Dynamics Clinical and Echographic Parameters Evaluation in Patients Prone to Diastolic Dysfunction Occurrence

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Abstract

Aim: The assessment of the clinical particularities and evolving echographic parameters evaluation in patients (p) examined in order to find the signs and symptoms corresponding to heart failure (HF), where the initial examination did not reveal echographic criteria of systolic and diastolic function alteration. *Material and Methods:* 40 patients were selected out of 200 examined, with pathologies frequently met in patients with manifest HF and EF [arterial hypertension (HTA), diabetes mellitus (DM), overweight), excluding the HF patients and the ones with echographic proves of systolic, diastolic function alteration and severe valvulopathies, as well as respiratory disease patients. They also have been clinically examined by echocardiography in the first 3 days from the first examination and then after 3, 6 and 12 months. The patients were divided in two samples, sample A, patients presenting $E/A < 1$ ratio, at least one examination out of the 4 carried out and sample B with $E/A > 1$. *Results*: Assessing the E/A ratio, sample A represents 70% of the patients. Assessing the whole sample, comparing just the first and the last examination highlights $E/A < 1$ in 35% of patients. E/Ea assessment at septal level shows a significantly difference between the samples, in all 4 examinations. The assessment of cardiac performance parameters (CPP) between the two samples shows a statistically significant difference. *Conclusions:* The study revealed that the presence of cardiovascular risk factors prepossesses to diastolic dysfunction development, frequently being also associated an alteration of systolic function.

Keywords: Diastolic dysfunction; Echocardiography; Heart failure

Introduction

The heart failure is a public health issue, representing an increasing pathology due to the evaluated therapy which, once with life expectancy extended in different cardiac pathologies, makes validate its evolution [1-3]. It determined discomfort, life quality diminishing, work inability and important costs. The heart failure is facilitated, besides the background diseases, by the precipitating and aggravating factors which recognized may be approached and corrected efficiently with the corresponding beneficial results [1,4]. As numerous studies showed, the heart failure with manifest systolic function, named also diastolic dysfunction, after the proved impairment of the diastolic function of the left ventricle is a common occurrence in the heart failure patients, as it most frequently remains undiagnosed [2,5,6].

The impairment of the diastolic function as well as of the systolic one, occurs relatively fast in cardiac diseases evolution. Due to these reasons, the last European guide of HF considers necessary to found the diastolic and systolic function impairment from the subclinical phases and simultaneously with the risk factors, in order to have an efficient prophylaxis avoiding as such the onset of HF. All HF phases present particularities detectable with the ultrasound scan, and as such one may act from the subclinical phases to prevent evolution to severe HF [1,3,7].

The sooner the diagnosis the efficient the therapy becomes and disease progress is prevented or delayed.

The aims of the research are the assessment of the clinical particularities and evolving echographic parameters evaluation in patients (p) examined in order to find the signs and symptoms corresponding to heart failure (HF), where the initial examination did not reveal echographic criteria of systolic and diastolic function alteration.

Material and Method

40 patients were selected out of 200 examined in ambulatory care or in emergency department, with pathologies frequently met in patients with manifest HF and EF (HTA, ischemic heart disease, (DM), overweight/obesity), excluding the HF patients and the ones with echographic proves of systolic, diastolic function alteration (EF < 50%) and severe valvulopathies, hemodynamic significant, as well as severe chronic respiratory disease patients. The clinical and dynamic evolution of the echographic parameters was followed, considering that early detection of the echographic modifications, suggesting the diastolic function impairment, requires therapeutic intervention upon the background diseases, precipitating and aggravating factors, with the corresponding beneficial results.

To each patient a standard echocardiography, using a 2.5-3 MHz probe, in M and 2D modes was performed. It was 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 Color Doppler, the calculation of the flow propagation velocity (PV) into the LV. It was calculated the ejection fraction (EF), the shortening fraction (SF), the velocity of circumferential shortening (VSC), the mitral annular systolic motion (MASM) and the myocardial performance index (MPI) [1,8]. The patients included in the study remained under observation and strict control of therapeutic indications compliance. The echocardiographic examination which initially was performed in the first 3 days from the first examination was subsequently repeated after 3, 6 and 12 months.

