

# Long-term prognostic significance of three-dimensional echocardiographic parameters of the left ventricle and left atrium

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## Aims

We sought to investigate the long-term prognostic significance of two- and three-dimensional echocardiography.

## Methods and results

One hundred and seventy-eight consecutive outpatients underwent two-dimensional echocardiography and three-dimensional echocardiography for the assessment of LV volumes, mass, ejection fraction, and LA maximum and minimum volumes. After 45 months of follow-up, 31 patients (17%) had major cardiovascular events (death, myocardial infarctions, or stroke). From the two-dimensional echocardiography data, a significant time relationship to cardiovascular events was achieved only by LV end-systolic volume [hazard ratio (HR): 1.047; 95% confidence interval (CI): 0.994–1.083;  $P = 0.031$ ] and mass (HR: 1.038; CI: 0.993–1.082;  $P = 0.019$ ), whereas from three-dimensional echocardiography, all the examined variables: LV end-diastolic (HR: 1.014; CI: 1.003–1.025;  $P = 0.014$ ) and end-systolic volume (HR: 1.018; CI: 1.006–1.029;  $P = 0.003$ ), ejection fraction (HR: 0.032; CI: 0.002–0.565;  $P = 0.019$ ), mass (HR: 1.030; CI: 1.016–1.045;  $P < 0.001$ ), LA maximum (HR: 1.055; CI: 1.031–1.080;  $P < 0.001$ ) and minimum (HR: 1.049; CI: 1.028–1.070;  $P < 0.001$ ) volumes, were found to bear a significant relationship to cardiovascular events. By multivariate analysis, three-dimensional echocardiography derived LA minimum volume was identified as the best independent predictor of adverse cardiovascular events (HR: 1.217; CI: 1.075–1.378;  $P = 0.002$ ).

## Conclusion

Owing to a superior accuracy, three-dimensional echocardiography derived parameters and most notably LA minimum volume provide more relevant information on outpatient prognosis.

## Keywords

Atrium • Ventricle • Echocardiography • Prognosis

## Introduction

Echocardiography plays a pivotal role in the diagnosis and management of cardiovascular disease. Diagnostic and therapeutic decisions are often guided by this technique and serial assessment of cardiac size and function has become a part of clinical and instrumental evaluation of cardiology and non-cardiology patients.<sup>1–3</sup>

Although conventional two-dimensional echocardiography is an accurate technique, is of widespread availability, and is relatively low cost, it has been demonstrated to routinely underestimate cardiac volumes compared with the 'gold standard': magnetic resonance.<sup>4–6</sup>

The assessment of heart structure and function by real-time three-dimensional echocardiography has emerged as a more

accurate and reliable technique.<sup>6–8</sup> Whether its higher accuracy in assessing quantitative parameters of the left ventricle (LV) and left atrium (LA) also reflects a different prognostic impact is not known.

Our hypothesis was that routine evaluation of cardiac volumes and mass by three-dimensional echocardiography is superior than conventional two-dimensional echocardiography in predicting major adverse cardiovascular events in a long-term follow-up study.

## Methods

Study was carried out at the 'Sapienza' University Hospital of Rome. A population of 224 consecutive outpatients in sinus rhythm were

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included in the study. They were referred to the echocardiography laboratory of the Department of Cardiovascular and Respiratory Sciences of the Policlinico Umberto I from May 2003 to September 2003, for a clinically indicated echocardiogram to assess LV function. Patients with primary valve disease were excluded. All subjects agreed to participate in the study and gave their informed written consent. The study protocol was approved by the institutional review board.

All patients underwent physical examination including clinical history and electrocardiogram. Patient age, sex, height, weight, and body surface area were recorded in our database.

Cardiovascular risk factors (hypertension, diabetes, hypercholesterolaemia, and familiar history of coronary artery disease) were evaluated for all patients on the basis of well-established criteria.<sup>9–11</sup> We recorded the presence of coronary artery disease on the basis of established angina, previous myocardial infarction, significant coronary stenosis or previous percutaneous or surgical coronary artery revascularization. Pharmacological treatment was also recorded in our database.

