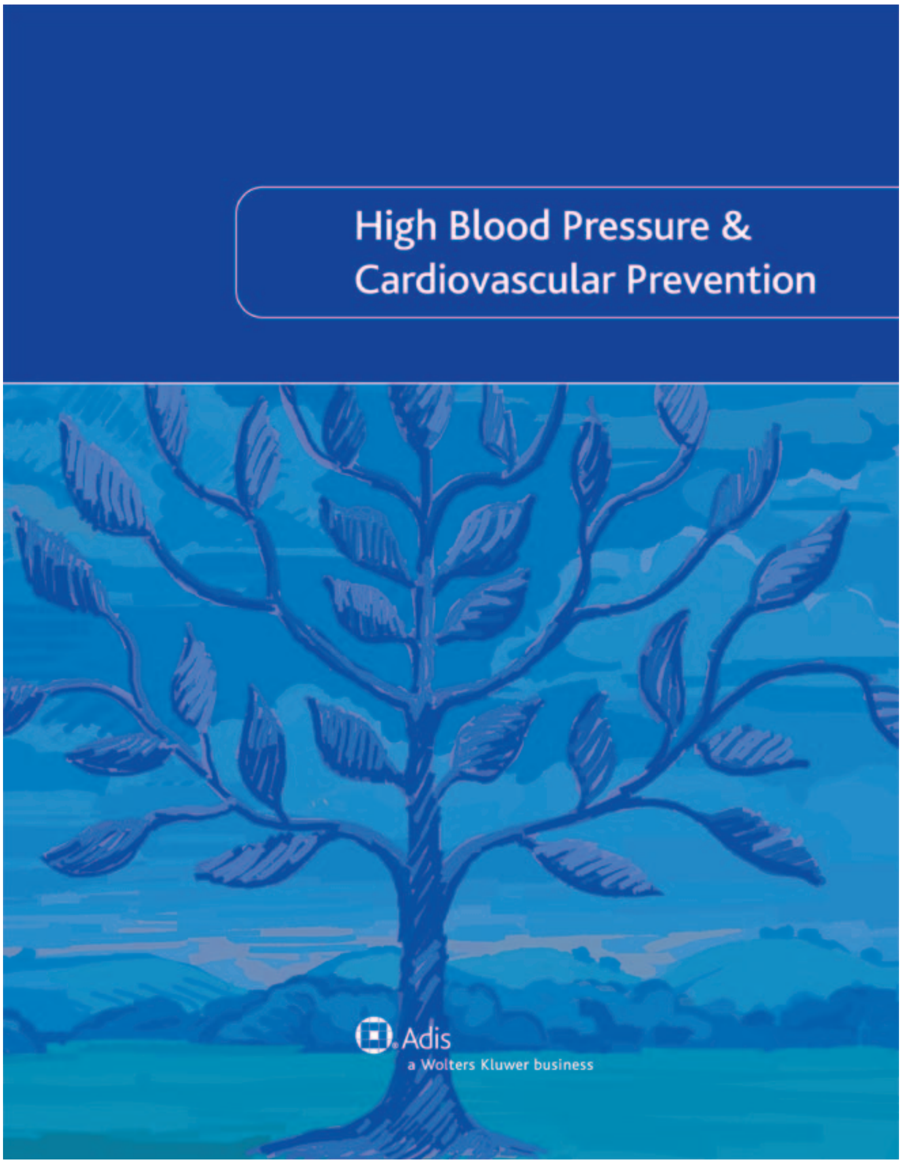
High Blood Pressure &
Cardiovascular Prevention
Adis
a Wolters Kluwer business

High Blood Press Cardiovasc Prev 2011; 18 (4): 187-193
1120-9879/11/0004-0187/$49.95/0

Role of Tissue Doppler Imaging for Detection of Diastolic Dysfunction in the Elderly

A Study in Clinical Practice

Francesca Negri,[1,2] *Carla Sala,*[3] *Cristiana Valerio,*[2] *Giuseppe Mancia*[1] and *Cesare Cuspidi*[1,2]

1 Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milan, Italy
2 Istituto Auxologico Italiano IRCCS, Milan, Italy
3 Heart and Lung Department, University of Milano and Fondazione Ospedale Maggiore Policlinico, Milan, Italy