The numerical data were generally reported as mean, ± standard deviation. The test "t" (Student) was used for the statistical comparison of the numerical results for paired samples, employing the initial value and that after 12 months for all variables of the study. The *p* values under 0.05 were considered significant for all data used. Where necessary, the confidence intervals (CI) were evaluated at the materiality threshold of 0.05. The statistical program used was Excel 2003 and MedCalc version 9.

Results

Of the 200 patients initially investigated based on the criteria mentioned in the methodology, 40 were selected, 22 patients (55%, 95%CI [39.58% - 70.42%]) were female and 18 patients (45%, 95%CI [29.58% - 60.42%] male. The patients' average age ranged 57.98 years old ± 10 years.

The reasons for hospital presentation were for most of the patients the dyspnea 30 (75%, 95%CI [61.58% - 88.42%]), effort tolerance decreasing in 25 patients (62.5%, 95%CI [47.49% - 77.51%]), cephalalgia 20 patients (50%, 95%CI [34.5% - 65.5%]) and to a less extent retrosternal pain, occurred in 15 patients (37.5%, 95%CI [22.49% - 52.51%]). Any of the patients presented acute ventricular or acute coronary syndrome type of failure phenomena.

The evaluation of the cardiovascular risk factors displayed the occurrence in 26 patients (65%, 95%CI [50.22% - 79.78%]) of HTA, dyslipidemia, in 24 patients (60%, 95%CI [44.81% - 75.19%]), in 32 patients (79%, 95%CI [67.6% - 92.4%]) displayed the increase of body mass index (BMI) associated with the increase in 33 patients (82%, 95%CI [70.72% - 94.28%]) of the abdominal circumference and in 13 patients (33%, 95%CI [17.98% - 47.02%]) diabetes mellitus occurred. Smoking is displayed in 8 patients (25%, 95%CI [7.6% - 32.4%]) of the males and in 7 patients (17.5%, CI: 5.72% - 29.28%) of the females. As a synthesis of the cardiovascular risk factors was performed, their frequent association was observed, most of the patients displaying at least two factors of cardiovascular risk.

On ultrasound scan examination, employing the transmitral flow, in the last examination was displayed the decreasing of E/A ratio in patients (35%, 95%CI [20.22% - 49.78%]) out of the 4o ones. Nevertheless, the evaluation of all E/A ratios during the examination, displayed that patients (70%, 95%CI [55.8% - 84.2%]) had during the 12 months of examination the ratio E/A < 1 at least in one examination. Starting from this ration, the patients were divided in two groups, as such, in group A all the patients who during the evolution displayed the report E/A < 1 in at least one examination and the group B those with E/A > 1 ratio, and a comparison was performed between them.