General exclusion criteria were atrial fibrillation (seven patients), moderate or severe heart-valve disease (five patients), or very poor echocardiographic image quality (four patients).

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

## Echocardiography

Echocardiographic examination was performed by using Sonos 7500 (Philips, Andover, MA, USA) with S3 probe (2–4 MHz) for two-dimensional and Doppler and with X4 matrix-array transducer for three-dimensional examination by two expert cardiologists (S.D.C. and S.C.).

Left ventricular volumes and ejection fraction were measured in apical four- and two-chambers windows by the modified Simpson's rule; mass was measured using the Devereux formula. Left atrial maximum and minimum volumes were calculated, by two-dimensional echocardiography, respectively, in LV end-systole (just before mitral valve opening) and in LV end-diastole (just after mitral valve closure) with biplane modified Simpson's rule from the apical four- and two-chamber views.<sup>12</sup>

Transmitral early (E) and late (A) diastolic peak velocities were measured from the apical four-chamber view, with the sample volume placed at the tip of the mitral leaflets to enable calculation of the  $E/A$  ratio. Pulsed tissue-Doppler measurements of mitral annulus motion were performed in the apical four-chamber view, with a 1.5 mm sample volume placed at the lateral corner of the mitral annulus. Early ( $E_m$ ) and late ( $A_m$ ) diastolic peak velocities and their ratio were recorded. The  $E/E_m$  ratio was also calculated.

Transthoracic three-dimensional full volume acquisitions were performed from the apical four-chamber view and collected within ~7–8 s of breath holding. Three datasets were acquired for each patient and exported on a dedicated work station. Off-line analysis was performed with 4D Echo-View (version 5.2, TomTec, Unterschleissheim, Germany) by an experienced cardiologist with specific training on three-dimensional echocardiography who was blinded on patient's clinical and echocardiographic data (S.C.).

Left ventricular end-diastolic and end-systolic volumes, ejection fraction, and mass were calculated by tracing epicardial and endocardial borders through eight different rotational cutting planes obtained by the LV long axis in end-diastole and end-systole; papillary muscles were excluded from tracing. Left ventricular mass was determined multiplying the volumetric parameter by the relative density of the myocardium (1.05 g/mL).

LA maximum volume was derived by tracing the endocardium of the LA, sequentially in eight equiangular planes, taking care to exclude pulmonary veins and the LA appendage from the tracing. The mitral annulus was taken to be the atrioventricular border.

Left atrial minimum volume was measured after atrial contraction, in end diastole, soon after mitral valve closure.

## Clinical follow-up

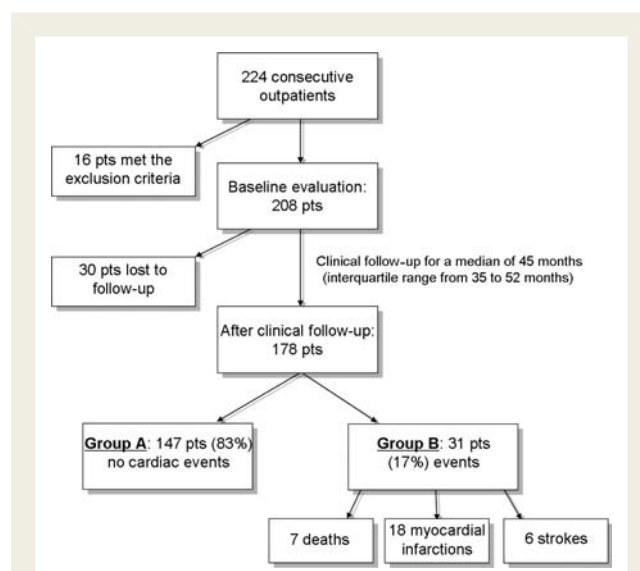
Study population was clinically observed for a median of 45 months (interquartile range from 35 to 52 months). Thirty patients (13%) were lost to follow-up. Baseline clinical and echocardiographic characteristics of these subjects were similar to those of the remaining population. Clinical data were obtained by periodical physical examinations and patients clinical records; autopsy reports and copies of death certificates were used to ascertain the cause of death and coded centrally by a nosologist according to the International Classification of Diseases, Ninth Revision.