Abstract

Background: The role of tissue Doppler imaging (TDI) in the assessment of diastolic dysfunction in elderly patients seen in echocardiographic practice is poorly defined.
Objective: The aim of this study was to investigate the prevalence of diastolic dysfunction in a cohort of elderly patients referred to an echocardiographic examination for routine clinical indications and to compare the findings obtained by conventional Doppler with those obtained by TDI.
Methods: A total of 457 elderly patients with preserved left ventricular (LV) systolic function (mean age 73 ± 5 years, 45% men, 76% with hypertension) underwent a comprehensive echo-Doppler examination; diastolic dysfunction was defined by the following conventional and TDI criteria: E/A ratio (ratio between transmitral peak velocity of E and A waves) <0.7 or >1.5 and lateral annular early diastolic peak velocity (Ei) <8 cm/sec, respectively.
Results: Diastolic dysfunction was present in 130 patients (28.4%) according to the conventional Doppler criterion, namely 119 (26.0%) because of E/A <0.7 and 11 because of E/A >1.5. A higher proportion of participants (60.1%) had LV diastolic dysfunction according to TDI. Notably, more than one-half of the patients with ‘normal’ diastolic function by conventional criterion exhibited an abnormal Ei value.
Conclusions: A large proportion of elderly patients with normal E/A ratios may have more subtle alterations in LV diastolic mechanics characterized by a reduced annular motion velocity. Thus, evaluation of diastolic function by the simple E/A ratio may markedly underestimate diastolic abnormalities. This finding supports the view that diastolic function should be routinely assessed by comprehensive Doppler methodologies including both conventional and tissue Doppler measurements in order to improve the management of elderly patients seen in clinical practice.

Received for publication 15 September 2011; accepted for publication 24 October 2011.

Keywords: conventional Doppler, tissue Doppler imaging, diastolic function, elderly.

Introduction

Heart failure represents the most common cause of hospitalization among major forms of cardiovascular disease, followed by cerebrovascular and coronary heart disease; hospitalization rates of congestive heart failure (CHF) are increasing worldwide.[1-3] Several factors have been advocated for this trend including aging of the population, substantial survival improvement among subjects with hypertension, diabetes mellitus, coronary disease and kidney disease.[4,5]

CHF related to left ventricular (LV) diastolic dysfunction, is an emerging clinical entity involving up to 50% of patients managed in current practice.[6] The likelihood of diastolic dysfunction as a leading cause of heart failure is high in the elderly population as a consequence of the high prevalence of hypertension, degenerative valve diseases, LV hypertrophy (LVH), large artery stiffness, metabolic syndrome and diabetes in this group.[7,8]

Echocardiography is recommended by international guidelines for identifying heart failure with preserved ejection fraction and detecting diastolic abnormalities in asymptomatic high-risk patients.[9] A large amount of evidence indicates that the assessment of diastolic parameters either by conventional Doppler or by tissue Doppler imaging (TDI) may provide independent predictive information about cardiovascular morbidity and mortality.[10-12]

In the last decade, the TDI technique has been extensively validated in a variety of cardiac pathologies.[13,14] At the present time, TDI (as well as new imaging technologies such as strain rate and speckle tracking) may offer incremental information on myocardial function compared with conventional echocardiography.[15] The role of these new technologies in the assessment of diastolic dysfunction in clinical practice remains undefined.

In the present study, we sought to evaluate the prevalence of LV diastolic dysfunction in a large cohort of elderly hypertensive patients with preserved LV systolic function seen in current echocardiographic practice; to this purpose we compared data obtained by conventional Doppler and TDI criteria to assess the role of TDI in detecting age-related diastolic abnormalities.

Methods

A total of 475 consecutive individuals aged ≥65 years, referred to the out-patient echocardiographic service of the Istituto Auxologico Italiano (Meda, Italy) by their general practitioners during a 15-month period from February 2009 to April 2010, were enrolled in the study. Main exclusion criteria were: (i) impaired LV ejection fraction (LVEF) [<40%]; (ii) previous myocardial infarction or coronary bypass history; (iii) previous hospitalization for heart failure; (iv) significant cardiac valve disease (regurgitation >1 at Doppler examination, stenosis of any degree, presence of prosthesis and mitral annulus calcification); (v) atrial fibrillation; and (vi) left bundle branch block.

After an informed consent had been obtained, patients' demographic data, medical history and medications were collected at the echocardiographic laboratory in a questionnaire administered by the attending physician. Obesity was identified as body mass index (BMI) ≥30 kg/m^2. High blood pressure (BP) was defined as systolic BP (SBP) ≥140 mmHg and/or diastolic BP (DBP) ≥90 mmHg in untreated subjects or current antihypertensive therapy regardless of BP values. Diabetes was defined by patients' self-reports.

