

Echocardiographic evaluation of left ventricular end diastolic pressure in patients with diastolic heart failure

A comparative study with real-time catheterization

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Abstract

To evaluate the left ventricular end diastolic pressure (LVEDP) in patients with diastolic heart failure by echocardiography and explore the clinical value of echocardiography.

From July 2017 to January 2018, 120 patients were prospectively selected from the affiliated hospital of Jiangsu university diagnosed as diastolic heart failure (York Heart Association class \geq II, LVEF \geq 50%). The patients were divided into group with LVEDP \leq 15 mm hg (1 mm hg=0.133 kpa) (43 cases) and the group with LVEDP >15 mm hg (77 cases) according to the real-time measurement of LVEDP. Receiver operator characteristic curves of each parameter of echocardiography in diagnosis of LVEDP were compared between the 2 groups.

Common ultrasonic parameters such as left ventricular inflow tract blood flow propagation velocity, mitral valve diastole e peak velocity/mitral valve diastole a peak velocity, e peak deceleration time, a peak duration, and early diastole interventricular septum bicuspid annulus velocity e' (e'sep) were used to evaluate LVEDP elevation with low accuracy (AUC is only between 0.5 and 0.7). Other ultrasonic parameters such as left atrial volume index (LAVI), tricuspid regurgitation maximum flow rate (TRmax), early diastole left ventricular sidewall bicuspid annulus velocity e' (e'lat), average e', E/e'sep, E/e'lat, average E/e' were used to evaluate LVEDP elevation with a certain improvement in accuracy (AUC between 0.7 and 0.9). Propagation velocity, mitral valve diastole e peak velocity/mitral valve diastole a peak velocity, e peak deceleration time, a peak duration, e'sep, average e', E/e'sep have very low correlation with LVEDP ($r=-0.283$ to 0.281); LAVI, TRmax, e'lat, E/e'lat, average E/e' and LVEDP are not highly correlated ($r=0.330-0.478$). Through real-time left ventricular manometry, multiple regression analysis showed that TRmax, average e', e'lat, LAVI were independently correlated with the actual measured LVEDP.

Echocardiography can recognize the increase of LVEDP in patients with heart failure preserved by LVEF, and estimate the value of LVEDP roughly, which can reflect LVEDP to a certain extent, with high feasibility and accuracy.

Abbreviations: A-dur = E peak persistence time, DHF = diastolic heart failure, DT = E peak deceleration time, E/A = E peak velocity of mitral valve opening in diastole/A peak velocity of mitral valve opening in diastole, E/e'lat = ratio of early diastolic mitral annulus velocity to early diastolic mitral annulus velocity, E/e'sep = ratio of early diastolic mitral velocity to early diastolic mitral annulus velocity, e'lat = diastolic left ventricular wall velocity of mitral annulus, e'sep = diastole velocity of mitral annulus at interventricular septal side, LAVI = left atrial volume index, LVEDP = left ventricular end diastolic pressure, LVEF = left ventricular ejection fraction, TRmax = maximum velocity of tricuspid regurgitation, VP = flow propagation speed of left ventricular inflow tract.

Keywords: echocardiography, left ventricular diastolic function, left ventricular end diastolic pressure

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1. Introduction

The current definition of heart failure classifies diastolic dysfunction as a clinically symptomatic stage, when in fact, the patient may present with asymptomatic structural or functional cardiac abnormalities (systolic or diastolic left ventricular dysfunction) before the onset of clinical symptoms, an early event of heart failure.^[1] It is important to identify these early events because they are associated with poor prognosis, and early intervention can significantly reduce patient fatality.^[2] Elevated left ventricular end-diastolic pressure (LVEDP) is the main index of left ventricular diastolic dysfunction. The gold standard for the determination of LVEDP is cardiac catheterization method, while cardiac catheterization technique is invasive, expensive and difficult, requiring appropriate equipment and trained operators, which is difficult to achieve in small and medium-sized hospitals.^[3] LVEDP is important not only for diagnosing heart failure, but also for understanding the severity and treatment of heart failure. Noninvasive evaluation of LVEDP is an important objective of echocardiography, and mitral valve flow, tissue doppler, tricuspid regurgitation rate (TRmax), and left atrial volume (LAVI) are the basis for evaluating diastolic function.^[4,5] In this study, the LVEDP value measured by left ventricular catheter in 120 patients was taken as the gold standard, and the comparison between non-invasive echocardiographic assessment and invasive real-time detection of LVEDP by left ventricular catheter was conducted. The purpose of this study was to explore the feasibility and accuracy of evaluating LVEDP by echocardiography, and to provide an optimal method for the clinical evaluation of left ventricular end-diastolic pressure in patients with diastolic heart failure.

