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ORIGINAL PAPER

Left atrial expansion index is an independent predictor of diastolic dysfunction in patients with preserved left ventricular systolic function: a three dimensional echocardiography study

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Abstract In the absence of mitral valve disease left atrial (LA) volume is a marker of diastolic dysfunction and its severity. This study investigated the relationship between left ventricular (LV) end diastolic pressure (LVEDP) and LA volumes and phasic atrial functions detected by real-time full volume three-dimensional echocardiography (RT3DE), in a patient population with preserved LV systolic function. Seventy-two (39 female and 33 male; mean age 56.1 ± 9.0 years) stable patients with normal LV ejection fraction (EF) undergoing cardiac catheterization were studied. All patients underwent comprehensive echocardiographic examination just before catheterization and LVEDP was obtained. In addition to conventional echocardiographic measurements and Doppler indices; by using RT3DE LA maximum, minimum and pre-a-wave volumes were measured; LA total, passive and active emptying volumes and fractions were calculated. LV systolic function was assessed by EF and global longitudinal strain by speckle tracking. RT3DE minimum LA volume index, RT3DE active LAEF and LA expansion index (EI) were statistically significant univariate predictors of LVEDP ≥ 16 mmHg. When age and hypertension adjusted multivariate analysis was performed EI [$\beta = -1.741$, $p = 0.015$; OR 0.175; 95 % CI (0.043–0.717)] was an independent predictor of elevated LVEDP. RT3DE evaluation of LA function during entire cardiac cycle has incremental value for the diagnosis of diastolic dysfunction in patients with preserved EF. We suggest that RT3DE evaluation of LA may find clinical application in this field.

Keywords Left atrial volume · Diastolic dysfunction · Left ventricular end diastolic pressure · Real-time three-dimensional echocardiography

Introduction

Changes in left atrial (LA) size and function are associated with major adverse cardiovascular outcomes such as atrial fibrillation (AF), heart failure, stroke and death [1–3]. LA plays an integral role in cardiac performance by modulating left ventricular (LV) filling with its reservoir, conduit and contractile functions. Routine measurement of maximum LA volume index (LAV max) represents only a snapshot of LA function at a specific point of cardiac cycle. Since during diastole the LA is directly exposed to the LV cavity pressure, events during each phase of "LA phasic function" are affected by factors from both the LA and LV [4]. LA phasic functions and volumes were reported to be valuable indicators of LV diastolic function [5–7].

Measurement of LA phasic volumes using two-dimensional echocardiography (2DE) is time-consuming, and errors can arise from the geometric assumptions of biplane volume calculations and from inappropriate timing of various atrial events. However, real time three-dimensional echocardiography (RT3DE) has been introduced to overcome these limitations and has acceptable temporal resolution, which is not easily achieved with cardiac computed

The study was conducted in Cardiology Department of Kartal Kosuyolu Heart Education and Research Hospital.

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tomography (CT) or cardiac magnetic resonance imaging (CMR) [8, 9]. Besides, LA volumes derived from RT3DE show good agreement with CMR derived volumes despite the fact that RT3DE significantly underestimates LA volumes compared to CMR. [10].

To the best of our knowledge, the direct relationship between invasively measured LV end diastolic pressure (LVEDP) and RT3DE derived LA volume curves has not been reported previously. We hypothesized that, LA phasic volumes and deriving LA stroke volumes detected using RT3DE may have an incremental value for the diagnosis of diastolic dysfunction in patients with preserved LV systolic function. In the present study, predictors of elevated (≥16 mmHg) LVEDP were assessed using univariate and multivariate models in patients with preserved (≥50 %) LV ejection fraction (LVEF) undergoing cardiac catheterization.

Methods

Study population

Our patient population consisted of 72 patients with preserved LVEF who underwent elective cardiac catheterization for the diagnosis of coronary artery disease or re-evaluation after coronary intervention. Exclusion criteria were; presence of LV systolic dysfunction (LVEF < 50 %), acute coronary syndrome, renal failure, more than mild aortic and mitral valvular regurgitation or stenosis, prosthetic valve, atrial septal defect or aneurysm, AF or conduction disturbances and inappropriate echocardiographic images. 120 consecutive patients referred to catheterization from outpatient clinic were evaluated and 72 of them were included. These patients underwent comprehensive echocardiographic examination just before cardiac catheterization and measurement of LVEDP was also performed in addition to conventional coronary angiography. The study was approved by the institutional ethical committee of Kartal Kosuyolu Heart Education and Research Hospital; oral and written informed consent was obtained from all study participants.