Measurements

Bodyweight was recorded to the nearest 0.1 kg using a calibrated electronic scale with the subjects wearing indoor clothing without shoes. Height was recorded to the nearest 0.5 cm using a standardized wall-mounted height board. BMI was computed as weight in kilograms divided by the squared height in metres.

Clinic BP was measured by mercury sphygmomanometer with appropriate-sized cuffs; measurements were performed after the subjects had been resting for 3–5 minutes in the sitting position. Three measurements were taken from the non-dominant arm at 1-minute intervals and the average was used to define the patients' representative values.

Echocardiography

Echocardiographic and Doppler examinations were performed according to a standardized protocol. In brief, M-mode, 2-dimensional and Doppler echocardiographic examinations were carried out with a commercially available instrument (Vivid 7, GE, Horten, Norway).

End-diastolic (d) and end-systolic (s) LV internal diameters (LVID), interventricular septum thickness (IVS) and posterior wall thickness (PWT) were measured from 2-dimensionally guided M-mode tracings recorded at a speed of 50–100 cm/sec, during at least three consecutive cycles according to the Penn convention. Relative wall thickness (RWT) was defined by the ratio of PWT plus IVS thickness to LVIDd; LV mass was estimated by Devereux's formula $\{1.04\,[(IVSd + PWTd + LVIDd)^3 - LVIDd^3] - 13.6\}$[16] and indexed to height to the allometric power of 2.7. LVH was defined as LV mass index >50 g/h$^{2.7}$ in both genders.[17] Patterns of abnormal LV geometry were defined as follows: (i) LV concentric remodelling (normal LV mass index combined with RWT ≥0.43); (ii) eccentric LVH (increased LV mass index combined with RWT <0.43); and (iii) concentric LVH (increased LV mass index combined with RWT ≥0.43).[18]

LVEF was measured from the four-chamber apical projection in the standard fashion from LV end-diastolic and LV end-systolic volume.

Left atrium diameter was determined at end-systole in the parasternal long-axis view, by the leading edge-to-leading edge maximal distance between end-systolic posterior aortic root wall and posterior left atrium wall.[18] Left atrium volume was measured at end-systole in the apical four-chamber view by planimetry.

Conventional Doppler Measurements

LV filling was assessed by recording mitral flow by standard pulsed Doppler technique in apical four-chamber view; the following parameters were considered: early diastolic peak flow velocity (E), late diastolic peak flow velocity (A), their ratio (E/A) and E-wave deceleration time (from peak E-wave to baseline).

Tissue Doppler Measurements

A TDI of the mitral annulus movement was obtained from the apical four-chamber view. A 2.0 mm sample volume was sequentially placed at the lateral and septal annular sites. Filters and gains were adjusted to minimize background noise and maximize tissue signal. Analysis was performed for early (Ei) and late (Ai) diastolic peak velocities and their ratio (Ei/Ai). LV filling index was determined by the ratio of transmitral flow velocity to annular velocity (E/Ei).

Definition of Left Ventricular Diastolic Dysfunction

The primary criterion for defining diastolic dysfunction was an E/A ratio (ratio between transmitral peak velocities of E and A waves) <0.7 or >1.5; these cut-off values were chosen based on the results of the Cardiovascular Health Study,[19] a prospective trial carried out in an elderly population, showing that these values are predictive of subsequent CHF. A lateral TDI-derived (Ei) velocity <8 cm/sec was considered an index of altered LV relaxation.[20,21]

Statistical Analysis

Statistical analysis was performed by SAS System (version 6.12; SAS Institute Inc., Cary, NC, USA) and was mostly descriptive; values were expressed as means ± standard deviations or as percentages. Mean values have been compared by Student's t-test for independent samples and categorical data analysed by chi-square test or Fisher's exact test when appropriate. The strength of correlation between variables was tested by linear correlation analysis and multiple regression analysis. A p-value <0.05 was considered statistically significant.

Results

A total of 457 of 475 elderly individuals (254 women, 203 men) fulfilled all study criteria and constituted the study population. Major indications for echocardiographic assessment were: arterial hypertension (36%); palpitations, presyncope or syncope (22%); dyspnoea (11%); suspected valve disease or murmurs (10%); chest discomfort (7%) and other reasons (14%). As reported in table I, 75% of the study sample were hypertensive, 34% were obese and 10% had type 2 diabetes.