A major cardiovascular event was considered the occurrence of a (fatal or non-fatal) myocardial infarction, stroke, or cardiovascular death.

On the basis of the follow-up data, study population was divided into two groups according to the absence (Group A) or presence (Group B) of any adverse cardiovascular event (Figure 1). All follow-up data were reviewed and inserted in our database by two trained doctors (E.C., M.L.F.).

## Statistic analysis

Continuous data are expressed as mean  $\pm$  standard deviation, categorical data are expressed as frequencies. Cardiac volumes and mass, measured by two- and three-dimensional echocardiography were indexed by body surface area. Statistical significance was set for a  $P < 0.05$ . Differences between continuous variables were assessed by Student's *t*-test for independent samples or Mann–Whitney's for



**Figure 1** Study population. Study population at baseline and after clinical follow-up; patients were divided into two subgroups according to the absence (Group A) or presence (Group B) of major cardiovascular events (death, stroke, or myocardial infarction) during clinical follow-up.

non-normal distributed variables. Differences between categorical variables were assessed by Pearson's  $\chi^2$  test.

Cox proportional hazard analysis was used considering the occurrence of adverse cardiovascular events as the dependent variable. The model included the study population's demographic characteristics and LV volumes, mass, ejection fraction, and LA volumes assessed by two-dimensional and three-dimensional echocardiography. Variables with a  $P$ -value  $\leq 0.25$  at univariate analysis were included in the final model. A stepwise method with forward variable elimination was used and corresponding hazard ratios (HR) with 95% confidence interval (CI) were calculated.

The most significant variable identified by multivariate analysis was used to stratify the study population in tertiles and Kaplan–Meier analysis was performed. Differences between curves were obtained by the log-rank test.

The association between three-dimensional measurement and  $E/E_m$  ratio was assessed by means of simple Pearson's correlation.

To assess the reproducibility of two-dimensional and three-dimensional echocardiography, measurements were repeated, in a random sample of 30 subjects, by the same investigator (intra-observer variability) and by an additional reader (inter-observer variability). Investigators were blinded from each other and patient's data. Inter- and intra-observer variability were calculated as the difference between the two measurements in terms of percentage of their mean.

Data were analysed using SPSS software v 15.0 (SPSS Inc., Chicago, IL, USA).

## Results

### Study population

Of the initial population of 224 consecutive patients, 16 (7%) met the exclusion criteria and 30 (13%) were lost to follow-up. Final study population therefore comprised 178 patients (81 males), aged  $57.9 \pm 16.3$  years (Figure 1).

The clinical indication to perform echocardiographic examination was the assessment of left ventricular function and the main clinical background included hypertension (56%), coronary heart disease (14%), heart failure (4%), diabetes (9%), or hypercholesterolaemia (17%).

After a median of 45 months (interquartile range from 35 to 52 months) of clinical follow-up, 147 patients (83%) were free from cardiovascular events (Groups A) and 31 (17%) had events (Group B): 7 deaths, 18 myocardial infarctions, and 6 strokes.

Clinical and demographic characteristics of our study population at the time of initial evaluation, including pharmacological treatment are reported in Table 1. Patients in Group B had a higher prevalence of hypertension, diabetes, hypercholesterolaemia, coronary artery disease, and positive familiar history as opposed to patients in Group A, whereas no differences were identified between groups in terms of age, sex, body surface area, and cigarette smoking.