Risk factors

Arterial hypertension was defined as blood pressure of >140/90 mmHg or in patients receiving anti-hypertensive therapy. Diabetes mellitus was defined as a fasting blood glucose level of >126 or >200 mg/dL 2 h after an oral glucose tolerance test or in patients receiving permanent medical anti-diabetic therapy. Hyperlipidaemia was defined as blood total cholesterol levels of >180 mg/dL or low density lipoprotein of >130 mg/dL or when patients were receiving permanent treatment with lipid-lowering agents. Coronary artery disease was defined as a history of myocardial infarction, coronary artery disease bypass grafting, percutaneous coronary intervention or an angiographic evidence of a significant coronary artery stenosis (≥50 %). Renal failure was defined as estimated creatinine clearance <30 ml/min/1.73 m^2 (calculated by Modification of Diet in Renal Disease formula).

Echocardiographic examination

All echocardiographic examinations were performed about half an hour before cardiac catheterization, using a commercially available system (iE 33, Philips, Bothel, USA) and recorded for offline analysis (Xcelera Workstation and QLAB; Advanced Quantification Software V.8.1, Philips).For the acquisition of 2DE images S5-1 and for RT3DE images X3 matrix array transducer was used. Individuals were instructed to hold their breath, and images were coupled with electrocardiographic recordings. Blood pressure was also recorded just before echocardiographic image acquisition. Measurements were done off-line later by a single investigator who was blinded to the clinical and catheterization data.

Two-dimensional echocardiography

M-mode measurements were performed according to the criteria of the American Society of Echocardiography. Three consecutive cycles were averaged for every parameter. LA dimension and LV end-systolic and end-diastolic diameters were measured. LVEF was estimated by biplane Simpson's rule. Inter ventricular septum, posterior wall thicknesses were measured and LV mass was calculated using the Devereux formula, subsequently it was indexed to body surface area (BSA) [11].

2DE LAV max volume was calculated at end systole of the LV using the biplane Simpson's method [11]. 2DE LAV max was calculated by dividing LA volume by BSA. 2DE minimum LA volume index (LAV min) was calculated at end diastole using the same method.

Early (E) and late (A) wave velocities, E/A ratio, E deceleration time (DT) were measured from the mitral inflow profile by placing a 1–3 mm sample volume between mitral valve leaflets using continuous wave Doppler. To acquire tissue Doppler imaging data the Nyquist limit was set at 15–20 cm/s, and minimal optimal gain was used. The myocardial systolic (S′), early diastolic (E′), and late diastolic (A′) velocities were obtained at the septal and lateral mitral annulus by placing a 5–10 mm sample volume. The E/E′ ratio was subsequently calculated for septal and lateral measurements, besides it was also averaged. Mitral regurgitation severity was semiquantified from none to severe based on integrated assessment.

LV diastolic dysfunction was classified according to previously defined standard criteria as normal (DT = 160–240 ms, E/A ratio = 0.9–1.5, $E' \geq 10$ cm/s), impaired relaxation; grade 1 (DT > 240 ms, E/A ratio < 0.9, $E' < 10$ cm/s), pseudo-normalised pattern; grade 2 (DT = 160–240 ms, E/A ratio = 0.9 to 1.5, $E' < 8$ cm/s) and restrictive pattern; grade 3 (DT < 160 ms, E/A ratio > 2.0, $E' < 5$ cm/s) [12].

Three-dimensional echocardiography

LA volume measurements were also performed by RT3DE echocardiography. Insufficient image quality for LA volume analysis was defined as inability to fully visualize the borders of atrial endocardium except atrial appendage and pulmonary vein ostia during image acquisition using apical four chamber view. Analysis time for the RT3DE dataset per patient was approximately 3 min. Apical full-volume images were acquired over four cycles. Semi-automatic LA border tracing was performed in LA systole and diastole by marking four mitral annular points (lateral, septal, inferior, anterior) and an atrial superior dome point opposite the annulus [9]. Manual corrections of the border tracings were avoided as far as possible. The LA maximal, minimal and pre a wave volumes were measured from the volume time curve automatically generated by the software (Fig. 1). All LA volume measurements were indexed to BSA. The parameters of LA size and function included in our analyses were:

- Total LA emptying volume = LA maximum volume− LA minimum volume
- Total LA emptying fraction (LAEF) = Total LA emptying volume/LA maximum volume
- Expansion index (EI) = Total LA emptying volume/ LA minimum volume
- Passive LA emptying volume = LA maximum volume- LA pre-a-wave volume