The evaluation of risk factors, in the patients of group A, displayed the frequent and simultaneous presence of more cardiovascular risk factors, with no significant statistical differences of the two groups as regarding the risk factors as taken individually. The cumulative risk analysis displayed a progressive increase of the diastolic disfunction risk onset, when linking 2 risk factors, the percentage of diastolic disfunction is 22.5%, when linking 5 risk factors the risk increases to 40% and the presence of 7 risk factors increases the cumulative risk at 70%, fact showed in Fig. 1.
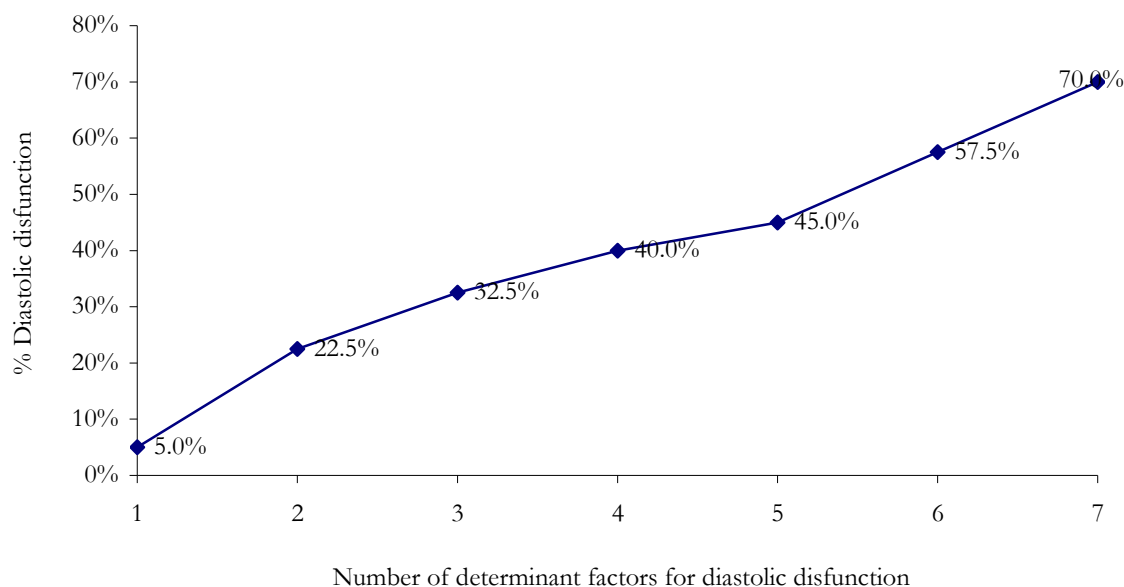

Figure 1. Cumulative risk of impaired diastolic function depending on the number of facilitating factors

The assessment of the diastolic function was performed by analyzing E/Ea, E/Vp, Ea/Aa septal, Ea/Aa lateral wall ratios for the global group and for the two groups by comparison.

The assessment on groups, A comparing with B of Ea/Aa ration during the evolution, both at lateral wall and septal level, had not displayed important changes between the two groups. The lateral and septal E/Ea evolution in all patients' group, between the first and last examination, reveals 9-12 E/Ea patients' percentage increase at the lateral region level (37.5% considering 10%) or septal region (82.5 considering 77.5%). The comparing on groups of E/Ea report, at the level of

the lateral wall, showed that are no statistical significant changes, as "p" of all four examination is insignificant statistically [the initial examination, p=0.83(NS), examination after 3 months, p=0.85 (NS), examination after 6 months, p=0.24 (NS), examination after 12 months, p=0.29(NS). In exchange, the evolution of septal E/Ea ratio during the 4 examination reveals a statistical significant difference between A and B group at all examinations with statistical significant "p", performed for the two groups (the initial examination, p=0.04; examination after 3 months, p=0.05; examination after 6 months, p=0.04; examination after 12 months, p=0.03).

Vp assessment shows a progressive decreasing of the value under 55 cm/s, between the first and last examination, 7 (17.5%, 95%CI [5.72% - 29.28%]) of the examined patients displayed a decrease of Vp value under 45 cm/s, considering the initial examination, when any patient outlined.

The comparative assessment of E/Vp ratio during the examinations reveals any statistical significant difference between the two groups of patients, aspects met also to the whole group, comparing with the first and last examination. Comparing assessments have been performed for estimation of possible correlations between different parameters used for the diastolic function evaluation. No statistical significant correlation have been displayed between the ratio Ea/Aa and E/Vp (r=0.25), E/Vp and lateral and septal E/Ea (r=0.46). The correlation evaluation between the minimum E/Vp and minimum lateral E/Ea, displayed a statistical significant correlation, with r=0.65.

MPI evolution analysis among the two groups reveals a different statistical significant evolution, with statistical significant impairment of MPI between the two groups, A and B. The statistical significant difference may be observed for all the evaluations, both at the (first examination, p=0.01; after 3 months, p=0.01; after 6 months, p < 0.01; and 12 months p=0.01). Any statistical significant influences outlined when taking into consideration separately the risk factors for the cardiac performance parameter.

