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Characteristics of heart failure course in patients with chronic myocarditis

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The aim of this study is to investigate the features of chronic heart failure (CHF) in patients with chronic myocarditis (CM) in the setting of left bundle branch block (LBBB).

Methods. To assess the severity of CHF depending on the degree of LBBB, 51 CM patients with signs of CHF were studied. Patients were divided into 2 groups. The first group consisted of 21 patients (mean age, 36.7±1.1 years) with LBBB and the second group consisted of 30 patients (mean age, 32.5±1.0 years) without conduction disturbances. All patients underwent resting electrocardiography and transthoracic echocardiography.

Results. As CHF progresses, patients with LBBB have statistically significant increases in left ventricular (LV) posterior wall and interventricular septum thickness, left ventricular myocardial mass index (LVMMI), and left atrial (LA) size compared to patients without conduction disturbances. End-diastolic size and end-diastolic volume were not significantly different between groups. A more pronounced deterioration of systolic cardiac function was observed in group 1 patients. In patients with functional class (FC) II CHF without LBBB, LV ejection fraction (EF) remained at the lower limit of normal (58.9±2.3%), whereas in patients with LBBB, LV EF decreased (47.1±1.0%). Patients in group 1 showed more pronounced signs of diastolic dysfunction at an early stage of CHF compared to patients in group 2. Thus, the pseudonormal type of diastolic dysfunction is diagnosed in the majority of group 1 patients with I FC CHF and the restrictive type in group 1 patients with II–III FC CHF.

Conclusion. Thus, complete block of LBBB in CM patients leads to earlier cardiac remodeling with marked impairment of myocardial systolic and diastolic functions.

Keywords: myocarditis, heart failure, left bundle branch block.

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Introduction

Cardiovascular diseases are one of the main causes of early disability and high mortality worldwide. Despite the fact that cardiovascular diseases associated with atherosclerosis take the leading position in the development of complications, still myocardial inflammatory diseases are important factors of cardiovascular morbidity and mortality [1-3]. In primary health care, verification of the causes, diagnosis and treatment of inflammatory myocardial diseases are challenging tasks [3-5].

Epidemiological studies have shown a steady increase in both non-coronary myocardial disease and chronic infections in young adults [3, 6]. Their late recognition leads to chronic inflammatory myocardial damage, progression of arrhythmias, and the development of chronic heart failure (CHF) [5, 7, 8]. There is no universally accepted scientific concept explaining the mechanisms of the onset and development of inflammatory myocardial diseases associated with chronic infections, which negatively affects treatment tactics [1, 4, 5].

Chronic myocarditis is a key pathology in the group of diseases called "inflammatory cardiomyopathy". Publications in recent years prove that the course and outcome of chronic inflammatory myocardial damage serve as the main pathogenetic mechanism for the development of congestive heart failure in young people [3, 8]. In recent years, special attention has been paid to the etiology of chronic myocarditis (CM), since the further management of the patient and the success of therapeutic measures largely depend on it [2, 4]. It is well known that the progression of CHF often leads to the development of dilated cardiomyopathy with the phenomenon of congestive CHF, which is resistant to optimal medical therapy and serves as an indication for heart transplantation [7, 8].

Despite its low sensitivity, electrocardiography (ECG) is widely used as a screening method. ECG changes in patients with myocarditis range from non-specific T-wave and ST segment changes to infarction-like ST elevations [1, 4]. Along with the development of CHF, arrhythmias and conduction disturbances become common and serious complications of CM [7, 9]. The presence of an abnormal Q wave and/or left bundle branch block (LBBB) is known to be associated with a higher incidence of fatal outcome in this group of patients [9–11].

The influence of intraventricular conduction disturbances on the course and outcome of CHF has been investigated in only a few studies [12, 13], and according to different authors, they are observed in 10–37 % of patients. At the same time, most attention has been paid to atrioventricular block, and complete LBBB, as well as the relationship of intraventricular conduction disturbances with the etiology and severity of CHF and with the contractile and diastolic function of the heart, have practically not been considered. According to some authors, LBBB is an independent predictor of death in patients with CHF [11-14]. Thus, the presence of complete LBBB, even in the absence of structural heart disease, has been shown to be an independent risk factor for the development and prognosis of CHF.