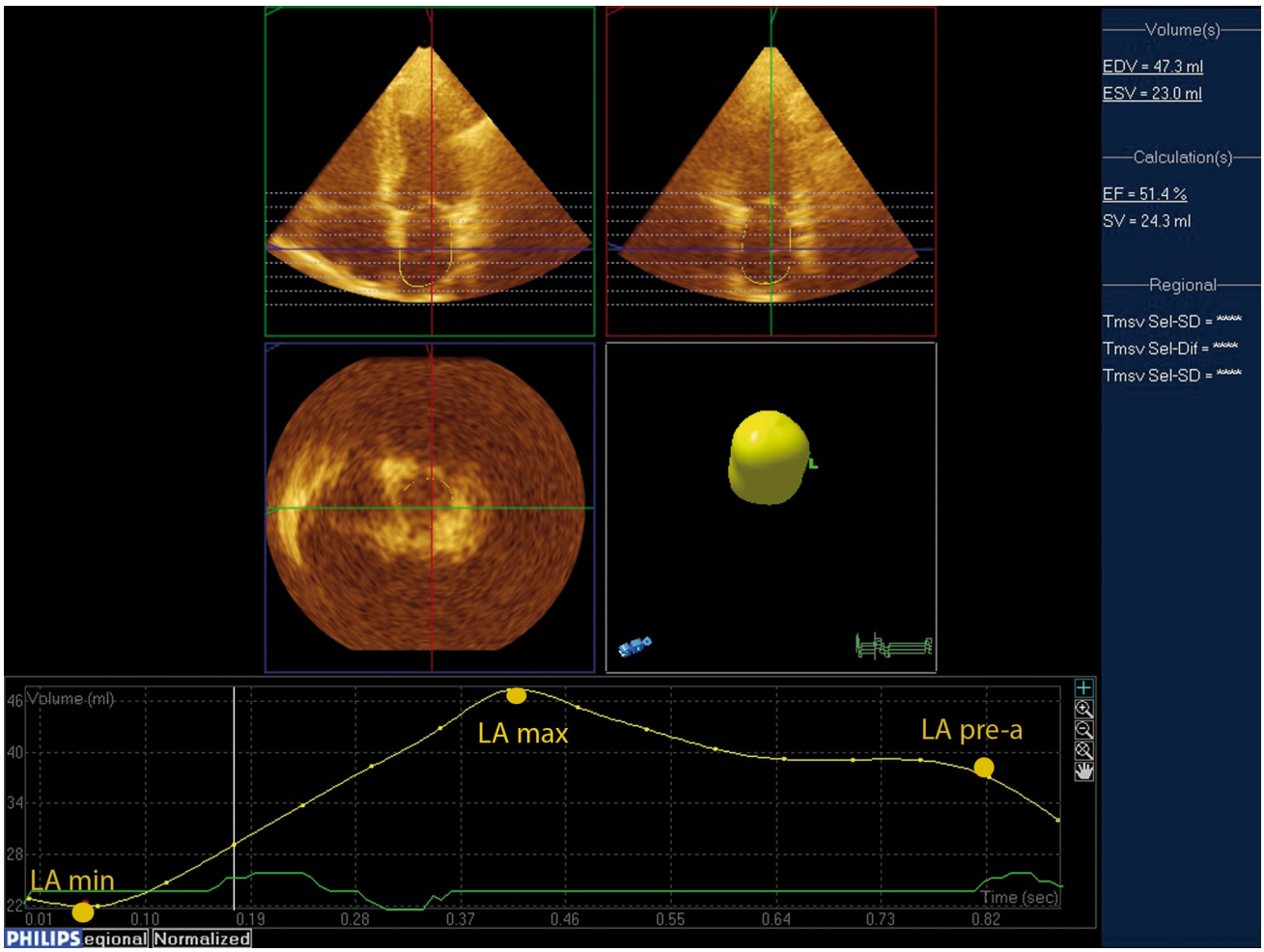

Fig. 1 An example of left atrial volume quantification by real-time 3-dimensional echocardiography. The graph shows left atrial volume variation throughout the cardiac cycle. LA max indicates, maximum left atrial volume; LA pre-a, pre-a-wave left atrial volume; LA min, minimum left atrial volume

- Passive LAEF = Passive LA emptying volume/LA maximum volume
- Conduit volume (CV) = LV stroke volume−(total LA emptying volume)
- Active LA emptying volume = LA pre-a-wave volume−LA minimum volume
- Active LAEF = Active LA emptying volume/LA pre-a-wave volume

In order to calculate RT3DE LVEF, non-foreshortened, anatomically correct apical 2- and 4-chamber views were extracted from the pyramidal dataset. On the frame in the loop corresponding to end-diastole five anatomic landmarks were manually selected and the program automatically identified the three-dimensional endocardial surface. Then, end-systole was selected by identifying the frame with the smallest LV cavity. The same process was repeated for this frame (Fig. 2). Using the time volume curve provided by the software EDV and ESV was measured and LVEF calculated [13].

Speckle tracking imaging

For speckle tracking analysis three cycles were recorded at a frame rate $\geq$ 45 fps, and were averaged for strain analysis. Aortic valve opening and closing times were measured from the LV outflow Doppler profile and were incorporated in the speckle-tracking strain profile in order to exclude post-systolic components. From three manually selected landmark points (lateral and septal mitral annulus and LV apex) in apical views, endocardial borders were automatically detected by the software. Subsequently, automatic tracking of myocardial speckles was performed throughout the whole cardiac cycle. Systolic global longitudinal strain (GLS) was calculated by averaging peak longitudinal strain of 16 segments from the apical four-chamber, three-chamber and two-chamber views.

