

Left atrial phasic echocardiographic functional analysis in relation to diastolic left ventricular hemodynamic parameters acquired during right heart catheterization

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ABSTRACT

Introduction: Doppler echocardiography has become the leading non-invasive tool for hemodynamic screening and follow-up in various clinical situations. Our objective was to assess whether left atrium (LA) functional echocardiographic parameters correlate with hemodynamic left ventricle (LV) filling parameters measured during right heart catheterization (RHC) in various disease states.

Methods: Echocardiographic examinations of 71 consecutive patients that had RHC within 24 h were studied retrospectively using LA/LV feature tracking analysis. Echocardiographic and myocardial mechanics characteristics were then correlated with the RHC findings.

Results: The best correlation were demonstrated between the *trans*-tricuspid gradient in the echocardiogram and the right ventricle (RV) systolic pressure in the RHC ($R^2 = 0.41$, $p < 0.0001$). Mitral E/E' annular velocity ratio did not correlate with capillary wedge pressure (CWP) while E velocity correlated significantly with CWP ($R^2 = 0.29$, $p = 0.0007$). Among 38 patients in sinus rhythm, echocardiographic diastolic dysfunction strongly correlated with elevated LA pressure in RHC ($CWP \geq 12$ mmHg, $p = 0.001$), with 96% sensitivity and 80% specificity. LA minimal volume index (LAVmin-i) as measured by echocardiogram was significantly correlated with elevated LA pressure in RHC ($p = 0.04$, criterion ≥ 27 ml) regardless of rhythm.

Conclusions: In patients with sinus rhythm, diastolic dysfunction was found to be sensitive and specific for elevated $CWP \geq 12$ mmHg at RHC. In all patients regardless of rhythm, LAVmin-i was found to correlate best with elevated LA pressure at RHC. This may suggest a new tool for assessment of diastolic dysfunction in all subjects.

1. Introduction

Echocardiography has become the leading non-invasive tool for hemodynamic screening and follow up of patients with heart failure (HF) symptoms in cardiovascular and pulmonary disorders [1]. Two-dimensional echocardiography provides structural and functional (mainly systolic) information and Doppler echocardiography provides estimates of pressure gradients, assessment of valvular function and determination of left ventricular (LV) diastolic function. Still, Right

heart catheterization (RHC) is considered the gold standard for assessment of cardiovascular hemodynamic parameters. Current guidelines require RHC in patients with dyspnea and echocardiographically measured pulmonary artery hypertension (PHTN) to elucidate etiology and to suggest therapeutic measures.

Echocardiographic assessment of left ventricular (LV) diastolic function is an integral part of the routine evaluation of patients presenting with symptoms of dyspnea or HF [2], and is crucial part of the diagnosis of heart failure with preserved ejection fraction. LV diastolic

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dysfunction is usually the result of impaired LV relaxation and increased LV chamber stiffness, increasing cardiac filling pressures [2]. Its diagnosis and grading of severity by echocardiography involves the assessment of multiple Doppler (mitral inflow and tricuspid regurgitation velocities) tissue doppler (mitral annular velocities) parameters, as well as the measurement of left atrial (LA) maximal (end systolic) volume indexed to body surface area (LAVmax-i). Different ratios between measurement have been suggested to estimate left atrial pressure [2,3]. Recent American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging [EACVI] [3] recommendations approached the diagnosis of diastolic dysfunction using a scoring system. Although better than previous suggestions – they still leave a fair percentage of patients with an undermined diagnosis, especially in patients that are not in sinus rhythm.

LA emptying dynamics represent LV filling. Assessment of LA function and phasic volumes (end diastolic, end systolic and pre-A volumes) – may enhance our ability to diagnose LV diastolic dysfunction. Contemporary myocardial mechanics, using echocardiographic 2D speckle tracking, allows for the evaluation of LA strain and volume changes throughout the cardiac cycle [5,6].

Our aim in this study was two-fold. First, we wished to validate common echocardiographic parameters that are assessed during RHC Contemporary myocardial mechanics, using echocardiographic 2D speckle tracking, allows for the evaluation of LA strain and volume changes throughout the cardiac cycle [4], especially ones involved in diastolic function assessment, and assess the accuracy of the latest guidelines in diagnosing diastolic dysfunction. Secondly, we wished to assess the added value of LA mechanics and volumetrics to the diagnosis of diastolic dysfunction, regardless of heart rhythm.