For the present analysis, patients were divided in two groups according to the E/A ratio: group 1 E/A ratio ≥0.7–1.5 (n = 327) and group 2 E/A ratio <0.7 (n = 119). A third group with an E/A ratio >1.5 was excluded from the study due to the small size of the sample (n = 11).

Table I. Demographic and clinical characteristics of the study population (n = 457)

Parameter	Data[a]
Age (y)	73.4 ± 5.3
Gender (men %)	44.5
Clinic BP (mmHg)	142 ± 18/80 ± 8
Heart rate (beats/min)	72 ± 10
Bodyweight (kg)	72.3 ± 13.8
Height (cm)	160.2 ± 9.1
BSA (m^2)	1.75 ± 0.19
BMI (kg/m^2)	28.1 ± 4.6
Hypertension (%)	75.7
Obesity (%)	34.2
Current smokers (%)	10.5
Type 2 diabetes mellitus (%)	10.7
LV mass (g)	207 ± 589
LV mass index ($g/height^{2.7}$)	58 ± 15
LVH (%)	64.9
E/A ratio <0.7 (%)	26.0
E/A ratio 0.7–1.5 (%)	71.5
E/A ratio >1.5 (%)	2.5

a Data are shown as mean ± SD or percentage.

A = late diastolic mitral flow; **BMI** = body mass index; **BP** = blood pressure; **BSA** = body surface area; **E** = early diastolic mitral flow; **LV** = left ventricular; **LVH** = left ventricular hypertrophy.

Table II shows the clinical characteristics of the study population according to such E/A categorization. SBP, anthropometric variables including BMI as well as prevalence of obesity, type 2 diabetes, hypertension and antihypertensive drugs were similar in both groups. Age, DBP and prevalence of current smokers were greater in group 2.

Echocardiographic parameters are depicted in table III. Mean values of LV internal diameter, interventricular wall thickness, RWT, absolute and indexed LV mass, did not significantly differ in the two groups. As expected, mitral E velocity and E/A ratio were higher in group 1 than in group 2. This was also the case for Ei, Ei/Ai and E/Ei ratio, whereas deceleration time was shorter.

When alterations in LV structure and geometry as well as in TDI relaxation pattern were analysed as categorical traits in the two groups, the following findings were observed: (i) LVH prevalence, in particular concentric LVH, was similar in both groups (40% group 1 and 42% group 2, p = not significant); and

(ii) an abnormal LV relaxation pattern was more frequently observed in group 2 (79% vs 54%, $p = 0.02$).

Reclassification of Diastolic Dysfunction According to Tissue-Doppler Criteria

As a result of the primary criterion (i.e. E/A ratio <0.7 or >1.5) 130 patients (28.4%) had diastolic dysfunction, defined as E/A ratio <0.7 or >1.5, in particular 119 (26.0%) because of E/A <0.7. When diastolic function was assessed by tissue Doppler parameters a markedly higher proportion of patients were classified as having a LV diastolic dysfunction, as in the total study population 275 patients (60.1%) were found to have an altered relaxation pattern.

Notably, 178 of 327 patients (54%) with 'normal' diastolic function according to the conventional criterion (i.e. E/A ratio 0.7–1.5) exhibited an abnormal TDI relaxation pattern. The components of this subgroup were slightly older (average difference in age was >1.2 years), had higher prevalence of LVH (76% vs 52%, $p < 0.05$), lower E/A ratio (0.80 ± 0.13 vs 0.93 ± 0.21, $p < 0.01$) and prolonged deceleration time (247 ± 63 vs 231 ± 52 msec, $p < 0.05$) when compared with individuals with normal Ei pattern.

Conversely, 25 of 119 patients (21%) with an altered E/A ratio (<0.7) showed a normal Ei velocity. These patients, compared with those with altered relaxation pattern defined by both conventional and TDI criteria, were slightly younger (average difference in age was >1.3 years), had a lower prevalence of LVH (46% vs 67%, $p < 0.05$), similar E/A ratio (0.58 ± 0.07 vs 0.56 ± 0.06) and shorter deceleration time.

Correlation Analyses

In the whole population, E/A ratio was positively associated with Ei ($r = 0.42$, $p < 0.0001$), LVEF ($r = 0.12$, $p = 0.02$) and inversely associated with deceleration time ($r = 0.20$, $p < 0.0001$), heart rate ($r = 0.19$, $p < 0.0001$), clinic DBP ($r = 0.15$, $p = 0.002$) and RWT ($r = 0.12$, $p = 0.02$). No relationship was found with age, SBP, BMI and LV mass index.