2. Methods

2.1. Patients

Prospectively, 120 patients (78 males and 42 females) who were diagnosed with diastolic Heart failure (New York Heart Association class \geq II and LVEF \geq 50%) at the affiliated hospital of Jiangsu University from July 2017 to January 2018 were selected, with an average age of (62.3 \pm 10.5) years. LVEDP $>$ 15 mm Hg (1 mm Hg = 0.133 kpa) was defined as the increased left ventricular filling pressure.^[6] Patients were divided into LVEDP \leq 15 mm Hg group (43 cases) and LVEDP $>$ 15 mm Hg group (77 cases) according to the real-time LVEDP measurement. Inclusion criteria: sinus rhythm, hemodynamic stability, LVEF \geq 50%, no primary cardiomyopathy or valvular heart disease, and no atrioventricular block. Exclusion criteria: atrial fibrillation, mitral valve surgery, mitral stenosis or severe mitral valve calcification, severe mitral valve or aortic regurgitation, patients with hemodynamic instability, heart transplant patients, patients with poor image quality, patients with a central rate of $>$ 100/min during examination. This study was approved by the medical ethics review committee of the Affiliated Hospital of Jiangsu University, and the ethics review committee number is SWYXLL20170601. The study conforms with the all outlined in the Declaration of Helsinki. All the patients and their families signed the informed consent.

2.2. Echocardiography

GE Vivid E 9 full digital color Doppler ultrasound diagnostic instrument, M5S probe, frequency 1.7 to 3.4 MHz were used for image acquisition. The patient was placed in a supine position and connected to the electrocardiogram, and dynamic images of the

4-chamber, 2-chamber, and 3-chamber hearts of the apex were taken to measure left atrial volume index (LAVI), LVEF, and TRmax according to the latest guidelines recommended by the American society of echocardiography.^[7] The sampling volume was placed at the level of the tip of the mitral valve on the 4-chamber view of the apex, and the probe direction and sampling site were appropriately adjusted to obtain the optimal mitral flow spectrum. Peak E (E), peak A flow rate (A), peak E deceleration time (DT), peak A duration time (A-dur, AD) in mitral diastole were measured, and the E peak velocity of mitral valve opening in diastole/A peak velocity of mitral valve opening in diastole (E/A) ratio was calculated. The PW-TDI program was started on the 4-chamber apex view, and the gain and frame rate were adjusted appropriately. The sampling volume was placed at the level of the mitral valve ring in the ventricular septum and the left ventricular lateral wall, respectively, to measure the mitral valve ring movement speed (e') in early diastolic period. The M-scan line was placed at the center of the inflow of the left ventricle from the mitral valve orifice to the apex of the heart. The baseline color blood flow was adjusted below the Nyquist limit to make the highest flow velocity in the center blue. The velocity of flow propagation (VP) in the inflow tract of the left ventricle was recorded.

2.3. Cardiac catheterization

Echocardiographic assessments were simultaneously performed during invasive measurements in the catheterization laboratory. Left cardiac catheterization examination shall be conducted by the same cardiologists in accordance with standard procedures, percutaneous puncture radial artery or femoral artery in sheath pipe, into 6 f pigtail catheter in left ventricular cavity, connect pressure transducer, ultrasonic doctor record echocardiography parameters associated with left ventricular diastolic function, meanwhile ecg stress system records for 3 to 5 electrical pressure curve of the cardiac cycle, measured in end-diastolic LVEDP, calculating the average of the 3 consecutive cardiac cycle, LVEDP $>$ 15 mm Hg defined as left ventricular filling pressure.

2.4. Statistical analysis

In this study, SPSS (20.0) software and Medcalc software were used to test the normal distribution (Kolmogorov-Smirnov test) and the homogeneity of variance (Levene test). The measurement data of normal distribution was expressed as mean \pm standard deviation, the measurement data of nonnormal distribution was expressed as M (Q1, Q3). The independent sample *t*-test was used to compare the measurement data of normal distribution between the 2 groups. Non-normal distribution data using nonparametric test (the Mann-Whitney *U* test). Enumeration data is expressed as absolute value or percentage, and Chi-square test is used for comparison between groups. Based on the gold standard of invasive manometry, Receiver operator characteristic (ROC) curve was used to evaluate the diagnostic efficacy of each echocardiographic parameter on LVEDP. ROC curve of each echocardiographic parameter was drawn and compared with each other. The sensitivity, specificity, 95% confidence interval, and area under ROC curve of echocardiographic parameters were calculated. The parameters of echocardiography were analyzed by stepwise regression equation and the Pearson method was used to analyze the correlation between the estimated value of LVEDP and the measured value of LVEDP. The Bland-Altman plot is used to analyze the agreement between

Table 1
Comparison of general data between 2 groups of patients ($\bar{x} \pm s$).