Neither the medication used did reveal significant statistical changes between the two groups.

The evaluation of the patients in B group during the 12 months, considering the four examination, reveals that only 4 patients (33%, 95%CI [6.66% - 60.01%]) did not present any parameters modification indicating diastolic dysfunction, 3 patients (25%, 95%CI [0.5% - 49.5%]) presenting one modification of a parameter, 3 patients (25%, 95%CI [0.5% - 49.5%]) modification of two parameters and 2 patients (16.6%, 95%CI [0% - 37.76%]) modification of three parameters.

The analysis of the therapy did not reveal significant statistical modifications from therapy point of view in these patients. Nevertheless, in patients with E/A > 1, it is displayed more frequently the use of IECA and diuretic.

Analyzing the patients just considering the final examination, the examination after 12 months, we observe that E/A < 1 ratio appears in 35% (14 patients), 65% of the patients, displaying E/A > 1 (26 patients).

By comparison, it is displayed with the ratio evaluation during the whole echographic observation, significant difference of the final examination, having the ratio E/A < 1 in only 35% at the examination after 12 months, comparing with the evaluation of E/A < 1 report during the whole observation and considering for calculation the modification, independently of the data of evaluation, during this interval.

Assessing the E/A > 1 patients, we observe the presence of other modified parameters, characterizing the diastolic function. As such, of the 26 patients with E/A > 1 ratio, 13 patients, representing 50 % (95%CI [30.78% - 69.22%]), display impairments of Ea/Aa ratio. Out of them, 4 patients (30.76%, 95%CI [5.67% - 55.86%]) displayed Ea/Aa < 1 at the septum and lateral wall level, most of the patients, namely 8 (61.55%, 95%CI [35.09% - 87.99%]), presenting modifications only at tissue Doppler evaluation at septum level.

Patients' distribution with E/Ea ratio modifications, comparing with the lateral and septal region, in E/A > 1 patients, shows us a higher frequency of the average, between 9 and 12, suggesting telediastolic pressure increase, if considering the ration at the lateral region level, comparing with the septal region (34% versus 27%). The assessment of Vp values show a significant percentage of 5 of the patients (42%, 95%CI [12.01% - 64.91%]) displaying Vp between 45 and 50 cm/s.

Frequently, the dilation of the LA is displayed at the last examination in 24 (60%, 95%CI [44.81% - 75.19%]) of the studied patients, the atrial flow was modified in 26.9%of the patients (7 patients). The systolic function evaluation, in E/A > 1 patients showed, besides EF >50%, the shortening fraction, MASM, the velocity of circumferential shortening between normal limits. In exchange, the MPI analysis showed an increase of over 0.47 in 46% of the patients, by MPI evaluation at the last examination.

Any statistical significant modifications were displayed, as reported to the therapy followed, combinations using IECA and diuretic, beta blockers and / or calcium blockers' therapy, having any significant influence upon the evolution of these patients.

Discussion

Of the 40 patients under study, 22 (55%) were female and 18 (45%) were male. The patients' mean age was lowered significantly comparing with the current studies, 57.98 years ± 10 years. The analysis according to the gender displays the high ratio of women of all ages, excepting the 61-70 years old period, over 70 years old, the women ratio being three times higher than the men's one. The men presents more frequently impaired HF and EF, as the women are prone to develop manifest HF and EF [1,2,9].