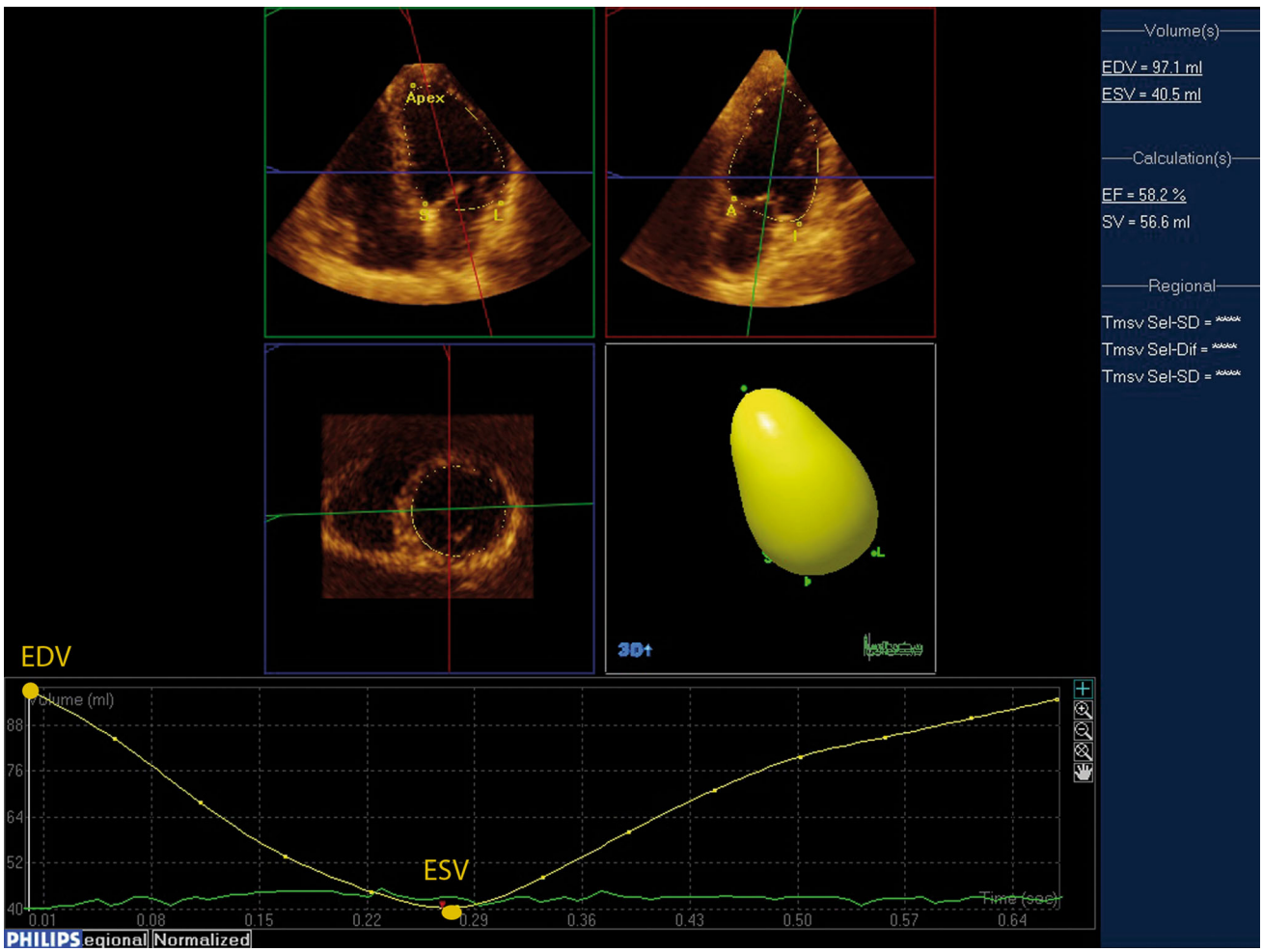

Fig. 2 An example of real-time 3-dimensional echocardiographic quantification of left ventricular volume. EDV indicates, end diastolic volume; ESV, end systolic volume; EF, ejection fraction

Cardiac catheterization

Cardiac catheterization was performed within 30 min after the echocardiographic image acquisition was completed. During cardiac catheterization, heart rate and blood pressure were continuously monitored. In all patients, a fluid-filled 6 F pigtail catheter was inserted percutaneously from the right femoral artery and advanced to the LV (retrograde left ventriculography is not a routine practice in our institution). Before the contrast agent was injected into the LV or coronary artery, the LV pressure was obtained. After 10 consecutive beats were recorded, the measurement of LVEDP was made at the peak of R-wave on electrocardiography and average of measurements made for five consecutive beats was recorded as LVEDP for the index patient. LVEDP $\geq$ 16 mmHg was considered to be increased according to the criteria proposed by the European Study Group on Diastolic Heart Failure and we used this value in our analysis [14].

