Frequency of Left Ventricular Diastolic Dysfunction by Mitral Doppler in Healthy Elderly Individuals

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Summary

Background : Healthy elderly individuals present alterations in mitral Doppler velocities, which are characteristic of left ventricular (LV) diastolic dysfunction with impaired relaxation.

Objective : To determine the frequency of LV diastolic dysfunction by mitral Doppler in healthy elderly individuals and identify clinical and echocardiographic characteristics associated to this finding.

Methods : Seventy-three apparently healthy individuals (64% women, aged 60 to 80) were carefully selected and submitted to clinical, laboratory and Doppler-echocardiographic assessment, with particular regard to the characteristics of the mitral flow.

Results : A total of 33 patients (45%) presented an impaired LV relaxation pattern (group I), characterized by the association between the maximum velocities of the mitral wave flow (E/A ratio) <0.75 or E-wave deceleration time >240 ms, and 40 (55%) with a normal pattern (group II). Group I presented a larger aortic root diameter (32.1±4.2 *vs*. 30.3±3.3 mm; p=0.044) and a longer PR interval (156±22 *vs*. 139±23 ms; p=0.002).

Conclusion : A large proportion of individuals aged 60 to 80 years present normal diastolic function at the Doppler-echocardiographic assessment of the mitral flow. Healthy elderly individuals with impaired LV relaxation filling have a larger aortic root diameter and longer PR interval.(Arq Bras Cardiol 2009; 93(3) : 304-309)

Key Words: Ventricular dysfunction, left; echocardiography, Doppler; mitral valve, elderly.

Introduction

One can observe significant modifications in the transmitral Doppler, tissue Doppler imaging of mitral annulus and pulmonary venous Doppler profiles at the older age ranges, similar to those found in diseases that course with impaired left ventricular (LV) relaxation filling[1-7]. However, not all elderly individuals exhibit altered mitral and pulmonary venous Doppler profiles[8,9]. More recently, it was demonstrated in a large epidemiological study with individuals older than 65 years that the diagnosis of diastolic dysfunction, based on a stricter criterion, was an independent predictor of congestive heart failure[10].

The objective of the present study was to evaluate the frequency of diastolic dysfunction by mitral Doppler in apparently healthy individuals aged ≥60 years, as well as to identify the clinical and echocardiographic characteristics associated to this finding.

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Manuscript received August 10, 2008; revised manuscript received October 16, 2008; accepted October 21, 2008.

Methods

Study population

Retired employees of the Federal University of Bahia and patients treated at a private health institution, aged 60 years or older, were invited to participate in the study. Individuals that met one or more of the following criteria were excluded from the study: (1) A diagnosis of systemic arterial hypertension based on the regular use of anti-hypertensive drug or persistently high blood pressure measurement by either the casual measurement with a sphygmomanometer or by ambulatory blood pressure monitoring; (2) a diagnosis of coronary artery disease, either by the history of angina pectoris or myocardial infarction, or the presence of myocardial ischemia or electrically inactive region at the ECG; (3) clinical picture of heart failure, or echocardiographic signs of LV systolic dysfunction (through the qualitative analysis of two-dimensional echocardiogram or ejection fraction <55%); (4) use of artificial pacemaker; (5) use of drug with cardiovascular action (diuretic, digital, beta-blocker, calcium channel antagonist, nitrate or antiarrhythmic); (6) presence of left branch blockage; (7) presence of atrial fibrillation; (8) diagnosis of hypertrophic cardiomyopathy, defined by the finding of interventricular septum diastolic thickness

≥15 mm and at least 1.3-fold the thickness of the LV posterior wall; (9) diagnosis of restrictive cardiomyopathy, such as endomyocardial fibrosis and amyloidosis; (10) presence of mitral or aortic valvular failure > mild; (11) presence of any degree of mitral or aortic stenosis; (12) diagnosis of diabetes mellitus, i.e., fasting glycemia ≥126 mg/dl, use of insulin, or use of oral hypoglycemic agents; (13) history of chronic disease capable of affecting the cardiocirculatory function, such as renal failure, hyperthyroidism, chronic pulmonary disease or collagenosis; (14) heart rate >100 beats per minute, at the moment of the echocardiographic assessment; (15) technically inadequate echocardiographic image ; (16) and refusal to participate in the study.

Clinical and Laboratory Data

All individuals enrolled in the study were submitted to a clinical examination, electrocardiogram and laboratory assessment, which included hematocrit, glycemia, creatinine, total cholesterol, HDL-cholesterol and triglycerides. Whenever possible, the LDL-cholesterol was calculated by Friedewald's formula[11].

