAFS) Study. *J Interv Card Electrophysiol.* 2011;32 (1):29–35.
7. Naruse Y, Tada H, Sekiguchi Y, et al. Concomitant chronic kidney disease increases the recurrence of atrial fibrillation after catheter ablation of atrial fibrillation: a mid-term follow-up. *Heart Rhythm.* 2011;8:335–41.
 8. Mainigi SK, Sauer WH, Cooper JM, et al. Incidence and predictors of very late recurrence of atrial fibrillation after ablation. *J Cardiovasc Electrophysiol.* 2007;18 (1):69–74.
 9. Sandhu RK, Kurth T, Conen D, et al. Relation of renal function to risk for incident atrial fibrillation in women. *Am J Cardiol.* 2012;109:538–42.
 10. Alonso A, Lopez FL, Matsushita K, et al. Chronic kidney disease is associated with the incidence of atrial fibrillation: the Atherosclerosis Risk in Communities (ARIC) study. *Circulation.* 2011;123:2946–53.
 11. Soliman EZ, Prineas RJ, Go AS, et al. Chronic Renal Insufficiency Cohort (CRIC) Study Group. Chronic kidney disease and prevalent atrial fibrillation: the Chronic Renal Insufficiency Cohort (CRIC). *Am Heart J.* 2010;159 (6):1102–7.
 12. Go AS, Fang MC, Udaltsova N, et al. Impact of proteinuria and glomerular filtration rate on risk of thromboembolism in atrial fibrillation: the anticoagulation and risk factors in atrial fibrillation (ATRIA) study. *Circulation.* 2009;119(10):1363–9.
 13. Charytan DM, Yang SS, McGurk S, Rawn J. Long and short-term outcomes following coronary artery bypass grafting in patients with and without chronic kidney disease. *Nephrol Dial Transplant.* 2010;25:3654–63.
 14. Iskenderov BG, Sisina ON. Risk factors and outcomes of acute kidney injury in patients with intact renal underwent coronary artery bypass grafting. *Nefrologiya.* 2013;4:63–7. Russian (Iskenderov B.G., Cicino O.N. Risk factors and outcomes of acute kidney injury by patients with preserved renal function undergoing coronary artery bypass surgery. *Nephrology.*2013;4:63–7).
 15. Kidney Disease: Improving Global Outcomes [KDIGO] CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013;3(1):1–150.
 16. Smirnov AV, Kayukov IG, Degtereva OA, et al. Problems of diagnostics and stratification of burden of acute kidney injury. *Nefrologiya.* 2009;3:9–18.
 17. Iskenderov BG, Rakhmatullof FK. Structural and electrophysiological predictors of paroxysmal atrial fibrillation. *Rossiyskiy kardiologicheskiy zhurnal* 2014;4:86–91. Russian (Iskenderov BG, Rahmatullah FK Structural and electrophysiological predictors of paroxysmal atrial fibrillation. *Russian Journal of Cardiology.* 2001;4:26–30).
 18. Iguchi Y, Kimura K, Kobayashi K, et al. Relation of atrial fibrillation to glomerular filtration rate. *Am J Cardiol.* 2008;102 (8): 1056–9.

The features of structural and morphometric parameters of the left ventricle in female chronic heart failure patients

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Summary

Object

Explore the structural-functional state of the left ventricle (LV) in female patients with post-infarction chronic heart failure (CHF) II–III functional class (FC) (NYHA).

Materials and methods

The study included 105 female patients with CHF II–III FC of non-valvular etiology; all of the patients were post-menopausal. The median age was 59 ± 6.7 years. All patients, included in the study, were performed echocardiography on ultrasound scanners «Vivid-7, Dimension» (USA).