Statistical analysis

Categorical variables were presented as number of cases (percentage) and mean $\pm$ SD, was used for continuous variables. Normal distribution was tested with Kolmogorov–Smirnov test. Unpaired t test was used to compare continuous variables that were normally distributed. Fisher's exact and Continuity Correction (Yate's Correction) tests were used compare categorical variables. Correlations between variables were tested by using the Pearson or Spearman correlation tests where appropriate. The baseline predictors of elevated LVEDP ($\geq$16 mmHg) that were statistically significant ($p < 0.05$) in univariate analysis (RT3DE LAV min, active LAEF and EI), were included in age and hypertension adjusted multivariate analysis (Backward stepwise model). The intraclass correlation coefficient (ICC) and its 95 % CI were used to assess intraobserver reliability for the first echocardiographer. Cronbach's α was used to evaluate internal consistency. The interobserver reliabilities were assessed by Bland & Altman plots. p value of <0.05 was considered significant for all tests. Statistical Package for the Social Sciences (SPSS version 11.0, SPSS Inc., Chicago, IL, USA) and MedCalc 12.4.0 software were used.

Results

120 consecutive patients referred for catheterization were evaluated; 8 patients were excluded for more than mild valvular disease, 6 patients for having AF; 12 patients had LV systolic dysfunction, 2 patients had conduction disturbances and 20 patients had insufficient echocardiographic images for LA analysis. Mean age of the 72 (39 female, 33 male) patients enrolled was 56.1 $\pm$ 9.0 years. There were no significant differences in heart rate, systolic and diastolic blood pressure obtained during cardiac catheterization, and echocardiographic examination (74 $\pm$ 9 bpm vs. 71 $\pm$ 8 bpm, $p = 0.074$, 155 $\pm$ 25 mm Hg vs. 153 $\pm$ 24 mm Hg, $p = 0.68$, 94 $\pm$ 15 mm Hg vs. 94 $\pm$ 15 mm Hg, $p = 1$, respectively). Patients' clinical characteristics and echocardiographic parameters grouped according to catheterization data are shown in Table 1. Mean LVEDP was 15.9 $\pm$ 4.2 mmHg and mean E/E′ averaged for lateral and septal measurements was 8.2 $\pm$ 2.0 for all patient population. 26 patients (36.1 %) had normal diastolic filling pattern, 36 (50 %) patients had impaired relaxation (Grade I) and 10 (13.9 %) patients had pseudo-normalised pattern (Grade II).

In patient group with elevated LVEDP; RT3DE LAV min was detected to be significantly increased (18 $\pm$ 6 ml/m^2 vs. 21 $\pm$ 6 ml/m^2; $p = 0.041$); however, RT3DE total LAEF (58 $\pm$ 5 % vs. 54 $\pm$ 8 %; $p = 0.022$), RT3DE active LAEF (35 $\pm$ 6 % vs. 32 $\pm$ 8 %; $p = 0.040$) and EI (1.4 $\pm$ 0.3 vs. 1.2 $\pm$ 0.4; $p = 0.011$) were reduced in this patient population.

In univariate analysis, RT3DE LAV min ($p = 0.041$), RT3DE active LAEF ($p = 0.040$) and EI ($p = 0.011$) were statistically significant predictors of LVEDP $\geq$ 16 mmHg. These predictors were included in age and hypertension adjusted multivariate analysis and only EI [$\beta = -1.741$, $p = 0.015$; OR 0.175; CI 95 % (0.043–0.717)] was determined as an independent predictor (Hosmer and Lemeshow test p: 0.752, Nagelkerke R^2: 0.120) (Table 2).

The impact of LV systolic function on LA volumetric parameters was evaluated and while GLS showed no significant correlation with LA volume parameters, RT3DE LVEF had low but significant correlation with CV (r = 0.366, $p = 0.002$), RT3DE active LAEF (r = 0.246, $p = 0.039$) and EI (r = 0.252, $p = 0.034$).

Reliability

Reliability of RT3DE LA volumes and GLS measurements were assessed in 25 randomly selected patients. Maximum LA volume, minimum LA volume, LA pre-a-wave volume and GLS were re-measured by the original reader and a second echocardiographer who was blinded to the first measures. ICCs for intra-observer reliability were significant for RT3DE maximum LA volume 0.88 (0.74–0.94); pre-a-wave LA volume 0.94 (0.88–0.97); minimum LA volume 0.95 (0.90–0.98), and GLS 0.90 (0.79–0.95). Cronbach's alpha coefficients were 0.93; 0.97; 0.97; 0.95, respectively. The inter-observer reliabilities for the same measurements were assessed by Bland & Altman plots and they revealed good agreement between measurements performed by two echocardiographers (Fig. 3).