	LVEDP ≤ 15 mm Hg (n=43)	LVEDP >15 mm Hg (n=77)	T (χ^2)	P
Male sex	29 (67.4)	49 (63.6)	0.2	.68
Height (cm)	167 \pm 9	165 \pm 7	1.5	.13
Body weight (kg)	68 \pm 13	68 \pm 10	0.2	.88
Body surface area (m ²)	1.8 \pm 0.2	1.8 \pm 0.2	0.5	.59
Hypertension (cases)	27	58	2.1	.15
Diabetes mellitus (cases)	5	13	0.6	.44
Coronary heart disease (cases)	25	41	0.3	.61
Emergency PCI (cases)	9	14	0.1	.71
Systolic pressure (mm Hg)	128 \pm 12	136 \pm 19	-2.4	.02
Diastolic pressure (mm Hg)	79 \pm 8	78 \pm 10	0.3	.75
Heart rate (b.p.m.)	70 \pm 10	69 \pm 11	0.5	.62
ACEI (cases)	27	40	1.3	.25
ARB (cases)	10	20	0.1	.74
Diuretics (cases)	5	6	0.5	.49
Receptor blocker (cases)	30	50	0.8	.68
Statins (cases)	29	42	4.2	.13
Nitrates (cases)	12	29	2.5	.28

ACEI = ACE inhibitor, ARB = ACE blocker, PCI = percutaneous coronary intervention.

estimated LVEDP by equation and measured LVEDP. *P*-value of $<.05$ was considered statistically significant.

3. Results

3.1. Comparison of general data between the 2 groups

In this study, there were 77 cases in the elevated LVEDP group and 43 cases in the normal LVEDP group. Except that systolic blood pressure in the increased LVEDP group was higher than that in the normal LVEDP group (*P* = .02), other basic data showed no statistical significance, as shown in Table 1.

3.2. Comparison of echocardiographic parameters between the 2 groups

LAVI, TRmax, E/e' sep, E/e' lat, and mean E/E' lat in patients with elevated LVEDP were greater than those in patients with normal LVEDP (*P* $<.05$). VP, e' sep, e' lat, and average e' at in patients with elevated LVEDP were lower than those in patients

with normal LVEDP (*P* $<.05$). There was no statistically significant difference between the 2 groups in LVEF, E/A, and DT (*P* $>.05$), as shown in Table 2.

3.3. Comparison of ROC curve of LVEDP estimation by echocardiographic parameters

The accuracy of commonly used ultrasonic parameters VP, E/A, DT, A-dur, and E' sep in the diagnosis of LVEDP was lower (AUC between 0.5 and 0.7), while the accuracy of other parameters LAVI, TRmax, E' lat, average e', E/e' sep, E/e' lat, and average E/e' lat in the diagnosis of LVEDP was somewhat improved (AUC between 0.7 and 0.9), but still lower, as shown in Table 3 and Figures 1 and 2.

3.4. Correlation between echocardiographic parameters and LVEDP

The correlation between VP, E/A, DT, A-dur, E' sep, average e', E/e' sep, and LVEDP was very low (*r* = -0.209, *P* = .023). *r* = 0.063, *P* = .492; *r* = 0.013, *P* = .891; *r* = 0.087, *P* = .344; *r* = 0.149,

Table 2
Comparison of echocardiographic parameters ($\bar{x} \pm s$).

	LVEDP ≤ 15 mm Hg (n=43)	LVEDP >15 mm Hg (n=77)	T	P
LVEF (%)	64 \pm 6	64 \pm 7	-1.3	.21
LAV I (mL/m ²)	29 \pm 6	35 \pm 9	-4.3	$<.001$
VP (cm/s)	55 \pm 17	46 \pm 15	2.9	.004
TRmax (cm/s)	241 \pm 34	264 \pm 35	-3.5	.001
E/A	1.0 \pm 0.3	1.0 \pm 0.4	-0.5	.65
DT (cm/s)	201 \pm 44	203 \pm 62	-0.1	.89
A-dur (AD, ms)	124 \pm 24	120 \pm 23	0.9	.38
e' sep (cm/s)	7 (6,8)	6 (4,7)	-3.1	.002
e' lat (cm /s)	9.7 \pm 2.2	7.9 \pm 2.0	4.7	$<.001$
Average e' (cm /s)	8.3 \pm 1.8	6.9 \pm 1.7	1.3	$<.001$
E/e' sep	11.0 \pm 3.5	14.5 \pm 4.6	-4.3	$<.001$
E/e' lat	7.8 \pm 2.5	10.7 \pm 3.5	-4.9	$<.001$
Average E/e'	9.4 \pm 2.8	12.6 \pm 3.7	-5.0	$<.001$