Results

Analysis of the ECG results showed, that CHF occurs predominantly in women with preserved LV systolic function. Restrictive type of the diastolic LV relaxation was defined only in 6 patients (6.2%), abnormal type of diastolic relaxation was observed in 32 patients (31.3%) and in 63 (61.7%) patients the type of violation of diastolic relaxation could not be determined. It should also be noted, that 8 patients (8.16%) had a combination of LV systolic dysfunction, defined in terms of LVEF, and signs of violation of diastolic relaxation, i.e. mixed LV dysfunction. In 23.5% cases concentric LV hypertrophy was defined, in 48% cases — eccentric hypertrophy without dilatation, in 15.7% cases — eccentric LV hypertrophy with dilatation and in 9.8% cases — mixed hypertrophy of LV.

Conclusion

Post-infarction CHF in women is combined with the preserved LV systolic function. In cases with post-infarction CHF II–III FC, the most common type of LV remodeling is eccentric hypertrophy without dilatation.

Key words

Chronic heart failure, *diastolic dysfunction*, remodeling

Introduction

Over the past decades, despite of the obvious achievements in the study of pathogenesis, clinic and treatment, chronic heart failure (CHF) still remains the most difficult and unfavorable prognostic complication of cardiovascular diseases. A significant number of clinical and epidemiological studies in Russia and abroad evidences this [1–6].

Over the past 20 years, the prevalence of CHF increased by more than 150%. The incidence of CHF in the United States was about 2.5% [7, 8], in the European population it ranged from 0.4% to 2% [9], in developing countries, this information is sparse. [10] The annual spread rate of CHF amounted 10 per 1 thousand people. Approximately 300 thousand people died from CHF, and treatment costs reached 1–2% of total expenditure on health [11–13].

According to current literature data, significant demographic changes in the population over the past decade are considered as the main cause of increase in the prevalence of CHF: the decrease in the proportion of young people and a significant increase in the number of elderly and centenarians, who are at risk for development of CHF. Currently, researchers are talking about the process of global “aging” of the population in the developed world [14–17]. In the UK over the past 40 years, the proportion of persons > 65 years old increased by 50%, and a 3-fold increase in the number of persons, who are 85 years old [18].

According to a recent registry of clinical entities, CHF is not the independent disease in the Republic of Azerbaijan, it is not included in statistical reports, but it is seen as a complication or outcome of major cardiovascular diseases. We know that as well as in Russia (before the study “Era” — epidemiological studies of patients in the European part of Russia), similar systematic data were not available [19].

This is due to the fact that CHF was not fixed both in the Russian and the national health statistics as a distinct disease, but it was dissolved in other diagnoses: coronary heart disease, rheumatic heart disease, myocarditis, cardiomyopathy, etc.

For decades, it was believed that the basis for the development of CHF was a violation of the LV contractile ability, which was revealed in the determination of its ejection fraction (EF). In the late 90s, there were

reports that the clinical manifestations of CHF are observed in 20–30% of patients with the preserved LV systolic function. This led to the assumption, that the cause of CHF could be extremely diastolic dysfunction with the preserved LV systolic function. Confirmation of this assumption has been possible thanks to the appearance of the Doppler method (Doppler-ECG) and its wider introduction into clinical practice. Essential significance of this method lies in the fact, that with its help there is a real opportunity to assess the global (systolic and diastolic) LV function in patients with CHF [20].

Most epidemiological studies indicate the predominance of men among patients with CHF [21]. A more serious epidemiological situation in terms of cardiovascular morbidity and mortality in men has led to an underestimation of the importance of this problem in women [22].

Therefore, the problem of the CHF treatment in women comes to the fore. It is necessary to define the peculiarities of CHF and its treatment in the female population, to communicate clinical manifestations with a hormonal status of women in different age periods. There is a need for a new epidemiological study, the results of which will be of great practical importance for the health system, in the development of guidelines and principles of CHF treatment in women.

Thus, considering the above definitions, the gender differences of CHF in women are interesting, which is reasonable and relevant to modern health care.

The object of research is to determine the characteristics of structural-functional state of LV in women with the post-infarction CHF II–III functional class (FC).