Echocardiogram

The echocardiographic assessment was carried out in an Apogee equipment (model CX 200) or Philips Envisor CHD, by the same professional.

The dimensions of the left atrium, left ventricle and aorta were obtained by the analysis of the M-mode, according to the criteria defined by the Penn Convention and corrected by height[12]. The relative thickness of the LV walls was determined by dividing the sum of the diastolic thickness of the interventricular septum (IVS) and the posterior wall (PW) by the LV diastolic diameter (LVDD). The ventricular mass was obtained through the formula: LV mass (g) = 1.04 [(LVDD + IVS + PW)^3 - (LVDD)^3 – 13.6)]; and corrected for the body surface area[13].

Doppler examination of the mitral inflow was performed from the apical 4-chamber view with the sample volume placed between the mitral leaflet tips. Doppler mitral inflow recordings were considered inadequate if the angle between the echo beam and the mitral inflow was >30°., the sample volume was inadequately positioned, and the Doppler envelope was too indistinct to measure accurately. The following transmitral flow variables were measured for each patient in three cardiac cycles: E-wave maximum velocity (EV_{max}), A-wave maximum velocity (AV_{max}), ratio between the maximum velocities of E and A waves (E/A ratio) and the E-wave deceleration time (EDT). The arithmetic means of these measurements were considered.

The reproducibility of the Doppler measurements was verified in 10 study patients, randomly selected by drawing lots. The videotape of selected cases was reviewed by a second echocardiographer blinded to the study data and then, Pearson's coefficients of correlation were calculated: E/A ratio = 0.91 and EDT = 0.82.

Individuals with an E/A ratio <0.75 or EDT >240 ms were considered as having impaired left ventricular relaxation.

Statistical Analysis

Categorical variables were compared between the groups with and without diastolic dysfunction by Chi-square test or Fisher's exact test, when appropriate. Student's *t* test or non-parametric Mann-Whitney test was used to compare the quantitative data when the variable did not follow the normal distribution. All tests were two-tailed. The level of significance was pre-established as 5%. The numerical data are expressed as means ± standard deviations. We also calculated the 5th and 95th percentiles of the mitral Doppler index.

Ethical Aspects

The research project was approved by the Committe of Ethics in Research of Hospital Universitario Prof. Edgard Santos. Each individual invited to participate in the study was informed on the nature, objective and possible consequences of the study and signed the free and informed consent form. All collected data were kept under complete confidentiality.

Results

Among the 73 individuals considered eligible for and included in the study, we identified 33 (45%; confidence interval: 34-57%) that presented an impaired LV relaxation pattern (Group I) and 40 (55%; confidence interval: 43-67%) with a mitral Doppler pattern considered normal (Group II).

The clinical and laboratory characteristics of each group are summarized in Table 1. The groups did not show any difference regarding most of the tested clinical and laboratory variables. However, Group I presented a longer PR interval (156±22 *vs*. 139±23 ms; p=0.002) and the diastolic arterial pressure was slightly higher in Group I, with a borderline statistical significance (80±5 *vs*. 77±6 mmHg; p=0.062).

The aortic root diameter was slightly larger in Group I (32.1±4.2 vs. 30.3±3.3 mm; p=0.044), with consequent decrease in the left atrium/aorta ratio (1.02±0.18 vs. 1.12±0.14 mm; p=0.007). None of the findings were modified after the echocardiographic dimensions were corrected for height (Table 2).

Table 3 shows the means, standard deviations, minimum and maximum values as well as the 5th and 95th percentiles of the mitral Doppler indexes. The EV_{max} and AV_{max} in the studied sample were, respectively: 0.75±0.16 m/s and 0.80±0.16 m/s, with E/A ratio = 0.96±0.24 and EDT = 234±42 ms.

Discussion

Few studies have described the frequency of impaired LV relaxation filling in the elderly population. In the subset of 114 healthy subjects of the Framingham Heart Study, aged 70 to 87 years, 87% had E/A ratio <1, which is a criterion of abnormal LV relaxation pattern recommended by the American Society of Echocardiography[8,14]. Subsequently, in a study with 288 normal individuals aged 20 to 80 years, a gradual decrease in the E wave and increase in the A wave were observed with aging, with most individuals presenting equivalent waves in the sixth decade[4]. Based on this observation, an E/A ratio between 0.75 and 1.5 is presumed as a criterion

Table 1 - Clinical characteristics of elderly individuals in the presence or absence of LV diastolic dysfunction.