**Table 1** Baseline characteristics of our study population

Variables	Group A	Group B	P-value
<i>n</i> (%)	147 (83%)	31 (17%)	
Age (y)	$56.8 \pm 15.7$	$65.3 \pm 11.3$	0.067
Sex, male (%)	63 (43)	18 (58)	0.095
Body surface area (m <sup>2</sup> )	$1.76 \pm 0.19$	$1.77 \pm 0.21$	0.779
Systolic blood pressure (mmHg)	$117 \pm 12$	$123 \pm 16$	0.081
Diastolic blood pressure (mmHg)	$78 \pm 9$	$84 \pm 10$	0.077
Hypertension, <i>n</i> (%)	69 (47)	24 (78)	<0.001
Smokers, <i>n</i> (%)	35 (24)	7 (24)	0.719
Diabetes, <i>n</i> (%)	16 (11)	16 (51)	<0.001
Hypercholesterolaemia, <i>n</i> (%)	56 (38)	21 (69)	<0.001
Positive familiar history, <i>n</i> (%)	47 (32)	21 (69)	<0.001
Coronary artery disease	15 (10)	11 (35)	0.042
Medications			
Beta-blockers (%)	21 (14)	9 (28)	0.541
Diuretics (%)	10 (7)	7 (21)	0.401
Calcium channel blockers (%)	7 (5)	5 (17)	0.625
ACE-inhibitors (%)	22 (15)	17 (56)	0.087
Angiotensin receptor blockers (%)	13 (9)	5 (17)	0.543
Statins (%)	16 (11)	15 (54)	0.017
Doppler			
<i>E/A</i> ratio	$1.1 \pm 0.4$	$1.1 \pm 0.8$	0.683
<i>E<sub>m</sub>/A<sub>m</sub></i> ratio	$1.16 \pm 0.57$	$0.95 \pm 0.53$	0.281
<i>E/E<sub>m</sub></i> ratio	$8.1 \pm 4.2$	$10.7 \pm 4.2$	0.001

Demographic characteristics, risk factors prevalence, pharmacological treatment, and Doppler measurements at baseline examination.

Univariate analysis showed a positive correlation with major adverse cardiovascular events for the following factors: age (HR: 1.060, CI: 1.027–1.094,  $P = 0.001$ ), sex (HR: 4.013, CI: 1.693–9.507,  $P = 0.002$ ), hypertension (HR: 19.911, CI: 2.68–147.58,  $P = 0.003$ ), diabetes (HR: 9.082, CI: 3.55–23.22,  $P = 0.001$ ), hypercholesterolaemia (HR: 7.40, CI: 2.20–24.89,  $P = 0.001$ ), positive familiar history (HR: 6.93, CI: 2.35–20.36,  $P = 0.001$ ), and coronary artery disease (HR: 1.78, CI: 0.88–3.591,  $P = 0.105$ ).

## Predictive value of two-dimensional and three-dimensional echocardiography

Table 2 shows cardiac volumes and mass assessed by two- and three-dimensional echocardiography and results from univariate analysis.

Among two-dimensional echocardiographic data, Group B had significantly higher LV end-systolic volume ( $P = 0.011$ ), mass ( $P = 0.037$ ), and lower ejection fraction ( $P = 0.010$ ) as opposed to Group A, whereas no significant differences were detected in terms of LV end-diastolic volume, LA maximum and minimum volumes. A significant time relationship to cardiovascular events was achieved only by LV end-systolic volume (HR: 1.047, CI: 0.994–1.083,  $P = 0.031$ ) and mass (HR: 1.038, CI: 0.993–1.083,  $P = 0.050$ ).

From three-dimensional echocardiographic variables, Group B had significantly higher LV end-diastolic ( $P = 0.038$ ) and end-systolic volumes ( $P = 0.004$ ), mass ( $P = 0.003$ ), LA maximum ( $P < 0.001$ ) and minimum volumes ( $P < 0.001$ ), and lower LV ejection fraction ( $P = 0.007$ ) as opposed to Group A. A significant time relationship to cardiovascular events was seen for all the examined variables: LV end-diastolic volume (HR: 1.014, CI: 1.003–1.025,  $P = 0.014$ ), end-systolic volume (HR: 1.018, CI: 1.006–1.029,  $P = 0.003$ ), ejection fraction (HR: 0.032, CI: 0.002–0.565,  $P = 0.019$ ), mass (HR: 1.030, CI: 1.016–1.045,  $P < 0.001$ ), LA maximum (HR: 1.055, CI: 1.031–1.080,  $P < 0.001$ ) and minimum (HR: 1.049, CI: 1.028–1.070,  $P < 0.001$ ) volumes.

Inter- and intra-observer variability of two-dimensional and three-dimensional measurements are reported in Table 3.

## Role of the left atrium

Among the study population's demographic variables, age, sex, hypertension, diabetes, hypercholesterolaemia, positive family history, and coronary artery disease reached statistical significance and were included in the multivariate analysis, along with LV end-diastolic and end-systolic volumes, mass, and ejection fraction, LA maximum and minimum volumes among two-dimensional and three-dimensional echocardiography variables.