A-dur = E peak persistence time, DT = E peak deceleration time, E/A = E peak velocity of mitral valve opening in diastole/A peak velocity of mitral valve opening in diastole, E/e' lat = ratio of early diastolic mitral annulus velocity to early diastolic mitral annulus velocity, E/e' sep = ratio of early diastolic mitral velocity to early diastolic mitral annulus velocity, e' lat = diastolic left ventricular wall velocity of mitral annulus, e' sep = diastole velocity of mitral annulus at interventricular septal side, LAVI = left atrial volume index, LVEF = left ventricular ejection fraction, TRmax = maximum velocity of tricuspid regurgitation, VP = flow propagation speed of left ventricular inflow tract.

Table 3
Correlations of established parameters with left ventricular end-diastolic pressure ($\bar{x} \pm s$).

		All (n = 120)	LVEDP ≤15 mm Hg (n=43)	LVEDP >15 mm Hg (n =77)
LAV I (mL/m ²)	r	0.478	0.454	0.357
	P	.000	.002	.001
VP (cm/s)	r	-0.209	0.257	-0.026
	P	.023	.096	.820
TRmax (cm/s)	r	0.330	0.397	0.220
	P	.000	.008	.054
E/A	r	0.063	0.234	0.062
	P	.492	.126	.594
DT (cm/s)	r	0.013	0.389	-0.010
	P	.891	.009	.929
A-dur (AD, ms)	r	-0.087	0.482	-0.104
	P	.344	.001	.367
e' sep (cm/s)	r	-0.149	0.334	0.095
	P	.104	.027	.411
e' lat (cm /s)	r	0.353	0.366	-0.137
	P	.000	.015	.234
Average e' (cm /s)	r	-0.283	0.378	-0.033
	P	.002	.011	.773
E/e' sep	r	0.281	0.211	0.017
	P	.002	.169	.883
E/e' lat	r	0.423	0.268	0.220
	P	.000	.078	.054
AverageE/e'	r	0.367	0.250	0.114
	P	.000	.101	.323

A-dur = E peak persistence time, DT = E peak deceleration time, e' lat = diastolic left ventricular wall velocity of mitral annulus, E/A = E peak velocity of mitral valve opening in diastole/A peak velocity of mitral valve opening in diastole, E/e'lat = ratio of early diastolic mitral annulus velocity to early diastolic mitral annulus velocity, E/e' sep = ratio of early diastolic mitral velocity to early diastolic mitral annulus velocity, e' sep = diastole velocity of mitral annulus at interventricular septal side, LAVI = left atrial volume index, TRmax = maximum velocity of tricuspid regurgitation, VP = flow propagation speed of left ventricular inflow tract.

P=.104; R=0.283, P=.002; R=0.281, P=.002); LAVI, TRmax, e'lat, e' /e' lat, and average E/e' had low correlation with LVEDP (r=0.478, P=.000). r=0.33, P=.000; r=0.353, P=.000; r=0.423, P=.000; r=0.367, P=.000), as shown in Table 4, Figures 3–6.

36 had elevated LVEDP, no false negative patients, 24 had false positive patients, and 24 were uncertain patients, with sensitivity of 100% and specificity of 60%, which was significantly higher than the diagnostic value of using a single indicator, but with slightly lower specificity.

3.5. 2016 EACVI/American Society for Echocardiography recommendations for evaluating LVEDP

The 120 patients in this study were evaluated according to the 2016 guidelines, among which 36 patients had normal LVEDP,

3.6. Correlation between LVEDP estimated value and LVEDP measured value of left cardiac catheter

Multiple regression analysis showed that TRmax, average e', e'lat, and LAVI were independently correlated with the actual measured LVEDP. When these 4 parameters entered the

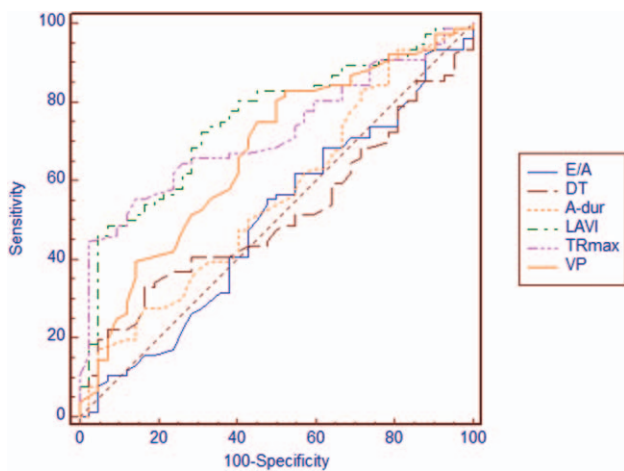


Figure 1. Comparison of ROC curve of LVEDP estimated by echocardiographic parameters. LVEDP = left ventricular end diastolic pressure, ROC = receiver operator characteristic curve.