Variable*	Diastolic Dysfunction Present (n = 33)	Absent (n = 40)	p value†
Categorical Variables			
Female gender	21 (64%)	26 (65%)	0.904
Regular physical activity	6 (18%)	10 (25%)	0.483
Smoking	3 (9%)	1 (3%)	0.322
Alcohol consumption	2 (6%)	3 (8%)	1.000
Estrogen use	5 (25%)	7 (29%)	0.757
Family history			
Coronary artery disease	6 (18%)	3 (8%)	0.284
Arterial hypertension	13 (39%)	14 (35%)	0.699
Heart failure	4 (12%)	3 (8%)	0.694
Diabetes mellitus	8 (24%)	10 (25%)	0.940
Quantitative Variables			
Age (yrs)	68±5 (60-80)	66±5 (60-78)	0.084
Body Mass Index (kg/m^2)	26.8±4.5	25.5±3.5	0.176
Systolic blood pressure (mmHg)	126±13	127±9	0.727
Diastolic blood pressure (mmHg)	80±5	77±6	0.062
Mean blood pressure (mmHg)	95±7	94±6	0.343
Pulse pressure (mmHg)	46±11	50±10	0.159
Heart rate at rest (beats/min)	68±10 (50-95)	64±8 (55-83)	0.090
PR Interval (ms)	156±22	139±23	0.002
Glycemia (mg/dl)	93±13	90±8	0.216
Total cholesterol (mg/dl)	212±38	223±43	0.234
HDL (mg/dl)	49±11	46±11	0.362
LDL (mg/dl)	137±40	149±45	0.237
Triglycerides (mg/dl)	130±65	121±45	0.475
Hematocrit (%)	42.3±2.4	41.9±3.6	0.558
Creatinine (mg/dl)	0.86±0.18	0.85±0.17	0.712
Estimated creatinine clearance (ml/min)	73±17	74±19	0.840

** Data in absolute numbers (percentage) — categorical variables — or mean±standard deviation — quantitative variables, except age and heart rate = mean±standard deviation (minimum value – maximum value). †Chi-square Test (categorical variables) or Student's t test (quantitative variables), except smoking, alcohol consumption and family history of coronary artery disease and heart failure (Fisher's exact test), in addition to PR interval (Mann-Whitney's test).*

of normality in the population older than 50 years[15,16]. The EDT undergoes less variation with aging and it is considered normal when <240 ms[17]. Using these criteria to diagnose diastolic dysfunction in the elderly population allowed the identification of those presenting a higher risk of death and congestive heart failure[10,18,19].

In our study, which involved apparently healthy adults between 60 and 80 years of age, 55% of the sample presented mitral Doppler results within the normal range. We then tried to find an explanation why the remainder of the population presented a pattern of impaired LV relaxation filling.

Age, gender, PR interval, arterial blood pressure and heart rate are physiological variables that interfere with the mitral Doppler parameters[5,20]. The present study showed a significant difference between the groups only regarding the PR interval, which was longer in the individuals classified as having diastolic dysfunction. That is in accordance with the data from the Framingham Heart Study, which showed an inverse correlation

Table 2 - Echocardiographic characteristics of elderly individuals in the presence or absence of LV diastolic dysfunction.

Variable*	Diastolic Dysfunction Present (n = 33)	Absent (n = 40)	p value†
Aortic root diameter (mm)	32.1± 4.2	30.3 ± 3.3	0.044
Aortic root diameter /height (mm/m^2)	20.1±2.1	18.9±2.0	0.013
Left atrial diameter (mm)	32.2 ± 3.6	33.7 ±4.1	0.102
Left atrial diameter /height (mm/m^2)	20.2±2.6	21.0±2.4	0.226
Left atrial/aortic root diameter ratio	1.02 ± 0.18	1.12 ± 0.14	0.007
LV diastolic diameter (mm)	44.7 ± 4.2	45.9 ± 5.0	0.285
LV diastolic diameter /height (mm/m^2)	28.1±2.9	28.5±2.7	0.483
LV systolic diameter (mm)	27.0 ± 4.1	27.3 ± 4.1	0.771
LV systolic diameter /height (mm/m^2)	16.9±2.6	16.9±2.4	0.966
Ejection fraction (%)	70 ± 7	71 ± 6	0.509
Septal wall thickness (mm)	9.6 ± 1.6	9.5 ± 1.9	0.512
Posterior wall thickness (mm)	9.3 ± 1.3	9.2 ± 1.6	0.339
Septal/posterior wall thickness ratio	1.03 ± 0.83	1.03 ± 0.11	0.812
LV relative wall thickness	0.43 ± 0.07	0.41 ± 0.09	0.450
LV mass index (g/m^2)	94.8 ± 24.3	98.4 ± 29.6	0.581

LV – left ventricular
** Data as mean ± SD — quantitative variables*
† Student's t Test, except septal wall thickness, posterior wall thickness and septal/posterior wall thickness ratio (Mann-Whitney's test)

Table 3 - Left ventricular diastolic function indexes in healthy elderly individuals (n=73).