Left atrial minimum volume obtained by three-dimensional echocardiography was found to be the best independent predicting parameter for cardiovascular events (HR: 1.217, 95% CI 1.075–1.378;  $P = 0.002$ ).

According to three-dimensional derived LA minimum volume, global population was divided into tertiles: in the lower tertile, the LA minimum volume ranged from 5.4 to 8.6 mL/m<sup>2</sup> (59 patients); in the middle tertile, the LA minimum volume ranged from 9.2 to 16.6 mL/m<sup>2</sup> (60 patients); in the upper tertile, the LA minimum volume ranged from 17.2 to 57.9 mL/m<sup>2</sup> (59 patients).

Kaplan–Meier analysis brought out significant differences in terms of event-free survival between tertiles of LA minimum volume ( $P = 0.03$ ; Figure 2).

Interestingly, among three-dimensional echocardiography derived variables, LA minimum volume had the best correlation with  $E/E_m$  ratio ( $r = 0.40$ ;  $P < 0.001$ ), followed by LA maximum volume ( $r = 0.29$ ;  $P < 0.001$ ) and LV mass ( $r = 0.23$ ;  $P < 0.001$ ).

## Discussion

To the best of our knowledge, this is the first study to assess the prognostic significance of three-dimensional echocardiography in a long-term follow-up study. Our study documented that cardiac volumes and function detected by three-dimensional

**Table 2** Data from two-dimensional and three-dimensional echocardiography

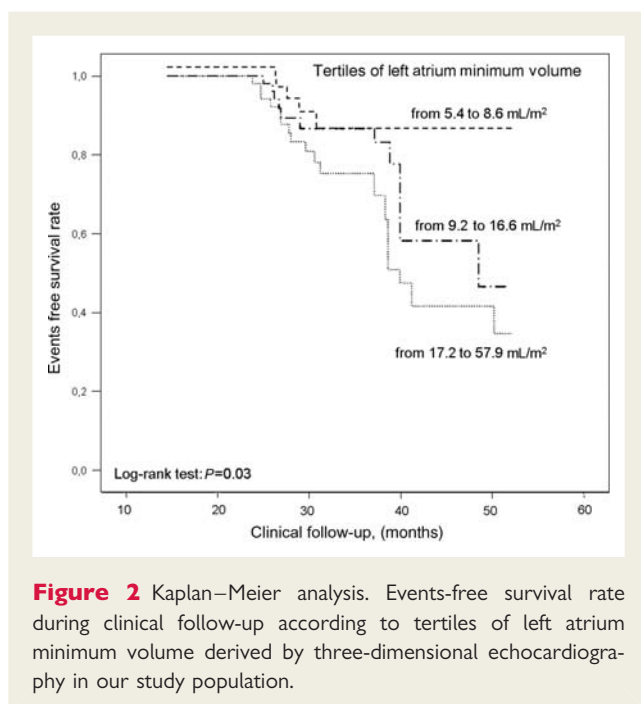
Parameter	Technique	Group A, n = 147 (83%)	Group B, n = 31 (17%)	P-value	HR	HR (95% CI)	P-value
LV end-diastolic volume (mL/m <sup>2</sup> )	2D	56.2 ± 11.2	62.3 ± 13.8	0.065	1.061	0.998–1.108	0.050
	3D	52.4 ± 28.2	63.9 ± 39.9	0.038	1.014	1.003–1.025	0.014
LV end-systolic volume (mL/m <sup>2</sup> )	2D	18.4 ± 13.6	27.7 ± 24.6	0.011	1.047	0.994–1.083	0.031
	3D	23.4 ± 15.6	34.2 ± 31.6	0.004	1.018	1.006–1.029	0.003
Ejection fraction (%)	2D	57.2 ± 5.0	53.6 ± 9.3	0.010	0.957	0.916–1.000	0.050
	3D	56.2 ± 7.4	51.3 ± 14.7	0.007	0.032	0.002–0.565	0.019
LV mass (g/m <sup>2</sup> )	2D	88.9 ± 51.7	97.5 ± 52.3	0.037	1.038	0.993–1.082	0.019
	3D	64.7 ± 23.1	78.0 ± 30.5	0.003	1.030	1.016–1.045	<0.001
LA maximum volume (mL/m <sup>2</sup> )	2D	28.1 ± 6.1	31.8 ± 7.7	0.065	1.096	0.955–1.048	0.128
	3D	30.1 ± 10.5	39.3 ± 18.0	<0.001	1.055	1.031–1.080	<0.001
LA minimum volume (mL/m <sup>2</sup> )	2D	11.9 ± 3.2	14.6 ± 7.7	0.081	1.018	0.958–1.083	0.240
	3D	13.4 ± 6.8	20.9 ± 13.6	<0.001	1.049	1.028–1.070	<0.001