Table 1 Baseline clinical, echocardiographic and laboratory characteristics of the study population

Variables	LVEDP < 16 mmHg (n = 42)	LVEDP ≥ 16 mmHg (n = 30)	*p* value
Clinical characteristics			
Age (years)	56.4 ± 8.2	55.7 ± 10.1	NS
Men [n (%)]	25 (59 %)	13 (43 %)	NS
Body mass index (kg/m^2)	28.3 ± 4.0	29.2 ± 4.4	NS
Hypertension [n (%)]	19 (45 %)	16 (53 %)	NS
Diabetes [n (%)]	12 (28 %)	8 (26 %)	NS
Hypercholesterolemia [n (%)]	22 (52 %)	20 (66 %)	NS
Coronary artery disease [n (%)]	29 (69 %)	13 (43 %)	NS
Smoking [n (%)]	27 (64 %)	15 (50 %)	NS
e GFR (ml/min/1.73 m^2)	115 ± 25	120 ± 34	NS
Heart rate (bpm)	74.2 ± 8.6	74.6 ± 11.4	NS
Systolic blood pressure (mmHg)	146 ± 22	163 ± 23	0.004*
Diastolic blood pressure (mmHg)	89 ± 13	100 ± 16	0.002*
LV and LA structure and function			
LVEDD (mm)	47 ± 5	48 ± 5	NS
LVESD (mm)	31 ± 6	32 ± 5	NS
LA (mm)	34 ± 4	35 ± 4	NS
LV 2D ejection fraction (%)	62 ± 7	59 ± 6	0.078
LV 3D ejection fraction (%)	60 ± 5	61 ± 8	NS
LV mass (g/m^2)	91 ± 21	97 ± 28	NS
GLS (%)	−15.1 ± 1.9	−14.9 ± 2.04	NS
2D LAV max, (ml/m^2)	26.3 ± 6.9	25.6 ± 7.6	NS
2D LAV max, (ml/m^2)	11.6 ± 4.8	10.6 ± 4.2	NS
2D LA total emptying fraction (%)	56 ± 10	58 ± 8	NS
3D LAV max, (ml/m^2)	44 ± 12	44 ± 12	NS
3D LAV pre-a (ml/m^2)	29 ± 9	31 ± 9	NS
3D LAV min, (ml/m^2)	18 ± 6	21 ± 6	0.041*
3D LA total emptying fraction (%)	58 ± 5	54 ± 8	0.022*
3D LA passive emptying fraction (%)	34 ± 6	31 ± 7	0.072
3D LA active emptying fraction (%)	35 ± 6	32 ± 8	0.040*
3D LA expansion index	1.4 ± 0.3	1.2 ± 0.4	0.011*
3D LA conduit volume, (ml)	27 ± 9	31 ± 15	NS
LV diastolic function			
E/A ratio	0.9 ± 0.2	0.8 ± 0.3	NS
E/E′ septal	9.7 ± 2.8	9.1 ± 2.2	NS
E/E′ lateral	7.4 ± 2.2	7.5 ± 1.5	NS
E/E′ average	8.3 ± 2.2	8.3 ± 2.3	NS

* $p < 0.05$

A mitral inflow late diastolic velocity, *E* mitral inflow early diastolic velocity, *E′* tissue Doppler early diastolic mitral annular velocity, *eGFR* estimated glomerular filtration ratio, *GLS* global longitudinal strain, *LA* left atrium, *LAV max* left atrial maximum volume index, *LAV pre-a* left atrial pre-a-wave volume index, *LAV min* left atrial minimum volume index, *LV* left ventricle, *LVEDD* left ventricular end diastolic diameter, *LVESD* left ventricular end systolic diameter, *3D* three-dimensional, *2D* two-dimensional

Discussion

LA size and function is increasingly used as a marker of diastolic dysfunction, therefore enlargement and changes in atrial function due to diastolic function need to be carefully quantified [3, 6, 7]. RT3DE, with its temporal resolution is able to detect phasic atrial volume changes accurately and as far as we are concerned, this is the first study reporting the relationship between invasively measured LVEDP and RT3DE LA volume parameters [10]. Our study demonstrated that in patients with preserved LVEF, EI detected with RT3DE is an age and hypertension adjusted independent predictor of elevated LV filling pressures. Interestingly, RT3DE LAV min was a univariate predictor of diastolic dysfunction in this patient population while routinely used 2DE LAV max was not. Additionally, RT3DE active LAEF was also a univarite predictor of high filling pressures.