The reasons for hospital presentation were usual, like dyspnea (75%), effort tolerance decreasing (62.5%), as frequently met symptoms in HF patients. The fact that neither patient of this group was hospitalized and that during the observation were performed only the periodical examinations are explained by the type of selected patient, without a severe pathology, the research aim being the evaluation of subclinical type of heart failure for their correction before the onset of obvious symptoms. The evaluation of cardiovascular risk factors displayed the frequent presence of the arterial hypertension in 65% of the patients, all patients displaying first and secondary level of HTA, hypercholesterolemia (60%), weight increase (79%) and diabetes mellitus (33%) [1,2,10,11]. This aspect is particular for the patients prone to develop diastolic dysfunction and to evolve to systolic impairment and heart failure onset [10,12]. As cardiovascular risk factors analysis is performed it is observed a frequent association of them, 38% of the patients displaying at least 3 cardiovascular risk factors [2,10,11].

Once clinically assessed, objectively and characterized from cardiovascular risk factors, the echographic analysis of these patients outlined two important aspects. The evaluation of the mitral flow showed a decrease of the E/A ratio, progressive between the first and last examination, leading to diastolic dysfunction onset. The assessment of E/A report was performed between the initial examination and the evaluation of all E/A ratios, during the whole observation, taking into consideration any examination, if E / A < 1 and between the initial and final examination. This parallel examination shows a significant difference, 70% of the evaluated patients during the observation had a ratio of E/A < 1, while, the comparative assessment between the first and last examination displayed only 35%. This aspect is very important to consider, proving the importance of the periodic assessment of the patients, the evaluation after a year, which may lead to early avoidance of the diastolic dysfunction and the rapid intervention to prevent the subclinical conditions to modify in clinical, symptomatic one [5,8,13,14].

The division in two groups, A and B, depending on E/A ratio assessment, during the whole time of observation and comparative analysis performance between the two groups brought data of interest.

The evaluation of risk or facilitating factors for heart failure onset, as taken individually, had not a statistical significant influence for the two groups.

 Although important differences are displayed between the two groups as considering the arterial hypertension (64.29% vs. 35.71%), dyslipidemia (76.92% vs. 23.08%) or diabetes mellitus presence (76.19% vs. 23.81%), however no significant statistical differences are displayed upon the E/A ratio evolution. Which outlines is the frequency of cardiovascular risk factors of group A patients. In exchange, the cumulative risk analysis shows us the increase of diastolic dysfunction onset riks, increasing the number of risk factors from 22.5%, with two associated risk factors up to

70% once with association of more involved factors [5,8,15]. The comparative assessment of septal and lateral Ea/Aa ratio in all patients' group, between the first and last examination, do not reveal significant statistical modifications between the two groups. The analysis of E/Ea ratio shows us the increa of patients' percentage with E/Ea between -12, at the level of lateral region (37.5% considering 10%) or septal (82.5 considering 77.5%), if the assessment is for the whole group of patients [1,5]. The comparison in exchange of E/Ea ratio at the septum and lateral wall level showed significant statistical differences between the two groups, especially at the septal assessment level (initial examination, $p=0.04$, examination after 3 months, $p=0.,05$, examination after 6 months, $p=0.04$, examination after 12 months, $p=0.03$). This parameter is useful, helping also in finding the ventricular telediastolic pressure increase [1,8]. The tissue Doppler evaluation, as it is much subtle, displays more frequently the occurrence of diastolic function impairment, the displayed modifications leading to diastolic dysfunction finding in patients with $E/A > 1$.

The Vp evaluation reveals us a progressive decrease of the value under 55 cm/s, between the first and last examination, 17.5% of the assessed patients presented a decrease of the Vp value below 45 cm/s, considering the initial examination when any patients outlined. This useful parameter, especially in association with E/Ea and E/Vp ratio, shows the telediastolic pressure increase for the studied patients, predicting the diastolic dysfunction onset. Although the two subgroups have different evolutions, the comparative evaluation of the E/Vp ratio during the examination does not display any significant statistical difference between the two patients' groups [8,13,14,15].

The attempt to settle different correlations between the E/Vp and lateral E/Ea, E/Vp and E/Ea ratios was not relevant, the correlation coefficient was statistically insignificant ($r=0,46$). In exchange, the assessment of the correlation between minimum E/Vp and minimum lateral E/Ea, showed a significant statistical correlation, with $r=0.65$. This aspect is important showing that if E/Vp converges to low values suggesting low pressures in telediastolic LV, this is correlated also with the other parameter used in telediastolic pressure estimation [5,16,17,18].