Materials and methods

The study included 105 women suffering from CHF II–III FC of non-valvular etiology, which are postmenopausal. Average age is 59 ± 6.7 years. All patients ($n = 105$), included in the study, was performed echocardiography (ECG) on the ultrasonic scanner «Vivid-7, Dimension» (USA). In the present study, this survey was not carried out in 3 women, for various reasons, so in the final data analysis, 102 patients suffering from the post-infarction CHF II–III FC were included.

The Ethics Committee of the Institute of Cardiology of Azerbaijan approved the study protocol. Work carried

out in accordance with the requirements of Good Clinical Practice (GCP), Good Epidemiology Practice (GEP) and the Helsinki Declaration of Human Rights. All patients signed the informed consent to the data analysis of records contained in their medical documentation.

The structure of complications is represented by a post-infarction stenocardia (71%), heart rhythm disorders (18%), the formation of a heart aneurysm (5%), blood clot in LV (2%) or ischemic cardiomyopathy (4%). Background increased BP was recorded in the whole group in 82% of patients, which is consistent with population-based studies on the higher frequency of arterial hypertension (AH) among women [23].

Patients, included in the study, were treated with antiplatelet agents (90%), β -blockers (85%), angiotensin-converting enzyme (95%), diuretics (68%), nitrate (41%), statin (22%).

Statistical analysis of the material was held by software packages the Microsoft Excel. The text, the data is presented as arithmetic mean and standard error of the mean ($M \pm m$).

Results and discussion

Analysis of the ECG study showed that CHF occurs in women predominantly with the preserved LV systolic function. Table 1 summarizes the main indicators characterizing the LV systolic function in women suffering from CHF II–III FC.

Numerous studies have shown that diastolic dysfunction developed more often in women than in men, and LVEF remained unchanged [24–29]. The prevalence of CHF in more elderly patients should be also considered. With an age increasing, the percentage of patients with the preserved LV systolic function increases [29, 30]. Thus, the prevalence of the LV diastolic dysfunction in women is associated with both the feature of a woman's heart reaction to damaging factors and gender characteristics of the CHF spread depending on age.

Table 1. **Indicators of the LV systolic function in women with post-infarction CHF II–III FC**

Indicator	Value (n=102)
ESD, mm	40.1±4.9
EDD, mm	57.0±5.2
ESV, ml	54.4±6.8
EDV, ml	109.1±11.2
LVEF, %	56.3±4.9
SV, ml	89.1±9.7

Features of cardiovascular continuum lie in the fact that at a certain stage of heart disease, progres-

sion of CHF occurs on general regularity, practically independent of etiologic factor. Perhaps this is the key to explaining the search of criteria of early diagnosis and prognosis of CHF [31–34].

Thus, when analyzing the results of ECG study of the heart, the LV systolic dysfunction is defined only in every fourth patient, whereas it is intact in other cases. To identify the etiologic and clinical-demographic indicators, which may be associated with the occurrence of LV systolic dysfunction, all the patients were divided into subgroups according to certain clinical-demographic characteristics (Table 2).

Table 2. **The incidence of the LV diastolic dysfunction, depending on the original characteristics of patients with CHF**

Subgroups of patients with CHF	The incidence of the LV diastolic dysfunction in subgroup, %
AMI in medical history	71
Age > 75 years old	53.4
Atrial fibrillation	33.2
AH as a cause of CHF	59.5
Diabetes mellitus as a cause of CHF	25.7

Thus, it was possible to determine the patient's premorbid background with CHF, in which systolic CHF is determined most likely. This form of CHF is specific in women after acute myocardial infarction (AMI), AH and in elderly patients aged ≥ 75 years.

The next logical step of the work was to determine the parameters of LV diastolic function. Table 3 summarizes the main indicators, characterizing the LV diastolic function in women with the post-infarction CHF II–III FC.

