

Evaluation of Patients with Heart Failure, Preserved Systolic Function and Diastolic Dysfunction

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Abstract

Aim: Assessment of the occurrence, severity and progress of the diastolic dysfunction in patients with clinically manifest heart failure with preserved systolic function, by analyzing the ultrasound parameters that define the diastolic ventricular function, recorded dynamically. *Material and Method:* The study involved 200 patients suffering from clinically manifest heart failure, admitted in Cardiology Department of Medical no 1, Cluj-Napoca; an echocardiographic study of the systolic and diastolic function was performed, by the same person, for each of them. The echocardiographic study was carried out dynamically, at first within 3 days of the first examination, then, after 9 months. In the present study we selected patients with an ejection fraction $\geq 50\%$ and diastolic dysfunction. *Results:* Of the 200 patients initially evaluated, 43 patients were selected based on the inclusion criteria for diastolic dysfunction. The E' / A' ratios in the lateral regions of the mitral annulus showed a statistically significant improvement when dynamically assessed (0.71 versus 0.6, $p = 0.016$). Also, E / E' ratio in the lateral portion of the mitral annulus significantly improved (6.15 vs. 5.44, $p = 0.016$) and *MPI* dynamical assessment shows a statistically significant improvement in this parameter (0.52 vs. 0.46 $p = 0.014$). *Conclusions:* Diastolic function assessment should be an integral part of the cardiac function assessment due to the increased prevalence of the patients with HF and preserved systolic function. Our study showed that the most reliable parameters used to assess the diastolic dysfunction in patients with preserved systolic function are the following: the E' / A' ratio at the level of the septum, the E / E' ratio at the level of the lateral wall, as well as the *MPI* estimate.

Keywords: Heart failure; Echocardiography; Diastolic function; Preserved ejection fraction.

Introduction

Due to the increase of life expectancy and of the risk factors such as hypertension, obesity and diabetes, heart failure (HF) has become a major public health issue. As in the case of impaired systolic function, impaired diastolic function occurs relatively fast in the development of heart conditions. Earlier studies have shown that mortality; readmission rates and the inpatient functional status were comparable between those with HF with preserved ejection fraction (EF) and those with impaired EF, which justifies the careful investigation and monitoring even of the patients who do not apparently display left ventricular dysfunction [1-3].

The purpose of this study was to dynamically assess the ultrasound parameters that define the diastolic function, as well as to establish correlations between the behaviour of these parameters and the clinical evolution of the patients.

Material and Method

The study was conducted on a group of 200 patients examined in the outpatient or emergency unit who showed symptoms of heart failure. Besides anamnesis, clinical examination, electrocardiogram, recording of the personal pathological history and of the cardiovascular risk factors, all patients were performed an echocardiography focusing on both the systolic and the diastolic function. The criterion of inclusion in the present study was the presence of heart failure signs, the echocardiographic finding of an EF $\geq 50\%$ as well as the absence of haemodynamically significant valvular diseases and of the severe chronic respiratory diseases. [4] A standard echocardiography was performed for each patient using a 2.5-3 MHz probe in the M and 2D modules. We performed pulsed Doppler evaluation of the transmitral flow, flow analysis in the pulmonary veins, segmental or global assessment of the myocardial relaxation by recording the motion velocity of the myocardium using tissue Doppler and M-mode colour Doppler, the calculation of the flow propagation velocity (PV) into the LV [1,14]. We calculated the ejection fraction (EF) by Simson's method, assessing the telediastolic volume and the telediastolic volume of the left ventricle (LV). We also calculated the shortening fraction (SF), the velocity of circumferential shortening (VSC), the mitral annular systolic motion (MAPS) and the myocardial performance index (MPI) [5-7]. For the systolic function the maximum systolic velocity (Sm) in the mitral annulus was also recorded by tissue Doppler. The patients included in the study remained under observation, and observance of the therapeutic regimen was strictly monitored. The echocardiographic examination initially performed within 3 days of the first examination, was later repeated after 9 months, in order to assess the evolution of cardiopathy under a correct and consistent lifestyle and therapy. Based on the transmitral flow, diastolic dysfunction was divided into mild / moderate / severe, based on the criteria used in the European Guidelines of Cardiology [1,3].