When these variables were tested in multiple regression analyses, Ei ($\beta = 0.303$, $p < 0.0001$), followed by deceleration time ($\beta = -0.217$, $p < 0.0001$), heart rate ($\beta = -0.147$, $p = 0.001$) and DBP ($\beta = -0.118$, $p = 0.008$) were the best correlates of E/A ratio.

Of note, at variance from E/A ratio, Ei was inversely and independently correlated to LV mass index ($\beta = -0.146$, $p = 0.001$).

Discussion

The principal finding of the present study is that in a cohort of elderly subjects, most of whom were hypertensive on anti-

Table II. Clinical characteristics of the study population categorized according to E/A ratio[a]

	Group 1 (E/A ratio ≥0.7–1.5; n = 327)	Group 2 (E/A ratio <0.7; n = 119)	p-Value[b]
Age (y)	72.8 ± 5.1	74.8 ± 5.7	<0.001
Gender (men %)	43.6	45.7	0.69
Clinic SBP (mmHg)	142 ± 18	142 ± 18	0.80
Clinic DBP (mmHg)	79 ± 9	81 ± 9	0.02
Heart rate (beats/min)	72 ± 10	72 ± 10	0.38
Bodyweight (kg)	72.7 ± 14.3	70.8 ± 12.2	0.39
Height (cm)	160 ± 9	160 ± 9	0.92
BSA (m^2)	1.75 ± 0.20	1.73 ± 0.18	0.32
BMI (kg/m^2)	28.3 ± 4.7	27.7 ± 4.0	0.23
Hypertension (%)	77.3	78.9	0.31
Obesity (%)	36.3	31.0	0.23
Smokers (%)	8.2	16.6	0.03
Diabetes mellitus (%)	12.8	8.8	0.29
Treatment (%)	76.2	77.3	0.79

a Data are shown as mean ± SD or percentage.

b p-Value: women vs men.

A = late diastolic mitral flow; **BMI** = body mass index; **BSA** = body surface area; **DBP** = diastolic blood pressure; **E** = early diastolic mitral flow; **SBP** = systolic blood pressure; **Smokers** = currently smoking; **Treatment** = antihypertensive treatment.

Table III. Echocardiographic findings of the study population categorized according to E/A ratio[a]

	Group 1 (E/A ratio ≥0.7–1.5; n = 327)	Group 2 (E/A ratio <0.7; n = 119)	p-Value[b]
LVIDd (mm)	47.2 ± 4.7	47.2 ± 4.9	0.37
LVIDs (mm)	28.0 ± 4.7	27.5 ± 4.8	0.03
IVSTd (mm)	10.8 ± 1.4	11.2 ± 1.5	0.03
PWTd (mm)	9.7 ± 1.2	9.6 ± 1.5	0.45
RWT	0.44 ± 0.05	0.44 ± 0.06	0.19
AR (mm)	33.6 ± 3.7	34.2 ± 3.8	0.10
LA (mm)	38.9 ± 5.4	38.6 ± 6.2	0.66
LVEF (%)	65.7 ± 4.8	64.2 ± 5.2	0.005
LVM (g)	204.9 ± 56.1	206.9 ± 56.9	0.81
LVM/h (g/m$^{2.7}$)	57.3 ± 14.7	58.3 ± 15.3	0.85
E velocity (cm/sec)	71.6 ± 17.4	53.1 ± 11.3	<0.0001
A velocity (cm/sec)	84.7 ± 64.6	95.1 ± 19.7	<0.0001
E/A ratio	0.86 ± 0.19	0.56 ± 0.06	<0.0001
DT (msec)	239.5 ± 56.9	262.5 ± 78.1	0.001
Ei velocity (cm/sec)	7.6 ± 2.5	6.5 ± 4.1	<0.0001
Ai velocity (cm/sec)	10.4 ± 3.0	11.2 ± 2.7	0.01
Ei/Ai ratio	0.73 ± 0.27	0.56 ± 021	<0.0001
E/Ei ratio	10.9 ± 3.8	9.8 ± 3.2	0.008

a Data are shown as mean ± SD or percentage.

b p-Value: women vs men.

