Diastolic Dysfunction of the Left and Right Ventricles in Patients with Ischemic Heart Disease at the Early Stages of Chronic Heart Failure

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ABSTRACT

The concept of "diastolic dysfunction" is based on both structural and functional remodeling of cardiomyocytes and the interstitial matrix, leading to increased myocardial stiffness [2,4]. Unlike systole, during which Ca^{2+} ions are actively released from the sarcoplasmic reticulum into the cytosol, myocardial relaxation is an energy-dependent process associated with the active transport of Ca^{2+} ions back into the sarcoplasmic reticulum against a concentration gradient [10]. This mechanism explains why disturbances in myocardial relaxation occur earlier than systolic dysfunction, particularly under conditions of myocardial ischemia in ischemic heart disease (IHD) [3,6,9]. The mechanisms underlying impaired diastolic function in IHD can be conventionally divided into two categories: disorders of active relaxation caused by the development of cardiosclerosis and those associated with myocardial ischemia [7,10].

Keywords:

Introduction. Chronic heart failure (CHF) is currently regarded as a syndrome that develops as a result of various cardiac diseases accompanied by systolic and diastolic dysfunctions [1,2,8]. Studies [1,3] have demonstrated the important role of diastolic dysfunction (DD) in the pathogenesis of heart failure. Isolated diastolic dysfunction is diagnosed in 30–40% of patients presenting with symptoms of CHF while maintaining normal myocardial contractility [4,6,10]. As systolic dysfunction progresses, diastolic abnormalities also become more pronounced [1,4,8]. Therefore, the assessment of left ventricular (LV) filling during diastole is crucial in evaluating the condition of patients with CHF.

The concept of "diastolic dysfunction" is based on both structural and functional remodeling of cardiomyocytes and the interstitial matrix, leading to increased myocardial stiffness [2,4]. Unlike systole, during which Ca^{2+} ions are actively released from the sarcoplasmic reticulum into the cytosol, myocardial relaxation is an energy-dependent process associated with the active transport of Ca^{2+} ions back into the sarcoplasmic reticulum against a concentration gradient [10]. This mechanism explains why disturbances in myocardial relaxation occur earlier than systolic dysfunction, particularly under conditions of myocardial ischemia in ischemic heart disease (IHD) [3,6,9]. The mechanisms underlying impaired diastolic function in IHD can be conventionally divided into two categories: disorders of active relaxation caused by the development of cardiosclerosis and those associated with myocardial ischemia [7,10].

The progression of diastolic dysfunction, accompanied by an increase in myocardial stiffness due to both muscular and interstitial components, leads to increased atrial workload and a greater contribution of active atrial systole to ensure normal ventricular filling during diastole [2,6]. Because of the thin myocardial wall of the atria and their limited compensatory reserves, adaptive mechanisms

eventually fail after a period of relative compensation. It is reasonable to assume that in patients with IHD, impaired perfusion and myocardial ischemia affect not only the LV but also the right ventricle (RV), leading to similar changes in RV diastolic function. The progression of diastolic dysfunction is manifested by a decline in diastolic filling velocities and an increase in left ventricular end-diastolic and end-systolic volumes (EDV and ESV), which contributes to the development of systolic dysfunction [4,8]. However, the state of right ventricular diastolic function at different stages of CHF has not been fully investigated to date, which determined the purpose of the present study.

Purpose to study diastolic function abnormalities of the left and right ventricles in patients with ischemic heart disease (IHD) at the early stages of chronic heart failure (CHF).

Materials and Methods. A total of 64 patients (31 men and 33 women), aged 44–76 years, with IHD and stable angina pectoris of functional class (FC) II–III according to the Canadian Cardiovascular Society (CCS) classification and CHF of class I–II according to the New York Heart Association (NYHA) classification, were examined. Among them, 72% of patients had concomitant hypertension. None of the examined patients had a history of myocardial infarction (MI). The diagnosis of IHD was established based on typical clinical symptoms, medical history, and instrumental investigations, including graded exercise testing (ETT). Exclusion criteria included cardiac rhythm disorders (atrial fibrillation), valvular heart defects, chronic pulmonary diseases, anemia, diabetes mellitus, malignant neoplasms, and other prognostically unfavorable conditions.

Symptoms of CHF in the examined patients included dyspnea, palpitations, cough, and fatigue occurring during moderate or significant physical exertion. According to the NYHA functional classification, all patients were divided into two groups:

Group I — 16 patients with CHF class I, average age 63.1 ± 5.2 years;
Group II — 48 patients with IHD and CHF class II, average age 58.9 ± 2 years.