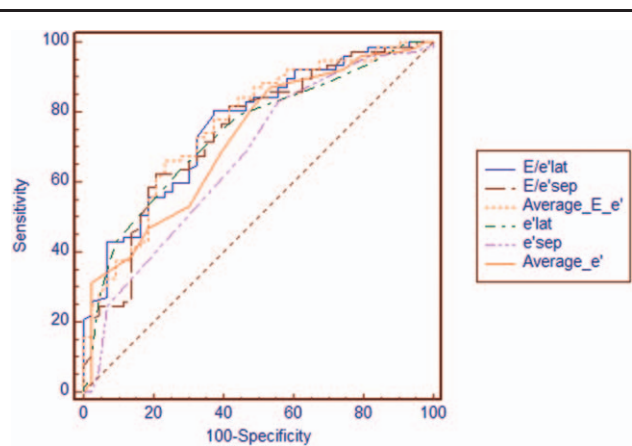


Figure 2. Comparison of ROC curve of LVEDP estimated by echocardiographic parameters. LVEDP = left ventricular end diastolic pressure, ROC = receiver operator characteristic curve.

Table 4
ROC curve comparison of LVEDP estimated by echocardiographic parameters.

Parameter	Cutoff value	Sensitivity	Specificity	Yoden index	95% CI	P	AUC
LAV I (mL/m ²)	>31.8	71.4%	69.8%	0.41	0.67–0.83	.0001	0.75
TRmax (cm/s)	>278	44.2%	97.7%	0.42	0.63–0.79	.0001	0.71
VP (cm/s)	<=55	83.1%	47.6%	0.31	0.57–0.75	.0027	0.66
E/A	>0.7	83.1%	25.6%	0.09	0.42–0.61	.7752	0.52
DT (cm/s)	<=168	32.5%	81.4%	0.14	0.41–0.60	.9498	0.50
A-dur(AD, ms)	<=99	16.9%	95.3%	0.12	0.46–0.64	.3594	0.55
e' sep (cm/s)	<=7	83.1%	44.2%	0.27	0.58–0.75	.0013	0.67
e' lat (cm/s)	<=8	63.6%	72.1%	0.36	0.62–0.82	.0001	0.74
Average e' (cm/s)	<=8.5	87.0%	46.5%	0.34	0.63–0.80	.0001	0.72
E/e' sep	>12.7	62.3%	79.1%	0.41	0.66–0.82	.0001	0.74
E/e' lat	>7.8	80.5%	62.8%	0.43	0.68–0.84	.0001	0.76
Average E/e'	>10.5	66.2%	76.7%	0.43	0.68–0.84	.0001	0.76

A-dur = E peak persistence time, DT = E peak deceleration time, e' lat = diastolic left ventricular wall velocity of mitral annulus, E/A = E peak velocity of mitral valve opening in diastole/A peak velocity of mitral valve opening in diastole, E/e' lat = ratio of early diastolic mitral annulus velocity to early diastolic mitral annulus velocity, E/e' sep = ratio of early diastolic mitral velocity to early diastolic mitral annulus velocity, e' sep = diastole velocity of mitral annulus at interventricular septal side, LAVI = left atrial volume index, TRmax = maximum velocity of tricuspid regurgitation, VP = flow propagation speed of left ventricular inflow tract.

equation, the optimal multiple regression equation could be obtained: $LVEDP = 0.046TR_{max} + 0.975e'_{sep} - 1.302e'_{lat} + 0.343LAVI + 3.854$. The sensitivity, specificity, positive predictive value, and negative predictive value of 15 mm Hg of LVEDP > were 70.1%, 80.0%, 96.1%, and 27.9%, respectively. The Pearson correlation coefficient between the estimated value of LVEDP and the measured value of LVEDP is $r = 0.61, P < .001$, as shown in Table 5. The Bland–Altman analysis for estimated LVEDP and measured LVEDP is shown in Figure 7.