A = late diastolic mitral flow; **Ai** = late diastolic peak velocity; **AR** = aortic root; **DT** = deceleration time; **E** = early diastolic mitral flow; **Ei** = early diastolic peak velocity; **IVSTd** = interventricular septum thickness diastole; **LA** = left atrium; **LVEF** = left ventricular ejection fraction; **LVIDd** = left ventricular internal diameter diastole; **LVIDs** = left ventricular internal diameter systole; **LVM** = left ventricular mass; **LVM** = left ventricular mass; **LVMI** = left ventricular mass index; **PWTd** = posterior wall thickness diastole; **RWT** = relative wall thickness.

hypertensive treatment, free from clinically evident CHF, from asymptomatic systolic dysfunction (LVEF <40%) or coronary artery disease, more than one-half of participants with a normal Doppler-derived index of LV diastolic function, defined according to prognostically validated partition values, presented an abnormal TDI-derived LV relaxation pattern.

This finding suggests that the assessment of transmitral E/A flow velocity ratio may not fully detect LV diastolic abnormalities; this is probably because E/A index is affected by several factors unrelated to intrinsic LV diastolic properties such as age, heart rate, pre-load and after-load.[22] In an elderly population, a normal E/A ratio (i.e. the so-called pseudo-normal pattern) may occur in the presence of a decreased LV compliance. This pattern can be differentiated from a 'true normal' pattern by taking into account other parameters such as isovolumic relaxation time, deceleration time or pulmonary vein flow; unfortunately, none of these time-consuming evaluations is routinely performed in echocardiographic practice. From our data, TDI may be regarded as an effective, easily implementable method for refining LV diastolic assessment in patients referred for routine echocardiography.

Several aspects of the present study deserve to be discussed.

At difference from previous reports, where diastolic dysfunction was defined by criteria proposed by guidelines or authoritative scientific bodies, in the present analysis we adopted the reference criteria provided by the Cardiovascular Health Study,[19] the first prospective survey performed in an elderly population, showing that diastolic dysfunction is predictive of incident CHF. In particular, E/A ratio was related to the relative risk of incident heart failure according to a U-shaped curve, namely for E/A values <0.7 the risk was 1.88 and for ratios >1.5 the risk was up to 3.50 compared with intermediate E/A values.

By using the same criteria, we found that LV diastolic abnormalities were present in about one-quarter of the sample. In the relatively healthy cohort such as the one we examined, with an average LVEF of 65%, diastolic abnormalities were mostly represented by an E/A ratio <0.7; the value >1.5 suggestive of a restrictive pattern was found in a small fraction of subjects (2.4%). Comparison of prevalence rates of diastolic dysfunction in the present study and in previous ones carried out in elderly populations is difficult due to differences in clinical characteristics of samples as well as in diagnostic criteria. Prevalence rates of diastolic dysfunction reported in recent literature ranged from 28% in the Olmsted County study including a relatively elderly population (mean age 63 years) to 45% in 331 hospitalized elderly.[23-25]

Our figures are similar to those reported (27%) in the APROS diadys (Assessment of Prevalence Observational Study of Diastolic Dysfunction) by Zanchetti et al.[26] in 2545 elderly hypertensive patients free of overt cardiovascular disease; also Zanchetti et al.'s study adopted the Cardiovascular Health Study E/A ratio thresholds as primary criterion for defining diastolic dysfunction.[19] In the APROS diadys study, patients with diastolic dysfunction more frequently presented LVH than their counterparts without it (55% vs 42%). This was not the case in our series as LVH rate was not different in patients with an E/A ratio <0.7 (64%) compared with those with an apparently normal ratio (65%). This finding supports the view that E/A ratio may be unrelated to LV mass and other factors (i.e. heart rate, BP, annular relaxation velocity) may influence mitral flow velocities in the elderly beyond ultrasonographic structural LV alterations. This observation is strengthened by univariate and multivariate analyses, which failed to demonstrate a significant correlation between E/A and LV mass index. In contrast, we found an independent, inverse relationship between annular relaxation velocity (Ei) and LV mass index in the total study population; this finding may reflect an interplay between reduced myocardial diastolic velocity and an increased cardiac mass.

A notable aspect of the study is that in our cohort differences in clinical characteristics between the two groups were small and limited to a slightly older age, higher DBP and greater prevalence of current smokers in patients with abnormal E/A ratio. This observation is in keeping with the results of the APROS diadys study[26] and suggests that alterations in conventional Doppler diastolic indexes in the elderly are largely independent from clinical and echocardiographic variables. This is not the case for alterations in TDI parameters. Indeed, patients with a reduced annular motion velocity exhibited a greater LV mass (data not shown) as well as a higher prevalence of LVH compared with their counterparts with normal TDI indexes (figure 1).