2. Material and methods

This single center retrospective cohort study was approved by the ethics committee and the Institutional Research Ethics Board (IRB) at the Baruch Padeh Medical Center, Poriya, Israel (0099-14-POR), and was conformed to the standards established by the Declaration of Helsinki.

2.1. Patients selection

Patients included in this study had RHC at the Baruch Padeh Medical Center for a wide spectrum of cardiac and pulmonary diseases and had a full echocardiography up to 24 h before or after RHC. Patients with low echocardiography quality that could not be submitted to 2D strain analysis were excluded from the study.

2.2. Data collection

Database was queried to identify consecutive patients that had RHC and same admission echocardiography, and the study cohort was defined. Conventional echocardiographic reports were retrieved and 4, 2 and 3 chamber echocardiography Digital Imaging and Communications in Medicine (DICOM) clips were downloaded for 2D strain analysis that was examined by an operator blinded to clinical and RHC findings.

2.3. Right heart catheterization (RHC)

RHC was performed per the clinical indications assessed by the attending cardiologist, for the evaluation of left and right heart disease and for pulmonary disease. Left heart parameters included capillary wedge pressure (CWP) measured at the end of expiration, LV end diastolic pressure (LVEDP), LV cardiac output (measured by the thermodilution and estimated Fick methods) and systemic vascular resistance (SVR). Right heart parameters included right atrial pressure (RAP), RV systolic and diastolic pressures, pulmonary arterial pressures (PAP, peak and mean) and pulmonary vascular resistance (PVR). All pressures were

measured using fluid filled catheters.

2.4. Two-dimensional (2D) doppler echocardiographic measurements

2D Doppler echocardiography was performed 24 h prior or 24-hours post RHC. Studies were carried out using various machine systems (GE Vivid 9, Vivid I, Siemens Acuson SC2000 prime and Philips Epic 7), according to the ASE/EACVI guidelines [2] by experienced sonographers. For interpretations of echocardiographs, blinding was necessary in cases when RHC preceded.

2.5. Speckle-tracking echocardiographic (STE) measurements

Myocardial mechanics were analyzed retrospectively from archived studies by a principal analyst. All analyses were reviewed and approved an echocardiographic experienced in strain methodology. Both observers were blinded to clinical, echocardiographic and RHC information at the time of analysis. LA and LV longitudinal and volumetric analyses were performed offline using dedicated software (eSie VVI, us v.3.0.1.45b.140211, Siemens Medical System, Mountain View, CA, USA). Apical views (4, 2 and 3 chambers) were analyzed for LV myocardial mechanics variables including strain (% shortening), global longitudinal strain (GLS), defined as the average strain at the aortic valve closure. Left atrial myocardial mechanics and phasic volumes assessed were: LA reservoir strain, LA maximal volume (Vmax), LA minimum volume (Vmin), total emptying volume = Vmax – Vmin, LA total emptying volume (LA TEV) = LA Vmax – Vmin. All atrial phasic volumes were indexed for patients' particular body surface areas (BSA, m²) to calculate the left atrial (LA) maximal (end systolic) volume indexed to body surface area (LAVmax-i), LA Vmin-i, and left atrial (LA) minimal volume indexed to body surface area (LAVmin-i) and LA Total emptying volume index (LA TEV-i), all in ml/m².

2.6. Statistical analysis

All data were presented as a mean ± standard deviation for continuous variables and as percentage for categorical variables. All analyses were performed using MedCalc Statistical Software version 18.11 (MedCalc Software bvba, Ostend, Belgium).

Minimal sample size estimation for parameters, estimated by echocardiogram and measured at RHC using Bland-Altman method, was 40 cases assuming 0 difference of means, an 0.6 expected standard deviation of the differences and a maximum allowed difference of 2 (0 ± 1.96). For LA volumes and function, correlates with RHC indicators of diastolic dysfunction (i.e., elevated LVEDP or PCWP) were evaluated.