Differences between events-free subjects (Group A) and patients with cardiovascular events (Group B) during follow-up in terms of baseline two-dimensional and three-dimensional echocardiography variables and results from univariate analysis.

**Table 3** Intra- and inter-observer variability

	2D echocardiography		3D echocardiography	
	Intra-observer	Inter-observer	Intra-observer	Inter-observer
LV end-diastolic volume (%)	13 ± 8	16 ± 7	6 ± 3	8 ± 4
LV end-systolic volume (%)	16 ± 8	18 ± 9	8 ± 4	9 ± 5
Ejection fraction (%)	12 ± 5	13 ± 6	4 ± 2	5 ± 2
LV mass (%)	16 ± 9	19 ± 11	8 ± 5	9 ± 6
LA maximum volume (%)	11 ± 4	15 ± 7	5 ± 2	4 ± 1
LA minimum volume (%)	13 ± 6	16 ± 8	7 ± 2	4 ± 2

Intra- and inter-observer variability assessed for two-dimensional and three-dimensional echocardiography in a random sample of 30 patients. Values are expressed as difference between measurements in percentage of their mean.



**Figure 2** Kaplan–Meier analysis. Events-free survival rate during clinical follow-up according to tertiles of left atrium minimum volume derived by three-dimensional echocardiography in our study population.

echocardiography were better correlated with the subsequent development of major adverse cardiovascular events than were the same parameters obtained by two-dimensional echocardiography.

With the exception of four patients who were initially excluded for suboptimal two-dimensional examination, three-dimensional full volume acquisitions, and off-line analysis were feasible in all the remaining study population.

### Predictive value of two-dimensional and three-dimensional echocardiography

The predictive value of two-dimensional and three-dimensional echocardiography in terms of fatal or non-fatal myocardial infarction and stroke or cardiovascular death was tested for the following variables: LV end-diastolic and end-systolic volumes, ejection fraction, mass, and LA maximum and minimum volume.

Left ventricular end-systolic volume and mass, detected by conventional two-dimensional echocardiography showed significant differences between groups at baseline examination and were able to predict events under univariate analysis. However, LV end-diastolic volume, ejection fraction, and LA volumes did not show predictive ability for death, stroke, or myocardial infarction.

On the contrary, we were able to observe very high significant differences between groups for three-dimensional based cardiac measurements. Univariate analysis showed that three-dimensional derived variables had a stronger and more significant time relationship to cardiovascular events.

Two-dimensional and Doppler echocardiography are extensively used in the current clinical practice for the diagnosis and management of cardiovascular disorders. The prognostic role of heart size and function assessment is well established and many parameters have been used in clinical and follow-up trials.<sup>13–15</sup> However, the assessment of cardiac chambers by two-dimensional echocardiography relies on the use of geometric models which assume that the geometry of the LV or the LA is the same in all the individuals. It has been demonstrated that as a result of different pathophysiological conditions, global or regional modifications of cardiac chamber shape may occur leading to worsened accuracy in volumetric measurements.<sup>16,17</sup>

To overcome these limitations, in the last decade increasing interest has been focused on the utility, accuracy, and reproducibility of real-time three-dimensional echocardiography. Its ability to accurately assess LV volumes and mass, ejection fraction, and LA volumes has been extensively reported as opposed to magnetic resonance.<sup>4–8,18,19</sup>

Volume assessment by three-dimensional echocardiography relies on the endocardial border tracing through a virtually infinite number of rotational planes, remarkably increasing its accuracy and reproducibility as demonstrated by the numerous studies.<sup>7,8,18,19</sup> In our study, increased reproducibility of three-dimensional as opposed to two-dimensional echocardiography derived parameters was confirmed by lower intra- and inter-observer variability in a random sample of 30 patients from our study population. Therefore, higher accuracy in the estimation of left ventricular and atrial volumes may be the reason for higher statistic significance obtained with three-dimensional echocardiography as

opposed to two-dimensional measurements in predicting adverse cardiovascular events.