It has been shown that invasive measures of diastolic function better correlate to early diastolic tissue velocity than to early mitral flow velocity or E/A ratio.[27] A reduced Ei velocity

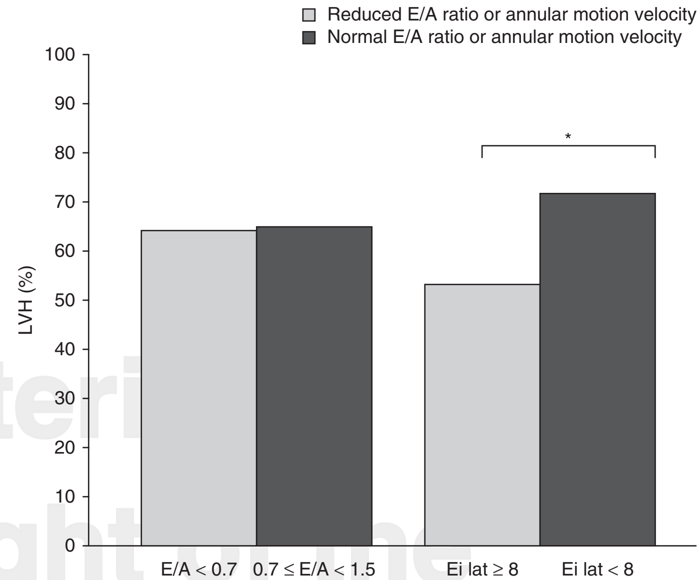

Fig. 1. Prevalence rates of left ventricular hypertrophy (LVH) in patients with reduced E/A ratio (ratio between transmitral peak velocity of E and A waves) or reduced annular motion velocity compared with their counterparts with normal E/A ratio or annular motion velocity. **Ei** = early diastolic peak velocity; **lat** = lateral annulus; * indicates Ei lat <8 vs Ei lat ≥8.

in patients with impaired LV systolic function as well as in those with hypertension and LVH has been reported to predict mortality more than clinical and echocardiographic data.[28,29] Furthermore, the E/Ei ratio reliably correlates with LV filling pressure and is an independent predictor of heart failure.[30]

Limitations of the study

As our data were obtained from a selected population of elderly Caucasians, the results may not be extended to different ethnic groups or clinical settings. Furthermore, it is worth noting that we could not access some clinical data including metabolic and renal parameters that were reported to correlate with diastolic dysfunction. Finally, our investigation was based on standard echocardiographic methods; more sophisticated methods such as strain imaging and colour flow propagation are not presently used as routine screening tools.

Conclusions

Overall, our finding indicates that evaluation of LV diastolic function by E/A ratio criteria is inaccurate and may underestimate the risk of incident heart failure in asymptomatic patients with preserved systolic function. Our data show that the association between an abnormal E/A ratio <0.7 with a normal Eì velocity identifies a subgroup of subjects with less advanced subclinical cardiac alterations compared with their counterparts with an altered relaxation pattern according to both criteria. Conversely, an abnormal TDI pattern in patients with normal E/A identifies a subgroup of subjects with a more pronounced risk for heart failure due to the higher prevalence of LVH. Thus, for a proper cardiovascular risk stratification and therapeutic-making strategy, diastolic function should be assessed in everyday clinical practice by a comprehensive Doppler methodology including both conventional and tissue Doppler measures.

Acknowledgements

No sources of funding were used to assist in the preparation of this article. The authors have no conflicts of interest that are directly relevant to the contents of this article. The authors alone are responsible for the content and writing of this article.