LA volume measurements by RT3DE correlate closely with those obtained on CT and on CMR, showing a better

Table 2 Age and hypertension adjusted multivariate logistic regression analysis for independent predictors of elevated left ventricular end diastolic pressure

	OR	*B*	*p* value	CI 95 %
3D LAV min	0.996	−0.004	0.963	0.832–1.192
3D active LAEF	0.128	−2.059	0.645	0.000–820.81
Expansion index	0.175	−1.7	0.015*	0.043–0.71
Hypertension	1.385	0.325	0.53	0.513–3.736
Age	0.980	−0.020	0.46	0.928–1.035

* $p < 0.05$

LAEF left atrial emptying fraction, *LAV min* left atrial minimum volume index, *3D* 3-dimensional

accuracy than 2DE methods [8, 9, 15, 16].In particular, 3DE reconstruction overcomes 2DE limitations, avoiding geometric assumptions for LA volume evaluation [15].

Diastolic dysfunction has a major role in producing signs and symptoms in patients presenting with heart failure [17]. Heart failure with preserved EF currently accounts for ≥50 % of the general heart failure population [18]. However, there are currently no unified criteria specified in the major guidelines for diagnosing diastolic dysfunction in patients with preserved EF. The value of the E/E′ ratio as a reliable estimate of LV filling pressures was endorsed by European and American consensus statements on diastolic HF and diastolic LV dysfunction [12, 14]. However, the existence of a "gray zone" between 8 and 13 represents a limitation for the application of E/E' ratio in clinical practice [19]. This may be particularly relevant among patients with normal EF, for whom the possibility of correctly estimating LV filling pressures is of key importance for the diagnosis of heart failure with preserved EF. Mean E/E' of our study population was in the "gray zone" and patients enrolled had many risk factors for diastolic dysfunction which is the usual case in clinical setting when an estimate of LV filling pressures is needed. Thus, we suggest that especially in this patient population which was represented in our study use of LA phasic functions and volumes may find a clinical application.