Numerical data were generally reported as mean \pm standard deviation. For the statistical comparison of numerical results to used the "t" test (Student) for paired samples, using the initial value and that recorded after 9 months for all study variables. P-values below 0.05 were considered significant for all the data used. Where necessary, confidence intervals (CI) were evaluated at the materiality threshold of 0.05. The statistical programme used was Excel 2003 and MedCalc version 9.6.

Results

Of the 200 patients initially investigated 43 patients were selected based on the inclusion criteria mentioned by the methodology, who represent the group in which the ultrasound parameters used in assessing the diastolic function were monitored. Of the 43 patients studied, 33 (76.75%, 95%CI: 64.11 to 89.37) were women and 10 (23.25%) were male. The average age of patients was 52 years \pm 2 years. The reasons for hospital admission / presentation to the emergency room or examination were: dyspnoea - all patients - 100%, palpitations - 39.53%, fatigue - 30.23% and angina - 46.51%. The personal pathological history analysis shows the occurrence of hypertension in 25 patients (58.13%, 95%CI 50.87 to 79.13) and of the coronary artery disease in 14 patients (32.55%, 95%CI: 18.55 to 46.57). 31 patients (73%, 95%CI: 58.68 to 85.5) had at least two cardiovascular risk factors, 70% of patients were overweight and 21% had serum cholesterol levels above 240 mg/dl.

Ejection fraction (EF) ultrasound revealed the following results: 30% of the patients had an EF between 50-55%, 23% of the patients had an EF between 56-60%, 21% had an EF between 61-65% and 26% had an EF $> 65\%$. Although 25 patients (58.13%, 95%CI: 50.87 to 79.13) suffered from hypertension and 80% of the patients displayed ultrasound signs of left ventricular hypertrophy (LVH), increased left ventricle (LV) muscle mass was confirmed in the case of only 13 patients (38%, 95%CI: 16.50 to 43.96).

The other parameters evaluated showed that 12% of the patients included in the study had a shortening fraction (SF) $< 25\%$, 61% showed a decrease in circumferential shortening rate, and 8%

of the patients experienced mitral annular systolic motion (MAPS) <7 mm.

The ultrasound evaluation of the diastolic function showed that only 10% of the patients initially assessed met all the criteria for inclusion in the diastolic dysfunction group. Based on the parameters chosen for characterizing the diastolic function, this was classified as follows: 20 patients (47%, 95%CI: 31.6 to 61.4) presented a mild impairment of the diastolic function, 16% a moderate and only 2% a severely impaired diastolic function. 15 patients (35%, 95%CI: 20.64 to 49.13) had a borderline form between mild and moderate impairment. Based on the transvalvular flow analysis 35 patients (82%, 95% CI: 69.76 to 93.03) were placed in stage I diastolic dysfunction group, 7 patients in stage II (16%) and only 2% in stage III, that is the restrictive dysfunction type group.

The patients with a quasi-normal aspect upon the assessment of the transmitral flow type were examined by tissue Doppler. At tissue Doppler examination 5% of them presented a normal appearance in one investigation, either in the septum or in the lateral wall. The evaluation of the pulmonary veins atrial reflux showed statistically significant improvement (139 ms versus 149.26, p = 0.003) of the telediastolic pressure in the LV, when dynamically assessed.

Table 1. The recorded parameters between the initial tissue Doppler examination and the examination performed 9 months later for diastolic dysfunction

	Baseline examination		Examination after 9 months		p
	Mean	Standard deviation	Mean	Standard deviation	
lateral E'/A'	0.71	0.16	0.60	0.17	<0.01
septal E'/A'	0.73	0.28	0.70	0.23	0.46
septal E/E'	7.80	2.25	7.80	2.08	0.99
lateral E/E'	6.15	2.11	5.44	1.33	0.01
MPI	0.52	0.17	0.46	0.15	0.01
E/Vp	1.22	0.31	1.24	0.18	0.75

E = early maximum diastolic filling velocity; E' = early annular maximum velocity ; A' = late annular maximum velocity measured by tissue Doppler at the level of the mitral annulus ; MPI = myocardial performance index ; Vp = flow propagation velocity into the left ventricle

The evaluation by tissue Doppler at the first examination and then 9 months later through the analysis of the E' / A' ratios in the septum and lateral regions of the mitral annulus showed a statistically significant improvement when dynamically assessed (0.71 versus 0.60, p = 0.016) in the case of the parameters recorded in the lateral area and an insignificant improvement in the septum area (0.73 versus 0.7, p = 0.46), as it can be seen in Table 1 and Figure 1.