Table 3. **Indicators of the LV diastolic function in women with the post-infarction CHF II–III FC**

Indicator	Value (n = 102)
The rate of early rapid filling of LV (peak E), m/s	0,89±0,17
The rate of late atrial filling of LV (peak A), m/s	0,71±0,02
The ratio E/A	1,49±0,21
Isovolumic relaxation time, ms	85±13
The deceleration time of early diastolic filling, ms	174±33

In the study sample, based on the method of determining the arithmetic mean of each specific indicator, it can come to the mistaken belief that the LV diastolic function is not impaired. However, although the restrictive type of the LV diastolic relaxation was defined only in 6 (6.2%) patients, abnormal type of diastolic relaxation was observed in 32 (31.3%) patients, and in 63 (61.7%) patients the violation type of diastolic

relaxation could not be determined. It should also be noted, that in 8 (8.16%) patients there was a combination of the LV systolic dysfunction, defined in terms of LVEF, and violation signs of diastolic relaxation, i.e. mixed LV dysfunction.

The analysis of remodeling features of LV based on the definition of indicators, such as LV myocardial mass index (LVMMI), relative wall thickness (RWT), shown that a change in the spatial architecture of LV is specific for women suffering from the post-infarction CHF II–III FC (Table 4).

Table 4. **The incidence of various types of LV remodeling, characterized by different ratios of wall thickness and size of its cavity**

Types of LV remodeling	Frequency, abs / %
Normal LV	1/0.98
Concentric hypertrophy of LV	26/23.5
Eccentric hypertrophy of LV without dilatation	49/48.0
Eccentric hypertrophy of LV with dilatation	16/15.7
Mixed hypertrophy of LV	10/9.8

Thus, we can conclude, that the presence of the post-infarction CHF II–III FC in women indicates the presence of some form of LV remodeling with approximately 100% probability. In 23.5% cases, the LV concentric hypertrophy is defined in patients (LVH), in 48% cases — the LV eccentric hypertrophy without dilatation, in 15.7% patients — the LV eccentric hypertrophy with dilatation, and in 9.8% patients — mixed LV hypertrophy.

In recent years, the gender characteristics of cardiac remodeling after myocardial infarction (MI) are discussed actively, despite the fact that the development of CHF after MI occurs on general mechanisms [33, 34]. In particular, the experiments show that fibroblasts of woman's hearts are more resistant to ischemia than men's, which determines their lower rate of the apoptosis of heart cells after MI [35]. This was confirmed in the clinic: in women, having MI, the degree of apoptosis of cardiomyocytes was 10 times lower than in men [36]. Consequently, the post-infarction remodeling occurs in women more favorably than in men. The thinning of the myocardium walls and enlargement of the heart chambers in women is less pronounced. As we age, women saved the total amount of heart muscle cells and muscle mass, but there is their steady loss in men. Often after MI, pressure overload develops. In this case, the majority of the women LV remodeling is on relatively favorable adaptive type of the heart remodeling, whereas there

is dilation of the LV chamber in men, which often leads to a decrease in systolic function.

Conclusions

Post-infarction CHF occurs predominantly with the preserved LV systolic function in women.

The presence in females of the post-infarction CHF II–III FC usually indicates the presence of some form of LV remodeling. At the same time, in 23.5% patients concentric LVH is defined, in 48% patients — eccentric LVH without dilatation, in 15.7% patients — eccentric LVH with dilatation, and in 9.8% patients — mixed LVH.

Conflict of interest: None declared.

References

1. Mareev VJu, Danieljan MO, Belenkov JuN. Comparative characteristics of patients with CHF, depending on the size of the ejection fraction by the results of the Russian multicenter study AGE-O-CHF: again about the problem of heart failure with preserved left ventricular systolic function. *Serdechnaya nedostatochnost*. 2006; 4: 164–71. Russian.
2. Roger VL, Mozaffarian D. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation* 2013; 127: e6–e245.
3. Lloyd-Jones D, Adams RJ, Brown TM et al. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. *Circulation* 2010;121:e46–e215.
4. Wong CM, Hawkins NM, Jhund PS, et al. Clinical characteristics and outcomes of young and very young adults with heart failure: The CHARM program [Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity]. *JACC* 2013; 62:1845–1854.
5. Lam CS, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2011;13:18–28.
6. Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. *Eur Heart J*. 2012; 33:1750–1757.
7. ACC/AHA Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines). S.A. Hunt [et al.]. *JACC*. 2005;46:1–82.
8. Peacock WF, Braunwald E, Abraham W. For the NHLBI Working Group on Emergency Department Management of Acute Heart Failure Research challenges and opportunities. *JACC*. 2010;56:343–51.