For the assessment of different LA volume and functional parameters as indicators of diastolic dysfunction, a minimum of 35 cases were required. This was assessed using the area under the receiver operator characteristic (ROC) curve with a desired area under ROC of at least 0.85.

2.7. General statistical methods applied

At the first stage, echocardiographic estimates were assessed for all RHC-measured parameters as a validation. Secondly, LV and LA volumetric/mechanic parameters were assessed for the association with RHC findings. Echocardiographic and RHC parameters were compared using the Bland-Altman analysis. A ROC curve was used to associate and estimate specificity and sensitivity. Categorical parameters were compared using Fisher's test. All statistical tests were two-sided, with a significance level of $p < 0.05$.

Table 1
Patient characteristics.

Patient's characteristics	
Age (years)	64 ± 15
BMI	30 ± 6
BSA (m ²)	1.9 ± 0.2
Sex (male)	44, (62%)
Smoker	17, (24%)
Hypertension (n, %)	52, (73%)
Dyslipidemia (n, %)	42, (59%)
Diabetes mellitus (n, %)	33, (46%)
Family history of CAD (n, %)	13, (18%)
Chronic renal failure (n, %)	19, (27%)
Coronary artery disease (n, %)	19, (27%)
Congestive heart failure (n, %)	49, (69%)
Chest pain (n, %)	7, (10%)
Rhythm	
Sinus (n, %)	49, (69%)
Atrial fibrillation (n, %)	16, (23%)
RV pacing (n, %)	2, (3%)
Biventricular pacing (n, %)	4, (6%)
BNP, median (IQR) (pg/mL)	610 (211,1321)

BMI = Body Mass Index; BNP = Brain Natriuretic peptide; BSA = Body Surface Area; RV = Right Ventricle.

Table 2
Conventional 2D Doppler echocardiographic characteristics and Left ventricular and left atrial myocardial mechanics (Strain).

Echocardiographic characteristics	
LV ejection fraction (%)	47 ± 19
LV End diastolic dimension (mm)	59 ± 12
LV End systolic dimension (mm)	45 ± 15
LV mass index (gr/m ²)	128 ± 44
LA systolic dimension	47 ± 8
Mitral valve regurgitation grade > 2	33 (46%)
Tricuspid valve regurgitation grade > 2	36 (50%)
Right ventricular systolic pressure (mmHg)	54 ± 17
Right atrial pressure (mmHg)	12 ± 5
Mitral E wave velocity (cm/s)	100 ± 39
Mitral E wave deceleration time (ms)	179 ± 57
Mitral E to A velocities ratio	1.8 ± 1
Average mitral E to E' velocity ratio	11 ± 5
Left atrial pressure (Nagueh's equation) (mmHg)	15 ± 7
Diastolic dysfunction in patient in sinus rhythm (ASE 2016)	No DDFx 13 DDFx 27 Undetermined 2
Left ventricle	
LV global longitudinal strain (%)	-12 ± 5.4
LV Ejection fraction (%)	41 ± 15
LV Cardiac Output (L/min)	4.4 ± 1.8
LV Systolic strain rate (%/s)	-4.5 ± 0.5
LV Diastolic strain rate (%/s)	1.3 ± 0.6
Diastolic to systolic strain rate ratio	1.1 ± 0.2
Left atrium	
LA Reservoir longitudinal strain	17.3 ± 11.8
LA Total emptying fraction (LAEF)	39 ± 17
LA End Systolic volume index, LAVmax-i, ml/m ²	53.5 ± 27.7
LA End Diastolic volume index, LAVmin-i, ml/m ²	35.2 ± 25.8
LA Total emptying volume index, TEVi, ml/m ²	18 ± 8
LA active strain (%)	-5.5 ± 7.5
LA Passive strain (%)	-11.8 ± 10

LV = Left Ventricle; LA = Left Atrium; LAV = Left Atrial Volume ASE = American Society of Echocardiography; DDFx = Diastolic Dysfunction.

Table 3
Right heart catheterization measurements.