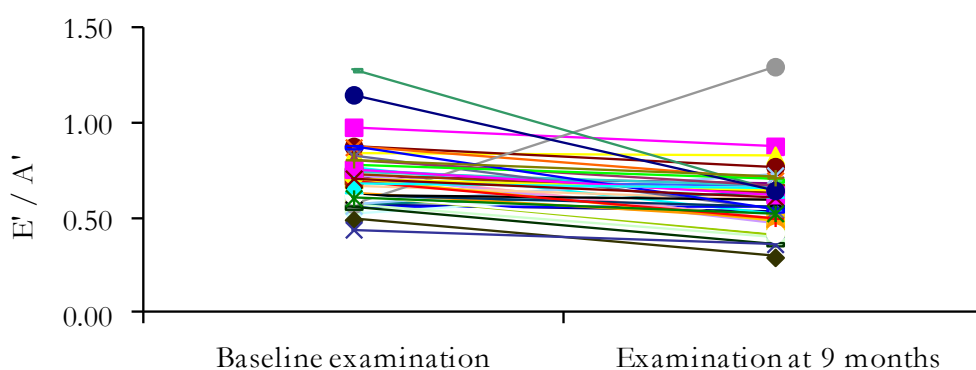


Figure 1. Evolution of the E' / A' (cm/s) ratio in the lateral portion of the mitral annulus (E' - early annular maximum velocity; A'- late annular maximum velocity measured by tissue Doppler at the level of the mitral annulus)

Also, as seen in Figure 2, the dynamically assessed E / E' ratio in the lateral portion of the mitral

annulus significantly improved (6.15 vs. 5.44, $p = 0.016$) under treatment.

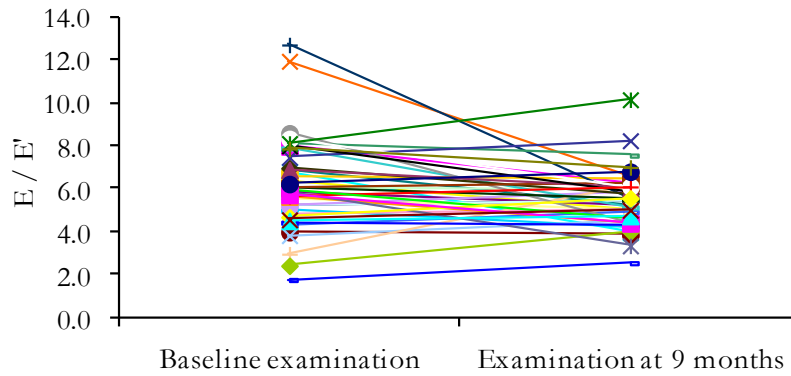


Figure 2. Evolution of the E (m/s) / E' (cm/s) ratio in the lateral portion of mitral annulus (E- early maximum diastolic filling velocity; E' - early annular maximum velocity)

Assessment of the MPI - myocardial performance index - revealed significant changes, especially when dynamically assessed. MPI alteration was evident in 33% of the patients. MPI dynamical assessment shows a statistically significant improvement in this parameter (0.52 vs. 0.46 $p = 0.014$) between the first and last examination. The results are showed in Figure 3.