The pathogenetic role of interventricular dyssynchrony caused by right ventricular apical pacing, which resembles the morphology of complete LBBB on ECG, is also known to contribute to the development of pacemaker cardiomyopathy with CHF phenomenon [15]. Obviously, in patients with CM, the risk of development/progression of CHF and the high incidence of fatal outcome are not only due to the presence of LBBB, but also to severe myocardial morphofunctional changes [1, 4, 5]. Thus, given the unfavorable prognostic value of complete LBBB in CM, the study of the hemodynamic mechanisms of CHF development and progression is relevant to justify the choice of therapeutic tactics, including the use of electrocardiotherapy.

The aim of the present study was to compare the characteristics of morphofunctional cardiac remodeling in patients with chronic myocarditis in relation to the presence of LBBB.

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Methods

Fifty-one patients (32 males and 19 females) diagnosed with CM with varying degrees of CHF severity were enrolled in an open-label, comparative clinical trial. The age of the patients ranged from 28 to 37 years (mean 34.2±1.4 years). Patients were divided into two groups according to the presence of LBBB: group 1 included 21 patients with LBBB and group 2 included 30 patients with normal QRS complex duration, i.e. without LBBB.

All patients underwent clinical examination (analysis of complaints and physical examination data), resting ECG recording in 12 standard leads, and Doppler echocardiography. Ultrasound examinations were performed with a color diagnostic scanner "Aloka SSd-2000" (Hitachi Aloka Medical, Japan) in M-mode with a 3.5 MHz pulse transducer in the left lateral position of the patient. Echocardiographic parameters characterizing chamber dimensions, wall thickness, and left ventricular (LV) systolic and diastolic function were calculated. LV diastolic function was assessed using transmitral diastolic flow and the following types of diastolic dysfunction were verified: hypertrophic, pseudonormal and restrictive.

Tolerance to physical activity was assessed by a standardized 6-minute walk test. Quality of life was assessed in scores using the Minnesota Questionnaire. The Clinical Status Assessment Scale (CSAS) modified by V.Y. Mareev was used to assess the clinical status of patients with CHF. Functional classes (FC) of CHF were determined according to the New York Heart Association classification.

Statistical analysis of the obtained data was performed in the system of statistical analysis IBM SPSS 20.0. Data input was carried out in Excel system of MS Office package. Qualitative parameters were described by relative frequencies in percentages. Normality of distribution of variables was determined by Kolmogorov-Smirnov test. Quantitative parameters were described by means and errors of means (M±m). The Student's t-test was used to evaluate differences between two independent samples for continuous parameters. For correlations, the Spearman rank correlation method was used. Differences were considered significant at $p<0.05$.

Results and the discussion

According to the clinical course of CHF, group 1 had 6 patients with I FC, 9 patients with II FC, and 6 patients with III FC. There were 10, 12, and 8 patients, respectively in group 2 (Table 1). Group 1 was predominantly presented by women. It should be noted that the mean age of the patients was not significantly different between the groups. However, the duration of the QRS complex width was significantly longer in group 1 than in group 2, which can be explained by the feature of this group — the presence of LBBB. In addition, group 1 was characterized by the predominance of cardiac rhythm disturbances, mainly in the form of supraventricular and ventricular extrasystoles or the presence of various atrial tachyarrhythmias. At the same time, the difference is not statistically significant, which is probably explained by the small sample in the study.

Table 1. **Clinical characteristics of patients in the compared groups**

Parameters	Group 1 (n = 21)	Group 2 (n = 30)
Males/females, n	18 / 3	14 / 16
Age, years (M ± m)	36.7±1.1	32.5±1.0
I FC CHF, n/%	6 (28.6)	10 (33.3)
II FC CHF, n/%	9 (42.8)	12 (40.0)
III FC CHF, n/%	6 (28.6)	8 (26.7)
QRS complex width, m/s (M ± m)	138.5±4.7	90.2±2.6
Rhythm and conduction disorders, n/%	6 (28.6)	5 (16.7)

Our findings in severe CHF may be explained by the fact that patients with complete LBBB are more likely to decompensate, require hospitalization or outpatient care, and have greater limitations in physical activity. Patients with early-stage CHF do not differ significantly in clinical manifestations, but in the absence of LBBB, they achieve compensation more quickly and have relatively high levels of quality of life indices. Table 2 shows the parameters of the morphofunctional state of the heart depending on the presence of LBBB, but without taking into account the FC of CHF. In this case, LV parameters were significantly larger in patients with complete LBBB than in patients without LBBB. In addition, the thickness of LV posterior wall and interventricular septum thickness was greater in group 1 than in group 2, although the difference was not significant ($p>0.05$). Importantly, the mean LV EF in group 1 was less than 40 % and significantly lower than in group 2: 29.3 % less on average ($p<0.001$).