The control group consisted of 19 practically healthy individuals aged 17–48 years. All patients underwent evaluation of left and right ventricular myocardial contractile function using equilibrium radionuclide ventriculography (RNV) with segmental and phase histogram analysis performed by standard methodology following administration of Pyrfotech and 555 MBq of 99mTc (in vivo labeling). Data were recorded using a BAZICAM gamma camera (Siemens) equipped with an automated system for segmental and phase histogram analysis (GoldRada+). The analysis of local myocardial contractility abnormalities was based on the standard 16-segment model of the left and right ventricles. Segments with a local ejection fraction (LEF) greater than 50% of the maximal value were considered normokinetic; segments with LEF = 25–50% were hypokinetic; LEF = 18–25% were akinetic; and LEF ≤ 0 were considered dyskinetic. All examinations were performed in the morning with patients in the supine position. Statistical analysis was carried out on a personal computer using Statistica v6.0 software, employing standard statistical methods. All results are presented as M ± σ.

Table 1

Indicators of systolic and diastolic function of the left ventricle (LV) in patients with ischemic heart disease (IHD) and chronic heart failure (CHF) of functional classes I and II, and in the control group

Indicators	CHF I FC (NYHA) (n=16)	CHF II FC (NYHA) (n=48)	Control group (n=19)
Heart rate (beats/min)	73.9±6.7	72±4.4	82.3±8
Ejection fraction (%)	65.2±4.3	62.1±2.3	64.6±4.1
Filling during the one third of diastole (%/s)	25.9±4.9*	24.9±2.1#	33.4±5

Ejection during the one third of systole (%/s)	18.9±2.3	18.6±2.6	22.7±5.5
Maximum ejection velocity (%/s)	325±17.3	311±24	344±27
Maximum filling velocity (%/s)	271±30.5*	247±20.3#	325±37.8
End-diastolic volume (EDV), ml	115.8±25*	121±7#	148.3±14.5
End-systolic volume (ESV), ml	40.6±10	46.4±4	51.7±6.6
Stroke volume (SV), ml	74±7*	74±5#	96.5±12

Note: * – $p<0.05$ compared to group I and control; # – $p<0.05$ compared to group II and control; HR – heart rate; SV – stroke volume.

Results and Discussion: to assess diastolic function of the left and right ventricles, the following parameters were analyzed: maximum filling velocity, filling during the first third of diastole, and end-diastolic volume (EDV). Among the parameters characterizing systolic function, maximum ejection velocity, ejection during the first third of systole, and end-systolic volume (ESV) were evaluated. Characteristics of the inotropic function of the LV myocardium in patients with IHD and CHF of functional classes I and II, and in the control group are presented in Table 1.

Diastolic dysfunction of the LV was observed in patients with CHF I–II functional classes in the absence of signs of LV systolic dysfunction. A statistically significant decrease in the rate-related indicators was observed: filling during the first third of diastole, maximum filling velocity, and EDV. This indicates increased stiffness of the LV myocardium and represents an early sign of diastolic dysfunction. Parameters such as ejection fraction, ejection during the first third of systole, maximum ejection velocity, and LV ESV in both patient groups remained within normal limits and did not differ significantly from those of the control group. In both patient groups, despite marked LV diastolic dysfunction, no significant changes in the velocity parameters of right ventricular (RV) diastolic function were observed (Table 2). The EDV of the RV in patients with early stages of CHF was significantly lower than in the control group, serving as an indirect indicator of impaired diastolic relaxation. Other characteristics of RV inotropic function in patients with IHD and CHF I–II FC did not differ significantly from those of healthy individuals [11].

Thus, diastolic dysfunction in patients with early-stage CHF manifested as a reduction in filling during the first third of diastole and a decrease in the LV maximum filling velocity (Figures 1, 2). Changes in these parameters, with sensitivity ranging from 93.2% to 96.6%, indicate diastolic dysfunction [7].

Therefore, clinical manifestations of CHF—such as dyspnea, palpitations, and reduced exercise tolerance—in patients with IHD and CHF of class III NYHA were associated with LV diastolic dysfunction.

A significant reduction in EDV in both ventricles was related not only to impaired diastolic filling ($p<0.05$) but also indirectly indicated increased myocardial stiffness with relaxation disturbance of the restrictive type [14,15].