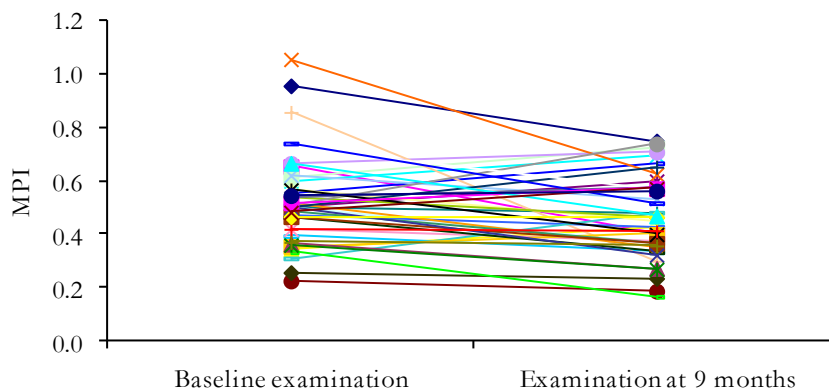


Figure 3. Evolution of the MPI during the evaluation (MPI -myocardial performance index)

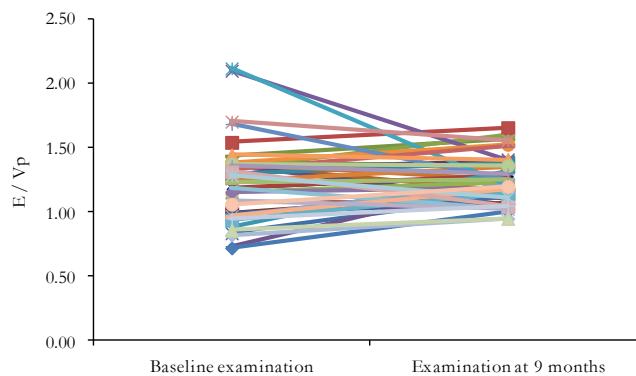


Figure 4. Evaluation of the ventricular filling pressure (E/Vp ratio - flow propagation velocity into the LV, measured in M colour mode)

The evaluation of the ventricular filling pressure by estimating the V_p highlights an increase of the telediastolic pressure in 16% of patients studied. At the same time, the dynamic assessment of the E/V_p ratio considered to be useful in a more sensitive assessment of the telediastolic pressure did not change significantly in the patients studied (1.22 versus 1.24, $p = 0.75$). (Figure 4.)

Discussion

In the group studied there is a predominance of women, a result confirmed in other studies in the literature [1,9,10]. It is not known precisely why there is a higher proportion of women among patients with heart failure with preserved EF, but the studies suggest that in women the left ventricle responds differently than in men, which is why left ventricular hypertrophy unaccompanied by dilation of the LV is more frequent in women [1,10]. The age of the patients studied was 52 years \pm 2 years, much reduced from that of the current studies [1,3,11]. A possible explanation of this is the absence of effective therapies of the cardiovascular risk factors and the ineffective control of blood pressure, leading to an early impairment of the diastolic function.

The patients studied presented no severe symptoms such as acute pulmonary oedema, hypertensive encephalopathy or acute coronary syndrome. Although the studies in the literature show a decline in the coronary artery disease in patients with heart failure with preserved systolic function, however, our group shows that angina was present in 46.51% of the patients [1,2,11].

The personal pathological history analysis revealed the frequent presence of hypertension in over half of the patients (58.13%) and of coronary artery disease in 32.55%. Based on the analysis of the cardiovascular risk factors we could notice their increased presence, as more than two thirds of the patients under study had at least two cardiovascular risk factors (most frequently BP and dyslipidemia). The current studies show that the increase in the prevalence and especially the lack of an efficient control of the cardiovascular risk factors greatly contribute to the occurrence and evolution of the heart failure [1,2,12,13].

Although the patients included in the study had an $EF \geq 50\%$, the assessment of the left ventricular systolic function revealed its alteration at segmental level, thanks to the more subtle parameters used. The EF assesses global systolic function and thus segment-level changes are not considered. In these conditions a SF, circumferential shortening velocity (CSV) analysis or MAPS assessment or by measuring systolic mitral annular velocity by tissue Doppler are extremely useful in the sensitive assessment of the systolic function. Thus, SF correlates well with the circumferential shortening velocity, which also reveals an alteration of the systolic function, probably still onset; 12% of the patients present a reduced SF, 61% of the patients in the study showed a decrease of the circumferential shortening velocity and 8 % of the patients experienced MAPS < 7 mm ($VM > 8$) [14,15].

An interesting parameter in terms of the data provided was MPI-1. This is a more sensitive indicator than EF and precedes EF decline, while being very sensitive when it comes to assessing diastolic dysfunction; it is independent of age, heart rate, post-pregnancy and LV geometry. What counts is that its change precedes the EF reduction [1,3].