With the progression of CHF, there is a statistically significant values increase in LV posterior wall and

Table 2. **Morphofunctional parameters of intracardiac hemodynamics in myocarditis patients depending on the presence of LBBB (M ± m)**

Parameters	Patients with LBBB (group 1)	Patients without LBBB (group 2)
LA, mm	4.5±1.3	4.3±0.9
LA volume index, ml/m^2	33.2±6.1	33.0±5.2
End diastolic diameter (EDD), mm	6.8±0.6	5.8±0.5*
End systolic diameter (ESD), mm	4.7±0.5	3.9±0.7*
End diastolic volume (EDV), ml	193±9.0	138±11.9*
End systolic volume (ESV), ml	120±6.9	69±9.0*
Indexed EDV (iEDV), ml/m^2	107±11.3	75.9±10.8*
Indexed ESV (iESV), ml/m^2	63.5±10.2	39.3±9.8*
Interventricular septum thickness, mm	10.1±0.4	9.2±0.4
LV posterior wall thickness, mm	11.2±0.3	10.2±0.3
LV EF, %	38.3±3.2	54.2±4.1*
Relative wall thickness (RWT)	0.35±0.04	0.35±0.03
Sphericity index	0.72±0.14	0.66±0.12
Pulmonary artery systolic pressure, mmHg	35±2.4	31.8±1.9

Note. * p<0,05 — statistically significant difference.

interventricular septum thickness, LVMMI and LA size, as well as of EDD and EDV indices in patients with LBBB compared to patients without conduction disturbances (Table 3). It should be noted that the severity of LV posterior wall hypertrophy increases with the FC of CHF, and LV posterior wall thickness directly correlates with the FC of CHF: r=0.49 (p=0.026).

Furthermore, a regular deterioration of LV systolic and diastolic function indices was observed with the progression of CHF. Thus, a physiological predominance of LV systolic function over RV systolic function is observed in I FC CHF in group 1 patients, regardless of the presence of LBBB. In addition, in patients with initially preserved LV systolic function (EF > 50 %), no significant difference was found. However, in II–III FC CHF, LV EF is moderately reduced or low (≤40 %), and RV EF is practically unchanged.

The evaluation of diastolic function of the heart taking into account the FC of CHF showed that patients with LBBB have more pronounced signs of diastolic dysfunction already in the early stage of CHF than patients without LBBB. Thus, "pseudo-normal" diastolic dysfunction was observed in group 1 patients at I FC CHF, and diastolic dysfunction worsened and became restrictive at II FC CHF. These marked disturbances in diastolic function associated with impaired active myocardial relaxation or a significant increase in ventricular diastolic pressure may characterize diastolic heart failure [7, 11]. Furthermore, it confirms the generally accepted hypothesis that diastolic dysfunction is a precursor or risk factor for the development of systolic heart failure in most cases of systolic heart failure [4, 12, 13].

When assessing the clinical status of patients according to the CSAS scale, no significant differences were found depending on the presence of LBBB (p>0.05). However, with the progression of hemodynamic disturbances, taking into account the FC of CHF, there was a regular and reliable increase in the average score of the CSAS scale, especially in pa-

Table 3. **Comparison of structural and functional parameters of the heart depending on the severity of CHF in groups (M ± m)**