9. Laribi S, Aouba A, Nikolaou M. Trends in death attributed to heart failure over the past two decades in Europe. *Eur J Heart Fail.* 2012;14:234–9.
10. Mendez GF, Cowie MR. The epidemiological features of heart failure in developing countries: a review of the literature. *International Journal of Cardiology.* 2001;80:213–9.
11. Lloyd-Jones D, Adams RJ, Brown TM. Heart disease and stroke statistics—2010 Update. *Circulation.* 2010;121:46–215.
12. Dunlay SM, Shah ND, Shi Q. Lifetime costs of medical care after heart failure diagnosis. *Circ Cardiovasc Qual Outcomes.* 2011;4:68–75.
13. Ross JS, Chen J, Lin Z. Recent national trends in readmission rates after heart failure hospitalizations. *Circ Heart Fail.* 2010;3:97–103.
14. Goyal A, Norton CR, Thomas TN. Predictors of incident heart failure in a large insured population. A one million person-year follow-up study. *Circ Heart Fail.* 2010;3: 698–705.
15. National guidelines GFCF and PRAs for the diagnosis and treatment of chronic heart failure (third revision). *Serdechnaja nedostatochnost* 2009;58:64–106. Russian.
16. Guidelines for the diagnosis and treatment of chronic heart failure. Task force for the diagnosis and treatment of chronic heart failure of the European Society of cardiology. *Eur Heart J.* 2008;4:2388–2442.
17. Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *JACC.* 2005;46–82.
18. British Heart Foundation. Coronary heart disease statistics: Heart failure supplement. 2002 ed. British Heart Foundation. 2002.
19. Belenkov JuN, Ageev FT, Mareev VJu. Paradoxes of heart failure: a look at the problem at the turn of the century. *Serdechnaja nedostatochnost.* 2000;1:4–6. Russian.
20. Belenkov JuN. The true prevalence of CHF in the European part of the Russian Federation (the study of the era, the hospital phase). *Serdechnaja Nedostatochnost'.* 2011;12:63–8. Russian.
21. Rodriguez F, Wang Y, Johnson CE, Foody JM. National patterns of heart failure hospitalizations and mortality by sex and age. *J Card Fail.* 2013; 19 (8):542–9.
22. Jessup M, Pina I. Is it important to examine gender differences in the epidemiology and outcome of severe heart failure? *J Thorac Cardiovasc Surg.* 2004; 127:1247–52.
23. Prevention, diagnosis and treatment of hypertension. Russian recommendations (third revision). Developed by the Expert Committee of All-Russian Scientific Society of Cardiology. Moscow; 2008. 32 p. Russian.
24. Anjan VY, Loftus TM, Burke MA, et al. Prevalence, clinical phenotype, and outcomes associated with normal B-type natriuretic peptide levels in heart failure with preserved ejection fraction. *Am J Cardiol* 2012;110:870–876.
25. Grewal J, McKelvie RS, Persson H, et al. Usefulness of N-terminal pro-brain natriuretic Peptide and brain natriuretic peptide to predict cardiovascular outcomes in patients with heart failure and preserved left ventricular ejection fraction. *Am J Cardiol.* 2008;102:733–737.
26. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *JACC* 2013 62:1495–539.
27. Lee DS, Gona P, Vasani RS, et al. Relation of disease pathogenesis and risk factors to heart failure with preserved or reduced ejection fraction: insights from the Framingham heart study of the National Heart, Lung, and Blood Institute. *Circulation.* 2009;119 (24):3070–3077.
28. Bursi F, Weston SA, Redfield MM, et al. Systolic and diastolic heart failure in the community. *JAMA.* 2006;296 (18): 2209–16.
29. Persson H, Lonn E, Edner M, et al. Diastolic dysfunction in heart failure with preserved systolic function: need for objective evidence: results from the CHARM Echocardiographic Substudy-CHARMES. *JACC.* 2007;49 (6):687–94.
30. Maestre A, Gil V, Gallego J, Aznar J, et al. Diagnostic accuracy of clinical criteria for identifying systolic and diastolic heart failure: cross-sectional study. *J Eval Clin Pract.* 2009;15 (1): 55–61.
31. Belenkov JuN, Mareev VJu, Ageev FT. Congestive heart failure. Selected lectures in cardiology. M.: GEOTAR-Media; 2006. p. 432. Russian.
32. Bokarev IN, Aksenova MB, Belikov VK. Heart failure is acute or chronic. *Grif UMO on medical education.* M.: Prakticheskaja medicina; 2006. 176 p. Russian.
33. Kaljuzhin VV. Congestive heart failure. Questions of etiology, epidemiology, pathogenesis (hemodynamic, neurohumoral, immune, genetic). Questions of diagnostics and treatment. M.: MIA; 2006. 288 p. Russian.
34. Okorokov AN. Diagnosis of internal diseases. M.: Medicinskaya literatura; 2007 (vol. 8). 432 p. Russian.
35. Zhao X, Eghbali, Webb M. Gender-related differences in basal and hypoxia-induced activation of signal transduction pathways controlling cell cycle progression and apoptosis in cardiac fibroblasts. *Endocrine.* 2002;8:137–45.
36. Biondi-Zoccai GGL, Abbate A, Bussani R, et al. Reduced postinfarction myocardial apoptosis in women: a clue to their different clinical course? *JACC.* 2003;41:753–760.