Table 2

Indicators of systolic and diastolic function of the right ventricle (RV) in patients with ischemic heart disease (IHD) and chronic heart failure (CHF) of functional classes I and II, and in the control group

Indicators	CHF I FC (NYHA) (n=16)	CHF II FC (NYHA) (n=48)	Control group (n=19)
Ejection fraction (%)	55.1±7.6	51.6±3	48.8±3.8
Filling during the one third of diastole (%/s)	17.8±3.7	19.7±2.2	19±0.3

Ejection during the one third of systole (%/s)	17.9±6.5	15.7±1.8	17±3.7
Maximum ejection velocity (%/s)	326.8±44.8	274.6±22.5	275.6±37
Maximum filling velocity (%/s)	206±24	182.5±14.3	201±23
End-diastolic volume (EDV), ml	117.7±20*	126±10#	150.7±15.7
End-systolic volume (ESV), ml	47.6±13.4	62.9±7.7	68.4±9.6
Stroke volume (SV), ml	68.6±16	63.1±4.8	65.1±8.3

Note: * – $p<0.05$ compared with group I and control; # – $p<0.05$ compared with group II and control; SV – stroke volume.

Impaired left ventricular (LV) filling, according to the Frank–Starling law, was accompanied by a decrease in stroke volume, which was observed in patients with CHF of functional classes I–II. Significantly lower EDV values of the RV in patients with early stages of CHF, compared to the control group, may also be due to decreased LV diastolic filling, elevated pulmonary circulation pressure, and increased RV preload. This explains the tendency toward increased indices of RV pumping function, such as ejection during the first third of systole, maximum ejection velocity, stroke volume, and ejection fraction ($p>0.05$).

A significant reduction in RV EDV may be associated with increased RV myocardial stiffness and elevated end-diastolic pressure within its cavity [6,7]. When comparing the parameters of myocardial inotropic function in groups I and II, no statistically significant differences were found, although a trend toward the progression of diastolic dysfunction in both ventricles was observed: a decrease in filling during the first third of diastole and in maximum filling velocity, along with a simultaneous increase in EDV ($p>0.05$) (Figures 1, 2).

Thus, the main intracardiac hemodynamic features in patients with early-stage CHF diagnosed via equilibrium radionuclide ventriculography (RNVG) included reduced filling during the first third of diastole and lower maximum LV filling velocity, along with decreased EDV in both ventricles, while maintaining ejection fraction (EF) and ESV within normal limits. Statistically significant differences in inotropic function between the two groups were not observed. To study local contractility (LC) indices in patients with early CHF, the contractility of 1024 LV and RV segments was analyzed. Signs of LC impairment were detected in all patients with CHF of functional classes I–II. In the LV, normokinetic zones were observed in 321 segments (62.9%), hypokinetic zones in 163 (31.8%), and akinetic zones in 28 (5.4%) (Figure 3). In patients with IHD and CHF I–III FC without a history of myocardial infarction, LV segments with hypokinesia and akinesia were identified. Analysis of the localization of impaired LC zones revealed that in 91% of cases, normokinetic zones were found in 488 segments corresponding to the apex, posterior, and lateral LV walls. Hypokinetic and akinetic zones (85.8% and 85.7%, respectively) were located in 183 segments, corresponding mainly to the upper part of the interventricular septum and the anterior LV wall. In the RV, the number of hypo- and akinetic zones was significantly higher compared to the LV, reaching 43.5% ($p<0.05$) (Figure 4).

In the RV myocardium, more pronounced segmental contractility disturbances were detected, with a greater number of zones exhibiting local dysfunction. Nevertheless, the RV ejection fraction in patients with CHF I FC (NYHA) tended to improve compared to healthy individuals, which may indicate compensatory adaptation of the RV. Similar to the LV, hypo- and akinetic segments in the RV were mainly located in the interventricular septum, while the free RV wall preserved satisfactory contractility. Thus, in patients with early CHF stages I and II (NYHA), diastolic dysfunction of the LV was

observed. The inotropic function of the RV at these early stages was not impaired and, in some cases, even improved, which may indicate an important compensatory and adaptive role of the RV during the initial development of CHF.

Disturbances of diastolic function in both LV and RV were accompanied by the appearance of local dysfunction zones in the myocardium of both ventricles even at the early stages of CHF. The most pronounced segmental contractility disorders were observed in the anterior–septal regions of the LV and RV, while the free walls of both ventricles preserved normal kinesis, likely explaining the maintenance of overall systolic performance in both ventricles.

Conclusion: The clinical manifestations of CHF I–II FC (NYHA) in patients with ischemic heart disease are due to LV diastolic dysfunction characterized by decreased filling during the first third of diastole and reduced maximum filling velocity.

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