## Role of the left atrium

Another of our study's interesting finding was the identification of LA minimum volume obtained by three-dimensional echocardiography as the best independent predictor of major adverse cardiovascular events.

Growing interest has been recently shown in the LA size and pathophysiology of its remodelling.<sup>20–22</sup> Several factors and cardiovascular disorders, most notably pressure and volume overload, affect the function and size of the LA.<sup>22–26</sup> The LA is directly exposed to LV filling pressure, and its enlargement is considered a sensitive indicator of chronic heart dysfunction and a negative prognostic factor for long-term survival in patients with stroke, congestive heart failure, and myocardial infarction.<sup>27</sup> In a previous study, we found a close correlation between the development of diastolic dysfunction and progressive increase in LA maximal volume, which may represent a cumulative effect of filling pressure over time.<sup>23</sup>

In our study population, a progressive dilation of LA minimum volume, as showed by Kaplan–Meier analysis, was associated with a higher cumulative incidence of death, stroke, or myocardial infarction during follow-up. In the lower tertile of LA minimum volume, three patients (5%) had myocardial infarction; in the middle tertile, 10 patients (17%) had events: three deaths, two strokes, six myocardial infarctions; in the upper tertile, 18 patients (30%) had events: 7 deaths, 4 strokes and 10 acute myocardial infarctions.

The occurrence and progression of diastolic dysfunction is characterized by increased myocardial stiffness, decreased LV compliance, LA enlargement, and reduced LA ejection force which is not able to overcome high LV end-diastolic filling pressure.<sup>28</sup> In this scenario, the LA progressively increases its volume. In particular, while LA maximum volume enlargement is mainly due to increased filling pressures, increased LA minimum volume also reflects the decreased ejection force of atrial pump. A Frank-Starling-like mechanism has been proposed to explain this phenomenon in patients with LA enlargement.<sup>29</sup> As a matter of fact in our study population, we found a significant positive correlation between LA volumes and  $E/E_m$  ratio which was stronger for LA minimum volume.

Finally, LA dilation has been associated with a higher incidence of embolic stroke; increased filling pressures and chamber dilation may be the cause for the onset of atrial fibrillation which increases the risk for embolic stroke.<sup>30,31</sup>

## Limitations

This study's main limitation is our patients' varying clinical background and risk profile. In attempt to overcome this limitation, multivariate analysis also included demographic variables like age, sex, hypertension, diabetes, hypercholesterolaemia, positive family history, and coronary artery disease and our results were then weighed on baseline differences among groups.

Other limitation is that our sample was relatively small and the number of patients with cardiovascular events, which composed Group B, was not high. However, the incidence of cardiovascular

events was not different compared with that observed in other follow-up studies with similar population.<sup>32,33</sup>

Furthermore, due to the study design, we were not able to assess the influence of pharmacological treatment on patients' prognosis.

Finally, diastolic function parameters, like Doppler derived  $E/A$  and  $E/E_m$  ratios, even though extremely important in patient assessment, were not included in the multivariate analysis and described only with Student's *t*-test. The reason for this lies in our study's objective, which was to compare the predictive ability of two-dimensional and three-dimensional echocardiography by considering the same parameters of the LV and the LA for both techniques.

## Conclusion

Three-dimensional echocardiography, with its superior accuracy in estimating quantitative parameters of the heart, provides important information on outpatients prognosis. LA minimum volume obtained by 3D echocardiography, an indicator of high left atrial pressure and low ejection force, could be useful in predicting major cardiovascular adverse events.

**Conflict of interest:** none declared.

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