The MPI analysis showed that this parameter changed in approximately 33% of the patients under study, which indicates that their evolution in time will be most likely followed by an impaired systolic function, according to the studies from the literature, showing an increase in mortality of the patients with CI and MPI changed by over 43% as compared to the general population [1,6].

The analysis in time of these patients under treatment shows an improvement of the MPI, which suggests that if we intervene early to control the various risk factors/precipitants, evolution could be soothed. However, in a large part of them, MPI did not improve, although they remained clinically asymptomatic, which suggests an unfavourable evolution in time, by altering the systolic function as well [3,6].

The ultrasound evaluation of the diastolic function showed an important aspect: only 10% of the patients studied met all the inclusion criteria. This suggests that the evaluation of the diastolic dysfunction requires an examination of as many parameters as possible, as their alteration in cardiovascular diseases is progressive and gradual [16,17,18].

Based on the criteria for assessing the diastolic function by transmitral flow analysis, venous flow analysis, tissue Doppler and VP analysis, the diastolic dysfunction was classified as follows: 47% of the patients had mild impairment of the diastolic function, 16% a moderate and only 16% had a severely impaired diastolic function. 35% of the patients presented a borderline form between mild and moderate impairment. These results are important because they show that timely intervention on the factors favouring the progression of the diastolic function impairment is very important and can reduce the unfavourable evolution of these patients [3,5,14].

In 25% of the patients the left atrial dilation occurs. This may explain the occurrence of atrial fibrillation in 11% of patients. It has been shown that atrial fibrillation is more frequent in patients with CI with preserved EF than in patients with CI and a low EF [1].

Tissue Doppler proved to be very important in assessing the systolic and diastolic function, proving particularly useful in patients whose transmitral flow evaluation showed a kind of quasi-normalization. The tissue Doppler dynamic evaluation at 9 months, based on the analysis of the E'/A' ratios in the septum and lateral wall showed a statistically significant improvement ($p = 0.016$) in the lateral wall, and an insignificant one ($p = 0.8$) in the septal area. Also, the E/E' ratio considered dynamically significantly improved from a statistic point of view ($p = 0.016$) under the therapy administered [1,3,14].

Assessment of the MPI (myocardial performance index) showed significant changes, especially when dynamically assessed. 33% of the patients had a reduced MPI. Dynamic evaluation of the MPI shows an improvement of this parameter under the therapy administered between the first and last examination, which is statistically significant ($p = 0.014$) [19,20].

Evaluation of the flow propagation velocity in the LV from the annulus to the apex, in diastole (VP) correlates well with the MPI and is generally independent of the filling conditions. Vp analysis highlights an increase of the diastolic pressure in 16% of the patients studied. E / VP is a parameter that correlates well with the LV pressure telediastolic pressure in the LV and the evaluation of the patients included based on this parameter showed that 15% of them have increased telediastolic LV filling pressures. Although considered useful in assessing the diastolic pressure, the E / Vp ratio did not change significantly in the patients studied [6,7].

The results of this study demonstrate that the assessment of the diastolic function should be part of the echocardiography evaluation algorithm and not determined only by evaluating the transmitral flow, but also by other means, more sensitive, such as tissue Doppler, VP, strain rates [1,6,7].

Thus, after evaluating the results of the ASCOT study, Dr. Hughes concluded: "I do not know exactly what is the proportion of doctors who send patients with hypertension to be performed a routine ultrasound, if only to assess the left ventricular mass. I think most specialty clinics would have to perform it, although I'm sure most doctors will not" [13].

Conclusions

Although the patients included in the study presented an apparently normal systolic function based on EF assessment, assessment of the LV systolic function by additional methods showed the presence of segmental alterations in the LV kinetics. The improvement of certain ultrasound parameters (E'/A', E/E') under treatment during the study underlines the importance of early diagnosis of the diastolic dysfunction in preventing the evolution of the heart failure. The use of the E'/A', E/E' and E/Vp ratio is useful in assessing the LV filling pressure, but it must be correlated with other parameters.

Conflict of Interest

The author declares that they have no conflict of interest.

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