Parameter	Average
Blood pressure – systolic (mmHg)	130 ± 26
Blood pressure – diastolic (mmHg)	77 ± 15
Peak Pulmonary arterial pressure (mmHg)	59 ± 19
Mean Pulmonary arterial pressure (mmHg)	38 ± 11
Mean Capillary wedge pressure (mmHg)	22 ± 9
Right atrial pressure (mmHg)	13 ± 6
Cardiac output (Fick) (l/min)	4.6 ± 2.0
Cardiac output (Thermodilution) (l/min)	5.0 ± 1.8
Diastolic pulmonary pressure gradient (mmHg)	5.3 ± 11.1
RV stroke work index (g*m/m ² /beat)	866 ± 444
Pulmonary vascular resistance (Woods)	4.7 ± 3.4
Pulmonary compliance (ml/mmHg)	1.3 ± 0.8
Systemic vascular resistance (Woods)	708 ± 806
RV systolic pressure (mmHg)	57 ± 18

RV = Right Ventricle.

3. Results

3.1. Patient clinical characteristics

The clinical characteristics of the study population are summarized in [Table 1](#).

A total of 71 consecutive patients were included in this study. All patients underwent RHC and echocardiography for the evaluation of dyspnea or HF.

The majority of patients had systemic hypertension and dyslipidemia. Nearly half had diabetes mellitus. Sixty-nine percent of the patients presented with congestive heart failure symptoms, and were mostly in sinus rhythm (69%), 23% were in atrial fibrillation and 9% were electronically paced ([Table 1](#)).

3.2. 2D Doppler conventional echocardiography

Echocardiographic findings are shown in [Table 2](#). These also represent the wide variety etiologies of patients referred for RHC. The average measurements of all parameters were pathologic, with a large range from normal to severely abnormal values. The left ventricle was large and hypertrophic with reduced systolic function and left atria were large. Mitral and tricuspid valve regurgitations were at least moderate in half of patients ([Table 2](#)).

3.3. Speckle tracking echocardiography (STE)

Myocardial mechanics through non-invasive evaluation of myocardial deformation (i.e., strain) was measured by a single observer using speckle tracking echocardiography (STE). Inter observer agreement in strain parameters was assessed after excessive training of the principal analyst in 17 cases. Supplemental Table 1 demonstrates the interclass correlation coefficients (ICCs) for strain parameters, validating the measurements for further analysis. Left ventricular and left atrial volumes were calculated using Simpson's biplane method which was applied automatically on all cardiac frames in cycles acquired by STE. As seen in [Table 2](#), GLS values were low (-12 ± 5.4%) compared to accepted normal values (ranging between -18% to -22%). Average ejection fraction (EF) was reduced at the mild to moderate range, while normal range cardiac output was maintained. Left atrial function was abnormal, demonstrated by low longitudinal reservoir strain of 17.3% (normal values range between 25 and 30), normal volumetric LA EF, yet showing reduced passive and active emptying strains (-11.8 ± 10% and -5.5 ± 7.5%, respectively). A moderate atrial enlargement, demonstrated by LAVmax-i of 53.5 ± 27.7 ml/m² was recorded.

Table 4
Conventional echocardiography correlations with right heart catheterization parameters.

Echo parameter	RHC parameter	R ²	p-value	Equation
Tricuspid regurgitation pressure gradient	RV systolic pressure	0.41	<0.0001	y = 27 + 0.72 x
RV systolic pressure	RV systolic pressure	0.38	<0.0001	y = 22.4 + 0.65 x
Right atrial pressure	Right atrial pressure	0.008	0.48	
Pulmonary compliance	Pulmonary compliance	0.22	<0.0001	y = 0.85 + 0.31 x
Mitral E to E' ratio	Capillary wedge pressure	0.06	0.18	y = 8.7 + 0.14 x
Mitral E	Capillary wedge pressure	0.29	0.0007	y = 0.46 + 0.024 x
Cardiac index (strain software, biplane)	Cardiac index, Thermodilution	0.17	0.0011	y = 3.19 + 0.4 x

RV = Right Ventricle; RHC = Right Heart Catheterization.

3.4. RHC measurements

Pulmonary hypertension (PHTN) was detected in 63 patients who underwent RHC, 52 of which had significant left heart pathologies. Primary idiopathic PHTN was noticed in 9 patients, and 8 patients did not have PHTN at all. Table 3 presents a wide range of average (38 ± 11 mmHg) and peak (59 ± 19 mmHg) pulmonary pressures which characterize a broad population spectrum. Variable CWP values and normal values of cardiac output were detected. Few patients had high PVR values (4.7 ± 3.4) (Table 3).