Parameters	I FC CHF		II FC CHF		III FC CHF	
	1 group	2 group	1 group	2 group	1 group	2 group
LA, mm	42.6±1.3	44.5±1.1	44.3±1.1	41.8±1.2	47±1.5	40±2.0*
ESD, mm	37.2±1.7	35.0±2.1	43.5±1.9	40.2±1.6	48.0±1.4	45.4±2.1
EDD, mm	48.5±3.9	50.8±3.4	54.6±2.8	52.0±3.3	58.3±3.5	63.0±3.0
LV EDV, ml	113.5±14.2	113±15.2	173.0±3.2	160±3.41*	192.3±9.1	173.13±8.8*
LV ESV, ml	52.3±7.9	42.7±5.3	65.2±2.5	61.8±2.2*	91.8±5.7	79.3±4.5*
LV posterior wall, mm	10.1±1.0	9.7±0.8	13.7±0.9	12.2±0.8*	16.4±1.5	14.0±0.9*
Interventricular septum, mm	9.1±0.5	9.2±0.7	11.6±0.7	10.1±0.9*	12.9±1.4	11.1±1.12*
RV EF, (%)	56.3±2.9	56.1±1.3	52.8±2.8	53.6±1.9	58.9±1.9	53.3±1.9*
LV EF (%)	65.0±3.3	66.2±1.2	47.1±1.0	58.9±2.3*	40.6±0.9	43.2±1.5
LVMMI, (g/m^2)	105.7±4.5	102.4±4.9	132.5±5.9	121.3±4.1*	156.4±3.9	135.1±4.1*
E/A	0.98±0.02	0.51±0.03*	0.96±0.04	0.99±0.02	1.11±0.01	0.98±0.01
IVRT, m/s	112.3±1.3	114.2±2.0	112.2±1.7	112.2±1.5	113.2±1.8	112.2±1.9
DT, m/s	242.0±7.2	228.2±7.0*	255.0±7.2	242.7±7.0	265.0±6.9	245.9±6.6*
CSAS, score	3.9±0.1	3.6±0.3	4.7±1.6	4.1±1.9	6.7±0.5	6.0±0.4

Note. * p<0,05 — statistically significant differences between groups 1 and 2: E/A — is the ratio of the early to lateventricular filling velocities; IVRT — isovolumic relaxation time; DT — deceleration time of early diastolic filling.

tients with the presence of LBBB. This means that the quality of life, including tolerance to physical activity, is reduced in patients of group 1 compared to group 2.

It should be noted that in patients with LBBB some patterns were revealed depending on the QRS complex duration. In group 1, out of 21 patients with LBBB, 8 patients had QRS complex width from 120 m/s to 150 m/s and 13 patients — more than 150 m/s. It is shown that LV EF value is inversely correlated with QRS complex duration: r = –0.53 (p=0.007). Moreover, in group 1, among patients with QRS complex duration more than 150 m/s, cases of severe CHF predominate: out of 15 patients, 12 patients were diagnosed with II–III FC CHF.

The data obtained by the authors confirm the underlying pathophysiological mechanisms of the development and progression of CHF caused by electromechanical dispersion due to complete LBBB, leading to mechanical interventricular dyssynchrony and global systolic dysfunction. In this regard, it is important to note that the therapeutic tactics of CHF treatment in the presence of LBBB with QRS complex duration greater than 150 m/s justified the introduction into clinical practice of cardiac resynchronization therapy as a highly effective method of biventricular electrical stimulation in patients with symptomatic CHF. It allows to improve the quality of life and the prognosis [16]. This method contributes to restoration of interventricular synchronization, improvement of systolic and diastolic functions of the heart, resolution/relief of CHF symptoms, especially with low LV EF. It should be noted that cardiac resynchronization therapy has shown particularly high efficacy in patients with CHF of non-ischemic genesis, including the fibrosis after myocarditis.

Conclusion

Thus, the characteristics of morphofunctional remodeling of the heart in patients with chronic myocarditis in relation to the presence of LBBB, as well as clinical and hemodynamic features of the course of CHF, which are important for predicting the outcome of the disease and choosing appropriate therapeutic strategies, were demonstrated.

Considering the leading role of conduction disturbances in the His-Purkinje system caused by chronic myocarditis in the development of CHF, in addition to the commonly used method of transthoracic echocardiography, it is advisable to use the method of tissue Doppler cardiac imaging to detect interventricular dyssynchrony, which causes disturbances in local myocardial contractility and a decrease in contractile and/or pumping function of the left ventricle. Diffuse inflammatory damage to the heart caused by myocarditis, especially in the case of complete LBBB, serves as the pathogenetic mechanism for the development of dilated cardiomyopathy, the adequate treatment of which requires the use of a wide range of therapeutic measures, including heart transplantation.

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