4. Discussions

The main cause of left ventricular diastolic dysfunction is abnormal cardiac relaxation caused by increased left ventricular stiffness, increased left ventricular filling resistance, and correspondingly increased LVEDP. Invasive cardiac catheterization is the gold standard for assessing left ventricular relaxation and stiffness, but due to its invasive and radioactive damage, it is

seldom used in clinical practice. Echocardiography is currently the only noninvasive imaging technique that can be used to diagnose diastolic dysfunction.^[8,9] Previous studies mostly supported the role of echocardiography in the assessment of left ventricular filling pressure in heart failure with reduced ejection fraction patients, while heart failure with preserved ejection fraction was rarely studied.^[10] The correlation between invasive LVEDP measurements and echocardiographic parameters in heart failure with preserved ejection fraction patients has not been fully demonstrated. Several studies have compared the relationship between hemodynamics and echocardiographic parameters, but the number of patients was small and the LVEDP and echocardiographic parameters were not obtained at the same time.^[11,12]

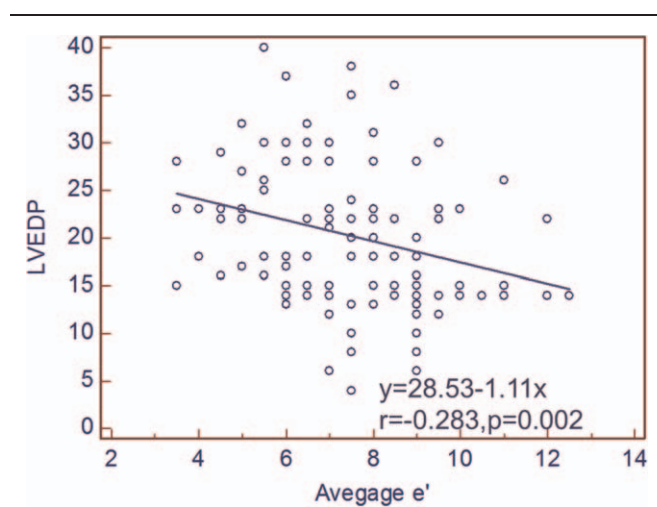


Figure 3. The 2016 ASE/EAVCI guidelines recommend indicators average e', average E/e', LAVI, TRmax have a low correlation with LVEDP. LAVI = left atrial volume index, LVEDP = left ventricular end diastolic pressure, TRmax = maximum velocity of tricuspid regurgitation.

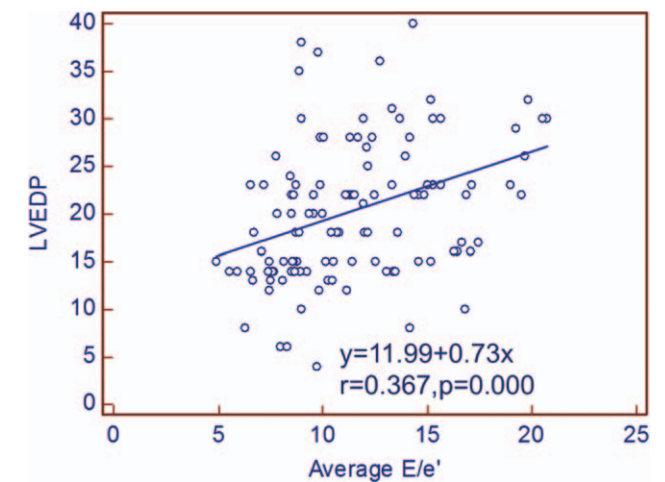


Figure 4. The 2016 ASE/EAVCI guidelines recommend indicators average average e', average E/e', LAVI, TRmax have a low correlation with LVEDP. LAVI = left atrial volume index, LVEDP = left ventricular end diastolic pressure, TRmax = maximum velocity of tricuspid regurgitation.

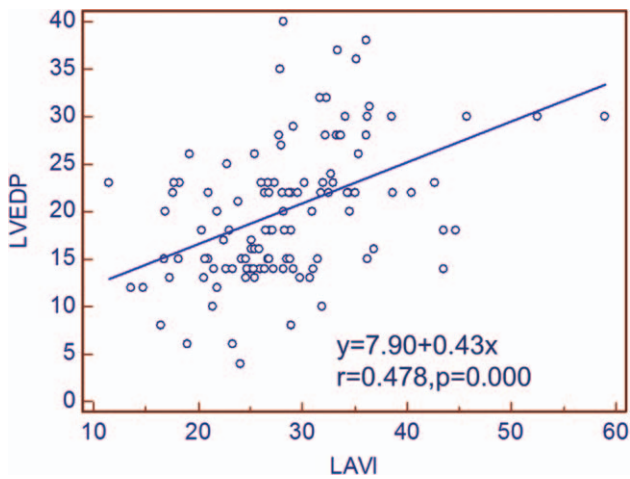


Figure 5. The 2016 ASE/EAVCI guidelines recommend indicators average e' , average E/e' , LAVI, TRmax have a low correlation with LVEDP. LAVI = left atrial volume index, LVEDP = left ventricular end diastolic pressure, TRmax = maximum velocity of tricuspid regurgitation.