Variable	Mean±SD	5-95th Percentile	Minimum-maximum value
E wave maximum velocity (m/s)	0.75±0.17	0.47-1.02	0.46-1.09
A wave maximum velocity (m/s)	0.80±0.16	0.53-1.09	0.52-1.27
E/A ratio	0.96±0.24	0.66-1.41	0.62-1.49
E-wave deceleration time (ms)	234±42	180-307	150-363

SD - standard deviation

between the PR interval and EV_{max}, in a population aged 20 to 80 years[20]. Two mechanisms can explain the contribution of the PR interval to the mitral Doppler pattern. First, the longer the PR interval, the higher the ventricular filling in the end-diastolic phase. Finally, the short time for the left ventricular passive filling results in a higher atrial volume at the beginning of the atrial systole, a principle of Starling's law.

In elderly individuals, the heart rate is positively associated with the AV_{max} and inversely associated with the EV_{max} and the E/A ratio[5,21]. In the present study, the heart rate variation was small, as we excluded individuals with more than 100 beats per minute, which can explain the similarity between the groups.

In the normal elderly population, there is evidence of an association between the mitral Doppler index and the diastolic blood pressure[22]. We restricted our study sample to normotensive individuals. We observed that the diastolic blood pressure was 3 mmHg higher in the group with diastolic dysfunction, with a borderline level of significance (0.062), which explains, in part, the alterations in the mitral Doppler pattern.

We tested epidemiological variables related to lifestyle habits and family history. Although it has been demonstrated that regular physical activity, alcohol consumption and estrogen replacement favorably alter the left ventricular relaxation[22,23] and that acute smoking causes a decrease in the E/A ratio[24,25], we did not observe any difference regarding the frequency of these variables between the groups. However, our study did not have enough power to measure the influence of these factors on the diastolic function.

Patients at older age ranges show a larger aortic root diameter[26,27]. In these individuals, the alteration in the composition of the central arterial walls has been considered responsible for the decreased arterial compliance observed[28]. We found a subtle, but significant difference between the studied groups, explained by the higher degeneration and lower distensibility of the aorta

in the group with diastolic dysfunction. Further studies are necessary to evaluate this hypothesis.

The groups did not differ regarding the linear dimensions of the left atrium and left ventricle, as well as the LV thickness, mass and ejection fraction. Although the volume measurement allows a more accurate assessment of the asymmetric remodeling of the left atrium, linear measurements are also useful in clinical and epidemiological researches[29,30].

To the best of our knowledge, this is the first study in Brazil that presents the 5th and 95th percentiles of the mitral Doppler in an elderly population selected as being healthy, which makes it useful in clinical practice. It can be considered that individuals in the distribution extremities are really pathological. Although we did not perform a broad epidemiological study to select the study sample, the patients were consecutively invited to participate in the study if they did not meet any of the exclusion criteria.

Study Limitations

We did not assess the Doppler of pulmonary venous flow or the tissue Doppler imaging in the studied sample. This could imply in the classification of some patients with a "pseudonormal" diastolic pattern as having a normal one. It is not possible to guarantee that all of them exhibited normal left atrial pressure, as the E/E' ratio was not calculated (the E/E' ratio >10 indicates elevated left atrial pressure[31]). However, the exclusion of several morbid conditions – such as the LV systolic dysfunction, hypertrophic cardiomyopathy and systemic arterial hypertension – makes these two situations very unlikely. The classification of the individuals as healthy was based on a noninvasive strategy, but an ergometric test for the detection of subclinical coronary artery disease was not performed. Nevertheless, all the individuals included in the study were asymptomatic for myocardial ischemia and exhibited normal overall and segmental LV contractility at the two-dimensional echocardiogram. The data were not analyzed in a multivariate model due to the study design. The authors plan to present more refined data in a new study.

Conclusion

A high number of individuals aged 60 to 80 years present normal diastolic function at the Doppler-echocardiographic analysis of the mitral flow. Healthy elderly individuals with impaired LV relaxation filling exhibit a longer PR interval and a larger aortic root diameter.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of Doctoral submitted by Luiz Sérgio Alves-Silva, from Escola Bahiana de Medicina e Saúde Pública.

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