Results of the European Congress of Cardiology 2015

On 29th August — 1st September 2015, London hosted the annual European Congress of Cardiology.

The congress was attended by 32 773 delegates from more than 50 countries. 440 delegates, including scientists, doctors and health managers from different cities of the country, represented Russia.

The organizing committee presented a number of new communication technologies. In the days of the Congress, daily e-mailing with the main news and press releases was carried out for all registered specialists on the official website. TV channel broadcasted scientific activities of the congress online. The project ESC365 is launched, allowing to get acquainted with videos, slides, theses and other materials of the Congress on the website of the European Society of Cardiology, during a year for free.

The scientific program of the Congress was intense; it included plenary sessions, symposia, discussions, poster sessions, presentations at exhibitions, interactive sessions and others.

The first day of Congress, the European Society of Cardiology provided 5 clinical guidelines:

- Recommendations for the diagnosis and treatment of pulmonary hypertension
- Recommendations for diagnosis, treatment and prevention of infective endocarditis
- Recommendations for the diagnosis and treatment of diseases of the pericardium
- Recommendations for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

- Recommendations for the management of patients with acute coronary syndromes without persistent elevation of ST segment.

In the near future, the Russian Society of Cardiology will feature Russian versions of these recommendations on section of the site http://www.scardio.ru/rekomendacii/rekomendacii_esc/.

Traditionally, HOT LINE sessions with the presentation of the results of major scientific and clinical studies have the greatest interest. During 3 days in 6 areas: acute myocardial infarction, atrial fibrillation / pacemakers, diabetes / pharmacology, hypertension, heart failure, coronary heart disease; the results of 28 studies, 18 clinical trials updates and 20 registers were presented. The following studies aroused the great interest and discussion among the delegates:

— PLATFORM: the use of diagnostic strategy of computed tomography with the fractional flow reserve method, which significantly reduces the number of patients with coronary artery disease, requiring invasive coronary angiography

— MATRIX: Is the continuous bivalirudin infusion effective?