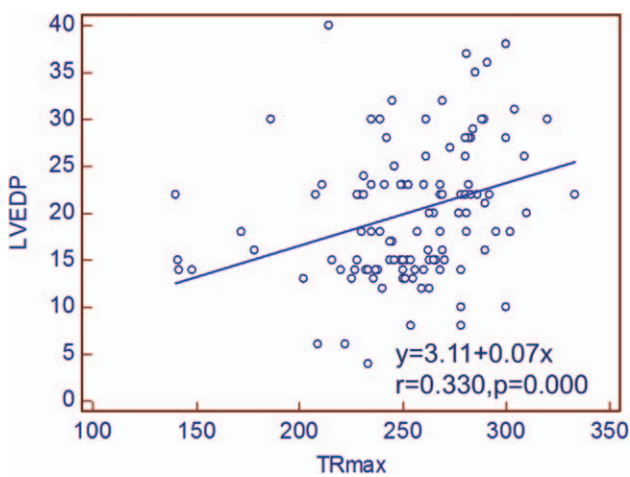


Figure 6. The 2016 ASE/EAVCI guidelines recommend indicators average e' , average E/e' , LAVI, TRmax have a low correlation with LVEDP. LAVI = left atrial volume index, LVEDP = left ventricular end diastolic pressure, TRmax = maximum velocity of tricuspid regurgitation.

4.1. Diastolic function parameters as estimates of LVEDP

The 2016 American Society for Echocardiography diastolic function guidelines mainly recommend 4 indicators for evaluation of left ventricular diastolic function in patients with normal LVEF:

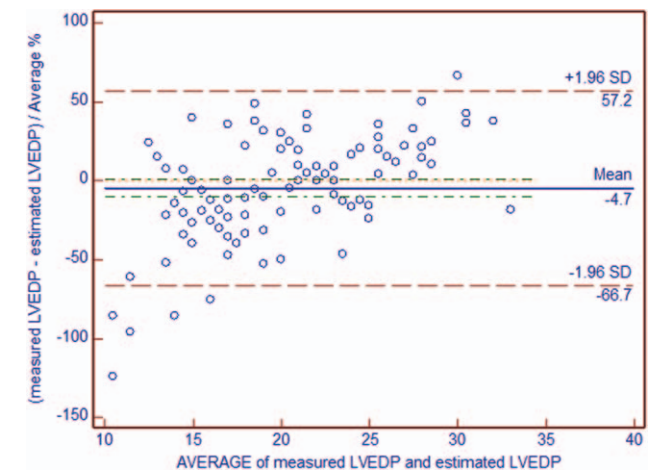


Figure 7. Bland–Altman analysis for estimated LVEDP and measured LVEDP. LVEDP = left ventricular end diastolic pressure.

- (1) wave velocity of mitral annulus e' (ventricular septum $e' < 7$ cm/s, left ventricular lateral wall $e' < 10$ cm /s);
- (2) Average E/e' ratio > 14 ;
- (3) The maximum volume index of the left atrium was > 34 mL/ m^2 ;
- (4) Peak tricuspid regurgitation velocity > 2.8 m/s.^[13]

The E/A of mitral valve blood flow spectrum is a traditional index reflecting the diastolic function, which is widely used in clinic. In clinical practice, $E/A < 1$ was used as the standard of diastolic function decline. However, E/A is affected by A variety of hemodynamic factors and age. With the increase of age, the relaxation speed of left ventricle slows down and the rigidity increases, which can lead to the normal filling mode of mitral valve in the elderly. The abnormality is similar to mild diastolic dysfunction. E/e' reflects left ventricular filling pressure, which has a good correlation with invasive cardiac function indexes such as left ventricular end diastolic pressure and hardness, pulmonary capillary wedge pressure (PCWP) and so on. Compared with E/A, E/e' has more advantages and is less affected by age. The left atrium acts as a channel between the pulmonary vein and the left ventricle, reflecting the filling load of the left ventricle during diastolic period.^[14] Studies have shown that LAVI has a good correlation with left ventricular end-diastolic pressure. $LAVI > 34$ mL/ m^2 is an independent predictor of heart failure, atrial fibrillation, ischemic stroke and death, as well as a key structural change of diastolic heart failure, which can be used as an indicator for clinical evaluation of left ventricular diastolic function.^[15,16]

Table 5
Results of multiple regression analysis.

variable	Non standardized coefficient β value	Standard error	Standardized coefficient β value	t	P
LAVI	0.343	0.072	0.380	4.742	.000
TRmax	0.046	0.016	0.227	2.925	.004
e' lat	-1.302	0.352	-0.398	-3.697	.000
e' sep	0.975	0.433	0.241	2.250	.026

e' lat = the velocity of diastolic mitral annular left ventricular wall motion, e' sep = the velocity of diastolic mitral annular septal motion, LAVI = left atrial volume index, TRmax = the maximum velocity of tricuspid regurgitation.