References

1. Koelling TM, Chen RS, Lubwama RN, et al. The expanding national burden of heart failure in the United States: the influence of heart failure in women. Am Heart J 2004; 147: 74-8
2. Fang J, Mensah GA, Croft JB, et al. Heart failure-related hospitalization in the US 1979 to 2004. J Am Coll Cardiol 2008; 52: 428-34
3. Liu L. Changes in cardiovascular hospitalization and comorbidity of heart failure in the United States: findings from the national hospital discharge surveys 1980-2006. Int J Cardiol 2011; 149: 39-45
4. Jugdutt BI. Aging and heart failure: changing demographics and implications for therapy in elderly. Heart Fail Rev 2010; 15: 401-5
5. Pagé M, Doucet M, Eisenberg MJ, et al. Temporal trends in revascularization and outcomes after acute myocardial infarction among the very elderly. CMAJ 2010; 182: 1415-20
6. Owan TE, Hodge DO, Herges RM, et al. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 2006; 355: 251-9
7. Abhayaratna WP, Marwick TH, Smith WT, et al. Characteristics of left ventricular diastolic dysfunction in the community: an echocardiographic survey. Heart 2006; 92: 1259-64
8. Cheng S, Xanthakis V, Sullivan LM, et al. Correlates of echocardiographic indices of cardiac remodeling over the adult life course: longitudinal observations from the Framingham Heart Study. Circulation 2010; 122: 570-8
9. Paulus WJ, Tschope C, Sanderson JE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. Eur Heart J 2007; 28: 2539-50
10. Bella JN, Palmieri V, Roman MJ, et al. Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults. The Strong Heart Study. Circulation 2002; 105: 1928-33
11. Temporelli PL, Giannuzzi P, Nicolosi GL, et al. Doppler-derived mitral deceleration time as a strong prognostic marker of left ventricular remodeling and survival after acute myocardial infarction. J Am Coll Cardiol 2004; 43: 1646-53
12. Wang M, Yip GWK, Wang AYM, et al. Peak early diastolic mitral annulus velocity by tissue Doppler imaging adds independent and incremental prognostic value. J Am Coll Cardiol 2003; 46: 272-7
13. Sutherland GR, Bijnens B, McDicken WN. Tissue Doppler echocardiography: historical perspective and technological considerations. Echocardiography 1999; 16: 445-53
14. Abraham TP, Dimano VL, Liang HY. Role of tissue Doppler and strain echocardiography in current clinical practice. Circulation 2007; 116: 2597-609
15. Kasner M, Westerman D, Steendijk P, et al. Utility of Doppler echocardiography and tissue Doppler imaging in the estimation of diastolic function in heart failure with normal ejection fraction: a comparative Doppler-conductance catheterization study. Circulation 2007; 116: 637-47
16. Devereux RB, Reickek N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. Circulation 1977; 55: 613-8
17. Verdecchia P, Angeli F, Gattobigio R, et al. Asymptomatic left ventricular systolic dysfunction in essential hypertension: prevalence, determinants, and prognostic value. Hypertension 2005; 45: 412-8
18. Lang RM, Bierig M, Devereux RB, et al., Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005; 18: 1440-63
19. Aurigemma GP, Gottdiener JS, Shemanski L, et al. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the Cardiovascular Health Study. J Am Coll Cardiol 2001; 37: 1042-8
20. Janardhan R, Daley WL, Naqvi TZ, et al. Rationale and design: the VALsartan In Diastolic Dysfunction (VALIDD) trial: evolving the management of diastolic dysfunction in hypertension. Am Heart J 2006; 152: 246-52
21. Ommen SR, Nishimurua RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. Circulation 2000; 102: 1788-94
22. Appleton CP, Hatle LH, Popp RL. Relation of transmitral flow velocity patterns to left ventricular diastolic function: new insights from a combined hemodynamic and Doppler echocardiographic study. J Am Coll Cardiol 1988; 12: 425-40
23. Fischer M, Baessler A, Hense HW, et al. Prevalence of left ventricular echocardiographic-based survey of a population sample. Eur Heart J 2003; 24: 320-8
24. Redfield MM, Jacobsen SJ, Burnett Jr JC, et al. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA 2003; 289: 194-202
25. Zhang Y, Safar MJ, Iaria P, et al. Prevalence and prognosis of left ventricular diastolic dysfunction in the elderly: the PROTEGER study. Am Heart J 2010; 160: 471-8
26. Zanchetti A, Cuspidi C, Comarella L, et al. Left ventricular diastolic dysfunction in elderly hypertensives: results of the APROS-diadys study. J Hypertens 2007; 25: 2158-67
27. Nagueh SF, Middleton KJ, Kopelen HA, et al. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am Coll Cardiol 1997; 30: 1527-33
28. Wang M, Yip G, Yu CM, et al. Independent and incremental prognostic value of early mitral annulus velocity in patients with impaired left ventricular systolic function. J Am Coll Cardiol 2005; 45: 272-7
29. Wang M, Yip GW, Wang AY, et al. Tissue Doppler imaging provides incremental prognostic value in patients with systemic hypertension and left ventricular hypertrophy. J Hypertens 2005; 23: 183-90
30. Liang HY, Cauduro SA, Pellikka PA, et al. Comparison of usefulness of echocardiographic Doppler variables to left ventricular end-diastolic pressure in predicting future heart failure events. Am J Cardiol 2006; 97: 866-71

Correspondence: Professor *Cesare Cuspidi*, Istituto Auxologico Italiano, Clinical Research Unit, Viale della Resistenza 23, 20036 Meda, Italy.
E-mail: cesare.cuspidi@unimib.it