— Treatment of central sleep apnea syndrome: a neutral impact on the final points with a trend of increasing mortality

— PARAMETER: LCZ696, compared with olmesartan, reduces the stiffness of arteries in aged people better

— Some hypoglycemic drugs increase cardiovascular complications

— OptiLink HF: Remote intrathoracic impedance monitoring does not improve survival in patients with chronic heart failure.

— PROMPT: Stimulants of left ventricular do not reduce a remodeling after extensive myocardial infarction.

— PATHWAY3: The combination of amiloride and hydrochlorothiazide effects neutrally on glucose metabolism; lowers blood pressure better than a monotherapy with each of them.

— DOPPLER-CIP: the small size of the heart and thickened walls are predictors of remodeling while coronary heart disease.

In science materials of congress, 4533 theses were published.

The next European Congress of Cardiology will be held from 27th to 31st August 2016 in Rome. More information on the materials of the European Congress of Cardiology, you can find on the official website of the European Society of Cardiology www.escardio.org.ru



Report from Russian National Congress of Cardiology 2015

From the 22th to 25th of September in Moscow annually Russian National Congress of Cardiologists was held.

The Congress was dedicated to the fight against cardiovascular disease and the search of new ways of helping patients with these conditions, and also introducing the most modern treatments and innovative methods into practice.

According to the organizers 6179 doctors have attended this meeting, from both the Russian Federation and 26 other countries. 2176 of the doctors have stated their will to participate in persistent medical educational system and they were able to obtain the Ministry of Health's certificates. The collection of scientific proceedings was published.

Scientific meetings took place in 11 halls and lasted for 4 days, including more than 150 plenary sessions, symposiums, clinical lectures, master classes, round tables. Within the Congress a contest among young scientist was organized, alongside poster sessions. The President of European Society of Cardiology, Fausto Pinto, ex-President of ESC Roberto Ferrari, Presidents of national societies of cardiology and leading experts in cardiology and cardiosurgery have attended the Congress

Within the National Congress an exhibition was organized, over 60 pharmaceutical companies and medical equipment developers took part in it. The Cardioprogress Foundation was represented by a stand in central exhibition ground of the Congress. The participants of the Congress found the stand very interesting and informative. Also a give-away of the last issues of International Heart and Vascular Disease Journal, a special limited issues of Cardioprogress Journal, methodical recommendations, manuals and souvenirs were organized.

Elections of President of the Russian Society of Cardiology took place, Academician Shlyachto E.V. was reelected as the President for the next 3 years. Also 5 vice-presidents and 25 members of presidium and council were elected.

The work of the National Congress was covered by Russian media. Live online translation of the work of Congress was organized. Also a press-center worked during the Congress.

The next annual Russian Congress of Cardiology will take place in the end of September, in Ekaterinburg. More detailed information about the event might be found on our website scardio.ru



Guidelines for authors

International Heart and Vascular Disease Journal Requirements for Submission and Publication

The requirements for submission and publication in the **International Heart and Vascular Disease Journal** are based on the 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals', developed by the *International Committee of Medical Journal Editors* (ICMJE), which can be found at www.ICMJE.org

These requirements form the basis for relations between the Editors of the **International Heart and Vascular Disease Journal**, further called "the Editors", and an author who submits a manuscript for publication, further called "the Author".

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Periodicals

Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the Anticoagulation and Risk factors in Atrial Fibrillation (ATRIA) Study. *JAMA*. 2001;285(18):2370-5.

Sources in Russian with transliteration:

Baevskiy RM, Ivanov GG, Chireykin LV, et al. Analiz variabel'nosti serdechnogo ritma pri ispol'zovanii razlichnyh jelektrokardiograficheskikh sistem (metodicheskie rekomendacii) [Analysis of heart rate variability using different ECG systems (guidelines)]. *Vestnik aritmologii*. 2002;24:65-86. Russian.

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These can be found on the Publisher's site or in the list of abbreviations of *Index Medicus*.