3.5. Validation of conventional echocardiographic parameters measured during RHC

Data correlations between echocardiographic and RHC parameters are presented in Table 4.

The best correlation was demonstrated between the echocardiographic parameter TR pressure gradient (calculated as 4 times the squared peak tricuspid regurgitation velocity, 4TRV²) and the RV systolic pressure measured by RHC (R² = 0.41, p < 0.0001), (Table 4).

The echocardiographic assessment of RV systolic pressure had a somewhat lower correlation to RV systolic pressure measured at RHC (R² = 0.38, p < 0.0001. Actually, 4TRV² > 35 mmHg was 100% specific and 67% sensitive for identifying elevated PAP measured during RHC (mean PAP > 25 mmHg) by ROC analysis with an area under the curve (AUC) of 0.873, CI 0.770–0.941, p < 0.0001 (Fig. 1).

LV diastolic parameters such as the mitral inflow E velocity to e' annular velocity ratio (E/e' ratio), forming the basis for the echocardiographic estimation of LAP², did not correlate with the actual assessment of LAP during RHC using PCWP. The mitral inflow E velocity correlated better and moderately with PCWP. Cardiac index, calculated from biplane endocardial contour by the echocardiography strain software only modestly correlated with thermodilution during RHC.

As shown in Fig. 2, among 38 patients in sinus rhythm, who were defined by echocardiogram for diastolic dysfunction according to current ASE/EACVI guidelines, dysfunction was strongly associated with elevated RHC-measured PCWP (p-value = 0.001). The diastolic dysfunction score sensitivity was 96% (CI 79.6–99.9%) and 80% specific (44.4–97.5%) for PCWP ≥ 12 mmHg at RHC, with a positive and negative predictive value of 92% and 89%, respectively.

Assessment of the individual parameters incorporated in the ASE/EACVI guidelines by the ROC analysis revealed that mitral E to A velocities ratio (E/A) and mitral E velocity were mostly associated with elevated LAP (supplemental Table 2).

Left atrial functional variables (volumetric, timing and strain) correlating with elevated LAP are shown in Table 5. Only LA minimal volume index >27 ml/m² demonstrated a statistically significant association with RHC elevated LAP. LA maximal volume index, LA ejection fraction (LAEF) and emptying duration, presented only a trend (p-values 0.09–0.06) for elevated LAP. Interestingly conduit volume, LV minus LA stroke volumes (LVSV - LASV), and reservoir strain were not associated with elevated LAP. LA volume indices were statistically non-significantly larger in patients with higher echocardiographic determined elevated LAP (Nagueh's equation), (Table 5).