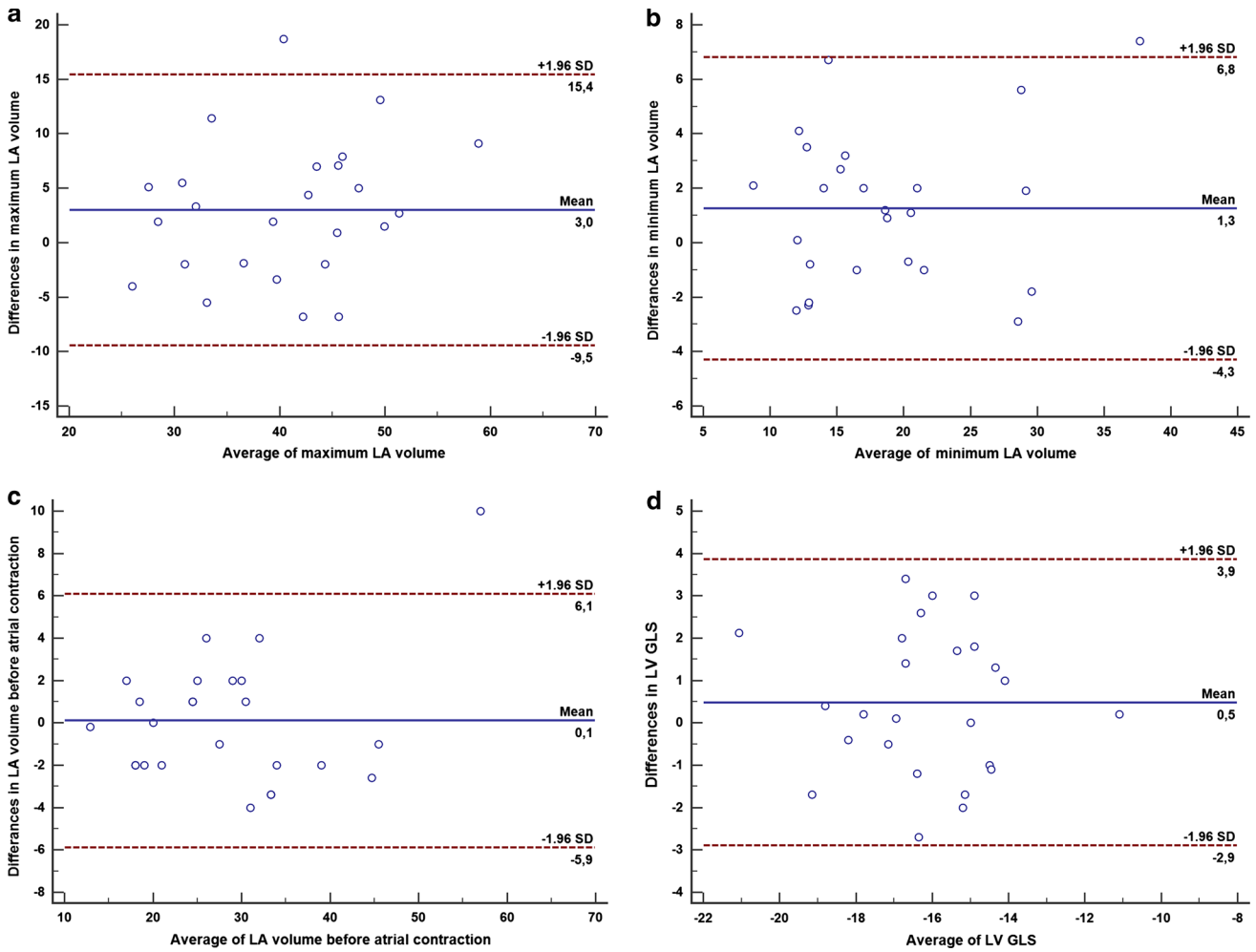

Fig. 3 Bland–Altman plots for inter-observer variability of maximum left atrial (LA) volume, minimum LA volume, LA volume before atrial contraction and left ventricular global longitudinal peak systolic strain (LV GLS)

Recently LA volume and diastolic function has been investigated in several studies, but only few of them included the measurement of LAV min and EI was rarely reported. Theoretical considerations and a growing literature suggest that perhaps LAV min should also be a parameter of interest [7, 20–23]. In our study, LA EI which is more closely related to LAV min was an independent predictor of elevated LVEDP. In parallel to our findings recently, Posina et al. reported that increased LAV min and decreased total LAEF measured by CMR were most closely associated with elevated LVEDP in ROC analysis [24]. However, they did not report EI in their study and LVEDP $\geq$ 12 mmHg was accepted as elevated. Russo et al. [20] also, suggested that RT3DE LAV min better correlated with LV diastolic function than LAV max. But in contrary to our findings in their study GLS was a significant predictor of maximum LA volume. We think that this difference resulted from the inclusion of patients with systolic dysfunction and the use of E/E' as a surrogate of LV filling pressure in their study. In a study by Appleton et al. [7], LAV min was related to the mean pulmonary wedge pressure in patients undergoing cardiac catheterization. Again in an invasive study by Hsiao et al. [6], EI better identified LV filling pressures than total LAEF and E/E′. Boyd et al. [5], also reported that impaired LV relaxation was associated with a shift in LA phasic volumes and EI decreased with increasing age.

LA function and volumes basically include three phasic parts known as a reservoir, conduit, and booster pump. All of these phasic volumetric changes modulate LV filling [3].The relationship between LAV min and diastolic function appears to be more direct, as in end diastole the mitral valve is open and the LA is directly exposed to the LV pressure. EI which is closely related to the LAV min, and total LAEF represent LA reservoir function that is determined by LA active relaxation and LA compliance as well as LV systolic function with apical displacement of mitral annulus [25]. The effect of LV systolic function was neutralised in our study by including patients only with normal EF. Besides, active LAEF which was also reduced in our patients with elevated LVEDP is determined by LA contractility and LV diastolic compliance [25]. An increase in interstitial atrial fibrosis caused by hypertension, diabetes and aging, similar to that observed in the LV, may contribute to LA noncompliance [26, 27]. Altered LA compliance prevents further compensatory augmentation of active atrial emptying and atrial enlargement occurs when the LA stroke volume has to increase beyond that of the Frank-Starling relationship. Atrial enlargement likely occurs as a consequence of long-term adaptation to LV diastolic dysfunction and reduced atrial compliance, as a consequence of interstitial fibrosis at more advanced stages of diastolic dysfunction [27]. Since EI represents combination of active atrial relaxation and compliance it is expected for EI to be an early indicator of atrial remodelling caused by elevated LVEDP. Thus we suggest that, LA phasic parameters and especially EI are more delicate measures for evaluating early stages diastolic dysfunction than LAV max.

The main limitation of our study was the small size of the study population. Besides, LVEDP was obtained using fluid-filled pigtail catheters. Although micromanometer-tipped catheters would have been ideal our method used to measure LVEDP is standard in clinical setting and well validated. Several studies show that echocardiography systematically tends to underestimate LA volumes when compared to MRI and LA appendix volume was not included in our study [13]. Our study could only detect cross-sectional relationships between the studied variables; long-term outcome studies are needed. Finally, the structural and functional changes of the LA express the chronicity of exposure to abnormal filling pressures, however LVEDP is an instantaneous measure better suited for monitoring the hemodynamic status in short term.

In conclusion, in patients with preserved LVEF, EI detected with RT3DE is an age and hypertension adjusted independent predictor of elevated LV filling pressures. We suggest that RT3DE LA phasic functions and volumes have incremental value for the diagnosis of diastolic dysfunction over conventional 2DE LAV max.

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Conflict of interest The authors report no conflict of interest. The authors alone are responsible for the content and writing of paper.

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