Punctuation in the list of references should be considered. A full stop should be put with a space between the name of the journal and the year of its release. After the year of release a semicolon is put without a space, then a colon follows the volume number, and finally page numbers are given. There are no indications like "volume", "№", "pages". Russian periodicals often have no indication of volume or numbering of pages within a year. In this case the number of an issue should be specified in brackets.

If the total number of authors exceeds four people, please provide the names of the first three authors and put "et al." afterwards. If there are not more than 4 authors, the full list of authors should be provided

Chapters in a book

Swanton RH, Banerjee S. Cardiac Failure. In: Swanton RH, Banerjee S., editors. *Swanton's Cardiology: A concise guide to clinical practice*. 6th ed. Oxford: Blackwell Publishing; 2008. p. 255-309.

Sources in Russian with transliteration:

Belenkov YuN. Kardiomiopatii [Cardiomyopathies]. In: Chazov EI, Belenkov YuN., editors. *Racional'naja farmakoterapija serdečno-sosudistyh zabolevanij: Rukovodstvo dlja praktikujushchih vrachej [Rationale for drug therapy of cardiovascular diseases: A guide for medical practitioners]*. Moscow: Litterra; 2006. p. 431-452. Russian.

Reference to a book chapter should be arranged in the following order: authors of the corresponding chapter; name of the chapter; «In:»; editors [title authors] of the book; name of the book; number of issue, publisher; city of publishing; year of publishing; pages of the corresponding chapter. Punctuation should be considered. There are no quotation marks.

Books

Sources in Russian with transliteration:

Shlyakhto EV, Konradi AO, Tsyrlin VA. Vegetativnaja nervnaja sistema i arterial'naja gipertenzija [The autonomic nervous system and hypertension]. St. Petersburg (Russia): Meditsinskoe izdatel'stvo; 2008. Russian.

Websites

Websites should be provided in the list of references, but not in the text. References to websites should be made only when original text is not available. References should be provided in the following way:

WHO. Severe Acute Respiratory Syndrome (SARS) [Internet]. [place unknown: publisher unknown]; [updated

2010 June 1; cited 2010 June 10]. Available from: <http://www.who.int/csr/sars/>.

7.8. Diagrams, charts, and figures

7.8.1. Diagrams, charts, and figures should be submitted electronically in the following formats: «MS Excel», «Adobe Illustrator», «Corel Draw» or «MS PowerPoint». Diagrams, charts, and figures must be allocated on separate pages, numbered in order of citation, and have names and notes if necessary. They must not repeat the content of tables. Please indicate the names and units of measurement for graph axes. Provide the legend for each graph (denote lines and filling). If you compare diagrams, provide significance of differences. Do not use 3-D models for histograms. If appropriate, please identify places in the text where you wish graphics, figures and graphs to be inserted.

7.8.2. Photographs must be submitted electronically with a minimum resolution of 300 dots per inch (dpi). Microphotos must be cropped so that only main content is left. Arrows should be used to show main features. All symbols, arrows and legends on gray-scale illustrations should be in contrast with the background.

7.8.3. Size of legends on images and photos should be big enough to be legible after compression for publication. The optimal size is 12 points.

7.8.4. All abbreviations should be defined either after the first citation in a legend, or in alphabetic order at the end of each legend. All symbols (arrows, circles, etc.) must be explained.

7.8.5. If data was published earlier, it is desirable to provide written permission from the publisher for the use of this data.

7.9. Tables

7.9.1. Tables should be typed with double spacing, have numbers in order of citation in the text, and names. Tables should be compact and demonstrative. Names of columns and rows must reflect the content. Data presented in tables should not be repeated in the text or images. Please clearly specify units of measurement of variables and form of data presentation ($M \pm m$; $M \pm SD$; Me ; Mo ; percentiles etc.). All figures, sums and percentages must be thoroughly checked and correspond to those in the text. Explanatory footnotes should be provided below the table if necessary.

7.9.2. Abbreviations should be listed in a footnote under the table in alphabetic order. Symbols of footnotes should be given in the following order: *, †, ‡, §, ||, ¶, #, **, † † etc.

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