4. Discussion

In this study, we aimed to evaluate the correlation of conventional

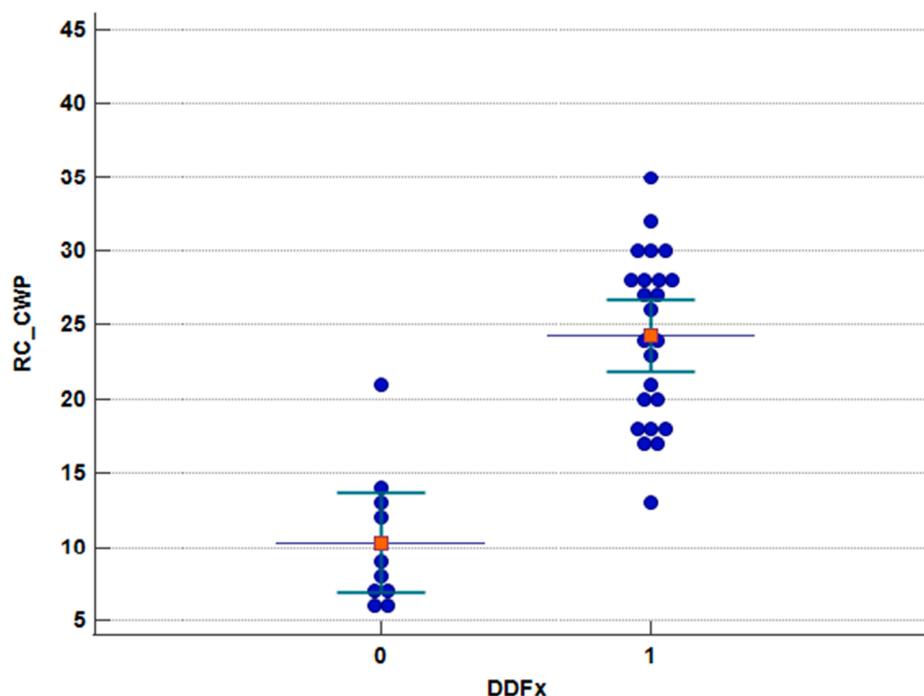


Fig. 1. American Society of Echocardiography (ASE) definition of diastolic dysfunction and elevated capillary wedge pressure at right heart catheterization.

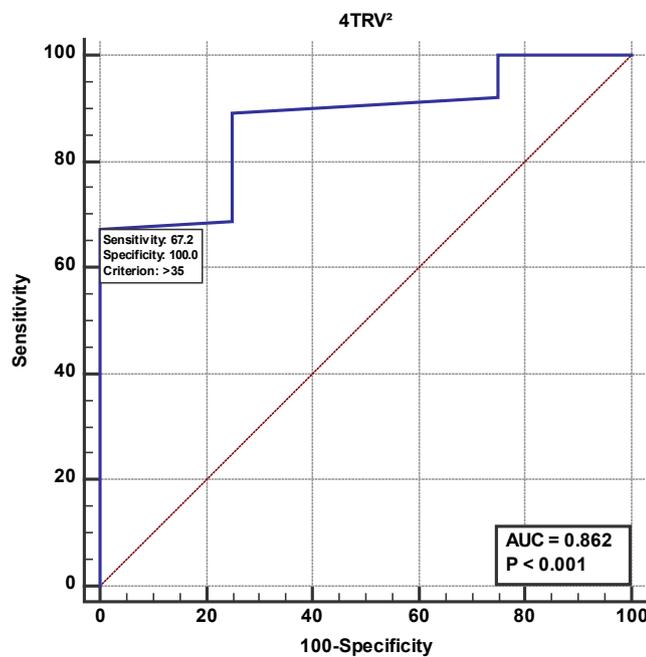


Fig. 2. Tricuspid regurgitation pressure gradient and elevated left atrial pressure at right heart catheterization, receiver operator characteristic (ROC) analysis.

echocardiographic parameters, elevated LAP, LA mechanics and phasic volumes, with LAP measured during RHC.

The best correlation detected was between the estimated echocardiographic TR pressure gradient and the RHC-measured peak pulmonary pressure. The estimated echocardiographic peak pulmonary pressure still correlated with the RHC peak pulmonary pressure with a lower correlation coefficient, probably because it included an estimation of RAP that did not correlate with the equivalent RHC measurement at all.

This discrepancy can be explained in two ways. RAP may be extremely variable and related to the patient fluid status, such that it may have changed during the 24-hour gap between the two procedures. The other reason may be related to the method of estimation of RAP in conventional echocardiography by scanning the diameter and collapsibility of the superior vena cava. This method probably needs to be reevaluated.

We found, according to the latest ASE/EACVI guidelines [2] for the diagnosis of diastolic dysfunction, the suggested score to strongly correlate with elevated LAP measured by RHC. Diastolic dysfunction defined by the score was both sensitive and specific for elevated CWP ≥ 12 mmHg at RHC, with high positive and negative predictive values. This is probably a major improvement over previous recommendations, as these have left many cases uncategorized for diastolic function and included patients with either normal or abnormal diastolic function, which are clearly divergent. Notably, the score comprises assessment of the tricuspid valve regurgitation velocity and not the RV systolic

Table 5

Left atrial mechanics associates of elevated left atrial pressure.