The assessment of the systolic function, by SF, MASM evaluation, the velocity of circumferential shortening, did not reveal significant statistical modifications, neither through group, globally assessing, nor by comparison between the two subgroups [5,8,17].

In exchange, the myocardial performance index assessment, revealed modifications in dynamics, with its impairment, both at the general group as by comparative assessment between the two groups, occurring statistical significant changes during the four examinations (initial examination, $p=0.01$, examination after 3 months, $p=0.01$, examination after 6 months, $p < 0.01$, examination after 12 months, $p < 0.01$). The association of the ischemic heart disease may constitute an explanation of the worsening of this index [8,16].

Another important aspect was observed when group B was analyzed, using also other echographic parameters. Only 4 patients (33%) did not present any modification of parameters indicating diastolic dysfunction, 25% of the patients presenting minimum two echographic parameters (using tissue Doppler, E/Ea, Vp, E/VP ratio).

The therapy assessment did not presented significant statistical changes from therapy point of view in these patients. Nevertheless in $E/A > 1$ patients, more frequently IECA and diuretic use is outlined. No significant statistical modifications displayed when employing beta blockers, calcium blockers comparing with IECA [1,2,19].

Analyzing the patients depending only by the final examination, after 12 months, we observe $E/A < 1$ ratio occurring in 35% (14 patients), 65% of the patients presenting $E/A >1$ (26p).

Considering just the patients with $E/A > 1$, we observe the presence of some modified parameters characterizing the diastolic function. As such, 50% of the patients present deficiencies of Ea/Aa ratio, more frequently at septum level, aspect often met also in literature, suggesting segmental kinetics disorders onset. At the same time Vp modification is displayed, explained by pressure increase in the LA, correlated also with the sizes increase, LA surface met in 60% of the patients. MPI, VP, Ea/Aa, E/Ea ratios modification in these patients raise questions about the presence of some subtle modifications, both of the systolic and diastolic function, which have not yet produced clinical conditions, but which undiscovered on time, may have repercussions upon the occurrence and progress of heart failure with diastolic and systolic function impairment. The

evaluation of the therapy, the separate evaluation of IECA and diuretic therapy versus beta blokers and/or calcium blockers, did not show significant statistical differences, considering the assessment of the whole group [5,18]

A possible explanation for therapy failure to correlate with the studies echographic indicators may be explained by relatively uncomplicated pathology of the patients, the administrated doses being relatively low, the patients not needing an aggressive therapy for symptoms control. Moreover, the observation during a relatively short period could not reveal the possible beneficial effects of the drugs over the systolic and diastolic function parameters [2,12,15].

Conclusions

The study revealed that the presence of cardiovascular risk factors predisposes to diastolic dysfunction development, proved by echographic parameters analysis (E/A, Ea/Aa, E/Ea, E/Vp – useful parameters in assessing these patients' evolution and behavior).

The outlining of some systolic function parameters strengthens the hypothesis of association of diastolic dysfunction with the systolic one, at least by segmental impairment, in heart failure patients and manifest systolic function. This aspect is proved by dynamic MPI increase, both in whole patients' group analysis and by comparing the groups A and B, under the conditions of an ejection fraction of > 50%.

The difference occurred (35% versus 70%) by analyzing the E/A ratio for all patients, only between the first and last examination and comparing assessment of E/A ratio in all examinations for A and B groups shows us the importance of the evaluation in shorter intervals of 3-6 months, avoiding as such the sub-estimation of the transient conditions of systolic and diastolic function impairment.

The therapy assessment by separate evaluation of IECA and diuretic therapy, versus beta blokers and / or calcium bloker, did not display significant statistical differences, comparing the two patients' groups.

Conflict of Interest

The authors declare that they have no conflict of interest.

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