4.2. Comparison of ROC curve of LVEDP estimation by echocardiographic parameters

In this study, the LVEDP was used as the gold standard, and the real-time cardiac catheter pressure measurement and echocardiographic data were recorded at the same time. While in most other studies, these 2 measurements were performed at different times and locations.^[17] The cut-off values of each parameter for the diagnosis of LVEDP were given, and the diagnostic efficacy of each echocardiographic parameter on LVEDP was evaluated by ROC curve. When E/A estimates LVEDP, the area under ROC curve is 0.52, the sensitivity is 83.1%, and the specificity is 25.6%. Because of its low specificity, the clinical diagnosis value is limited. When E/e' estimated LVEDP, the area under ROC curve was 0.76, the sensitivity was 66.2%, and the specificity was 76.7%. In this study, multiple regression analysis shows that TRmax, average e', e'lat, and LAVI are independently related to the actual measured LVEDP. When TRmax, e'sep, e'lat, and LAVI enter the equation, an optimal multiple regression equation can be obtained, from which the LVEDP >15 mm Hg can be estimated. The sensitivity and specificity of mm Hg were 70.1% and 80.0%, respectively. According to this equation, we can get the accurate value of LVEDP of patients, rather than simply be judged as increasing or decreasing. This study shows that echocardiography can identify the elevation of LVEDP in patients with heart failure retained by LVEF, and estimate the LVEDP value roughly, reflecting LVEDP to a certain extent, with high feasibility and accuracy.

4.3. Correlation between echocardiographic parameters and LVEDP

In this study, the correlation coefficient between E/A and LVEDP is $r=0.063$. Some scholars found that the correlation between E/A ratio and left ventricular filling pressure was related to LVEF. Because the velocity of blood flow through the mitral valve depends on the pressure gradient on both sides, the velocity of E wave is affected by early diastolic relaxation and left atrial pressure. In patients with reduced LVEF, the correlation between E wave of mitral velocity and left ventricular filling pressure is better; in patients with LVEF >50%, the correlation between E wave of mitral velocity and left ventricular filling pressure is poor.^[18,19] A-wave velocity reflects the left atrial left ventricular pressure gradient in late diastolic period, and is affected by left ventricular compliance and left atrial systolic function.^[20] It is worth noting that E-wave, A-wave, and E/A are age-dependent and should be used cautiously in patients with arrhythmia.^[21] Some studies have shown that there is no nonlinear relationship between the change of mitral valve flow spectrum and cardiac function, which is only a comprehensive reflection of the dynamic change of left atrioventricular pressure gradient.^[22] Previous studies have verified E/e' and LVEDP, PAWP, LV pre-A-wave.^[11,12,23,24,25] In this study, the average correlation coefficient between E/e' and LVEDP was $r=0.367$. Lancellotti et al showed a significant correlation between E/e' lat and invasive LVEDP in normal LVEF patients.^[17] Yasuyuki et al found that when LVEF > 50%, E/e' had a good correlation with LVEDP and PCWP.^[26] When EF ≤50%, E/e' was moderately correlated with LVEDP and PCWP.

4.4. Limitations

It must be pointed out that all patients in this study have normal LVEF, and the application value of echocardiography in patients

with reduced LVEF needs further study to confirm. Doppler echocardiography is affected by age, heart rate, heart load, left atrial left ventricular size and systolic function, and the design of this study is still relatively shallow. The cut points that were obtained from ROC curves for our population may not be applicable to other populations. Our proposed algorithm is hypothesis generating and its accuracy will need to be re-validated in additional patient groups with normal LVEF. Whether echocardiography can be used as a noninvasive method to estimate left ventricular function remains to be verified by large samples.

5. Conclusion

In this study, we measured LVEDP by real-time cardiac catheter, and evaluated the diagnostic value of echocardiography parameters on LVEDP by ROC curve. The results showed that single echocardiography parameters had their potential advantages and limitations, and could not accurately determine whether left ventricular diastolic pressure was increased or not. It further confirms the diagnostic value of multi-parameter echocardiography in evaluating left ventricular diastolic function, which will provide important information for future research.

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