	AUC	CI	p-value	Criterion	Sensitivity	Specificity
LAVmax-i	0.66 \pm 0.09	0.534–0.776	0.07	>37	76	57
LAVmin-i	0.69 \pm 0.09	0.559–0.797	0.04	>27	66	79
LA EF (%)	0.68 \pm 0.09	0.549–0.789	0.06	<56	90	50
LA reservoir strain (%)	0.61 \pm 0.10	0.477–0.727	0.29	<23	80	57
LA emptying duration (% cycle length)	0.66 \pm 0.10	0.533–0.778	0.09	>27	64	86
Conduit Volume (LVSV-LASV)	0.55 \pm 0.08	0.423–0.677	0.55	<21	58	71

AUC = Area Under the Curve; CI = Confidence Interval; LAV = Left Atrial Volume; LA = Left Atrium; EF = Ejection Fraction; LVSV = Left Ventricle Stroke Volume; LASV = Left Atrial Stroke Volume.

pressure estimate, ignoring the RAP estimate, which was confirmed by our findings.

There is benefit of LA minimal volume to the estimation of elevated LAP regardless of rhythm. The LA remodels in patients with LV diastolic dysfunction [7]. This remodeling is multifaceted and includes geometric adaptations (size and shape), changes in tissue characteristics (dispensability and compliance) as well as mechanical modifications (ability to relax and contract) that interplay and change in response to the severity of LV diastolic dysfunction [6]. Large LA end diastolic volume (LAVmax-i, indexed to body surface area) has been shown to aid in the diagnosis of LV diastolic function and demonstrated evidence regarding grim prognosis in various diseases [8]. However, as simple as it may be, the effect of diastolic dysfunction on LA is more complex than what is represented in a single echocardiographic end systolic frame. In fact, even in sinus rhythm patients, the LAVmax-i showed to be least associated with elevated LAP. Moreover, patients with HF have frequent atrial fibrillations. The assessment of diastolic dysfunction by echocardiography in these patients is indirect and requires evaluation of many time-dependent parameters. These are notorious for having a large beat-to-beat changes as well as large intra and inter-observer variabilities.

According to our findings, replacing LAVmax-i > 34 ml/m²i by LAVmin-i > 27 ml/m² in the ASE/EACVI algorithm would probably yield more accurate predictions of elevated LAP and improve definition of diastolic dysfunction. Incorporating LAEF (representing normal vs abnormal emptying of the LA) would probably enhance this prediction further. Actually, creating a diastolic index LAEF(%) / LAVmin-i(ml/min) / mitral E(m/s) < 3.1 was 89% specific and 69% sensitive to diagnosing elevated LVEDP (ROC = 0.76, P = 0.015). Similar approaches using ECG time intervals criteria were also found to be specific and sensitive to echocardiographically defined diastolic dysfunction [9,10].

We have shown herein that LAVmin-i significantly correlated with elevated LAP, with a high specificity criterion of ≥ 27 ml. LAEF $< 56\%$ demonstrated a trend for high sensitivity for elevated LAP. LAVmin-i remained the sole associating factor of elevated LAP in multiple logistic regressions, including all geometric and functional LA parameters performed, regardless of the presence of sinus rhythm or atrial fibrillation. LA maximal and minimal volumes most likely rise in tandem in response to LV diastolic dysfunction. With worsening LA function, LA minimal volume may be increasing disproportionately, thus its size might bear both geometric and functional characteristics that may explain the superiority over maximal size and function. Clinically, these data support the notion of a new tool to define diastolic dysfunction using LAVmin-i in patients regardless of their rhythm or pulmonary disease.

In conclusion, we compared conventional echocardiography parameters to those quantified during RHC and discovered that estimated tricuspid regurgitation pressure gradient determined by standard echocardiography best correlated with RHC-measured peak pulmonary pressure. The 2016 ASE/EACVI guidelines [2] for the diagnosis of diastolic dysfunction suggested a score, which strongly correlated with elevated LA pressure measured by RHC, in sinus rhythm patients. Diastolic dysfunction defined by the score was both sensitive and specific for elevated CWP ≥ 12 mmHg at RHC, with high positive and negative predictive values.

When assessing the LA volumes to estimate elevated LA pressure in

all patients, regardless of sinus rhythm presence or regional wall motion abnormalities, LAVmin-index is the best tool to define elevated LA pressure using echocardiography.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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