Left Ventricular Global Strain for Estimating Relaxation and Filling Pressure

– A Multicenter Study –

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Background: Speckle-tracking echocardiography (STE)-derived parameters may have better correlation with left ventricular (LV) relaxation and filling pressure than tissue Doppler-derived parameters. However, it has not been elucidated which parameter – strain or strain rate – and which direction of myocardial deformation – longitudinal or circumferential – is the most useful marker of LV relaxation and filling pressure.

Methods and Results: We conducted a prospective multicenter study and compared the correlation of tissue Doppler- and STE-derived parameters with the time constant of LV pressure decay (τ) and LV mean diastolic pressure (MDP) in 77 patients. The correlation of early-diastolic mitral annular velocity (e') with τ was weak ($r=-0.32$, $P<0.01$), and that of peak longitudinal strain (LS) was the strongest ($r=-0.45$, $P<0.001$) among the STE-derived parameters. There was a modest correlation between LVMDP and the ratio of early-diastolic inflow velocity (E) to e' (E/e') ($r=0.50$, $P<0.001$). In contrast, the ratio of E to LS (E/LS) correlated strongly with LVMDP ($r=0.70$, $P<0.001$). The correlation of E/LS with LVMDP was significantly better than that for E/e' ($P<0.01$). Receiver-operating characteristic analysis showed that E/LS had the largest area under the curve for distinguishing elevated LVMDP (E/LS 0.86, E/e' 0.74, E/A 0.67).

Conclusions: STE-derived longitudinal parameters correlated well with LV relaxation and filling pressure. In particular, E/LS could be more accurate than E/e' for estimating LV filling pressure. (*Circ J* 2016; **80**: 1163–1170)

Key Words: Diastolic dysfunction; Heart diseases; Heart failure; Speckle-tracking echocardiography

Elevated left ventricular (LV) filling pressure results in shortness of breath, which is both a major symptom and a prognostic predictor for heart failure. Therefore, noninvasive estimation of LV filling pressure is considered a goal of routine echocardiography. Recent recommendations encourage using tissue Doppler-derived early-diastolic mitral annular velocity (e') as a parameter of LV relaxation and the ratio of early-diastolic LV inflow velocity (E) to e' (E/e') to indicate LV filling pressure.¹ However, recent reports suggest

that these parameters do not necessarily correlate with invasively measured LV filling pressure in patients with hypertrophic cardiomyopathy,² severely reduced LV systolic function,³ and heart failure with preserved ejection fraction (EF).⁴

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Reasons for inaccuracies with tissue Doppler-derived parameters could include angle dependency and myocardial tethering,

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which are well-known limitations of tissue Doppler imaging.⁵ Because e' reflects the rate of longitudinal LV wall expansion in early diastole, a deformation parameter for the entire LV wall could be an alternative or even more useful marker of LV relaxation. Based on this hypothesis, myocardial strain and strain rate measured by 2-dimensional (2D) speckle-tracking echocardiography (STE) have been tested as estimates of LV relaxation and filling pressure.^{5–11} Several single-center studies have demonstrated that STE-derived parameters correlate with LV relaxation and filling pressure better than tissue Doppler-derived parameters.^{5–10} However, it has not been elucidated which parameter – peak strain, strain rate during the isovolumic relaxation (IVR) period or during the early-diastolic phase – and which direction of the myocardial deformation – longitudinal or circumferential – are the most useful markers of LV relaxation and filling pressure. Accordingly, we conducted a multicenter study of Strain/strain rate versus Myocardial velocity for Assessing left ventricular relaxation and filling Pressure (SMAP study). The aims of this study were to (1) re-examine the correlations between invasively measured LV hemodynamic parameters and tissue Doppler-derived parameters and (2) determine the most useful marker(s) of LV relaxation and filling pressure among STE-derived parameters.

Methods

Study Population and Protocol

We prospectively enrolled 84 patients who underwent cardiac catheterization for clinical diagnosis of cardiac diseases, including angina pectoris, prior myocardial infarction, dilated cardiomyopathy, hypertrophic cardiomyopathy, and hyperten-

sive heart disease, from 5 university hospitals in Japan (Hokkaido University Hospital, Nagoya City University Hospital, Mie University Hospital, University of Tsukuba Hospital, and Tokushima University Hospital). We excluded patients with atrial fibrillation, frequent supraventricular or ventricular premature contraction, moderate to severe aortic or mitral valve disease, and inadequate echocardiographic images. Patients who had undergone mitral valve plasty, replacement, or aortic valve replacement, and those who underwent hemodialysis were also excluded. Echocardiography was performed within 3 h of cardiac catheterization. The study protocol was approved by the institutional review board of each hospital and all patients gave written informed consent.

LV Pressure Measurement

LV pressures were recorded prior to coronary angiography. A high-fidelity, 5-French (Model SPC-454D, Millar Instruments, Houston, TX, USA) or 6-French (Model CA-61000-PLB, CD Leycom, Zoetermeer, The Netherlands) pigtail micromanometer-tipped catheter was balanced to the zero level at the mid-axillary line. The catheter was then placed in the LV chamber via the femoral or brachial artery and calibrated against the pressure measured simultaneously with the fluid-filled lumen at end diastole. LV pressure was recorded at end expiration for 3 consecutive cardiac cycles and digitized with a 1-ms sampling frequency using a data analysis system (PowerLab and LabChart software version 7.3.4, ADInstruments, NSW, Australia). The time constant of LV pressure decay (τ) was derived from a monoexponential fit to the LV pressure decay with a zero asymptote.¹² The τ with the zero-asymptote method may be less sensitive for the detection of impaired LV

relaxation than that with a non-zero-asymptote method; however, many clinical studies and the European guidelines for the diagnosis of heart failure with preserved EF¹³ have used the τ derived from the zero-asymptote method. We thus followed the prior standards in the present study. LV mean diastolic pressure (LVMDP) was measured as previously described.¹⁴ Abnormal LV relaxation was defined as $\tau \geq 48$ ms and elevated LV filling pressure was defined as LVMDP ≥ 12 mmHg.¹⁵ All parameters were averaged over 3 consecutive cardiac cycles.

Echocardiography

Echocardiography was performed using 1 of 2 commercially available systems (Aplio Artida SSH-88-CV or Aplio SSA-770A, Toshiba Medical Systems, Tochigi, Japan). LV mass was calculated according to the recommendations.¹⁶ LV hypertrophy was defined as LV mass index ≥ 115 g/m² in males and ≥ 95 g/m² in females. LVEF was calculated using the biplane method of disks. Patients were divided into 2 groups: with reduced LVEF ($<50\%$) and with preserved LVEF ($\geq 50\%$). LV inflow E and atrial-systolic peak velocity (A) were measured using pulsed-wave Doppler. Using the apical 4-chamber view, e' was measured at the septal and lateral sides of the annulus and averaged. The IVR period was defined as the time from aortic valve closure, determined by the end of LV outflow on the pulsed-Doppler image, to mitral valve opening, determined by the beginning of LV inflow.

STE Analysis

LV myocardial strain was analyzed offline using STE software (Toshiba Medical Systems). First, the endocardial border was manually traced, and the myocardial motion was tracked frame-by-frame on every view. The longitudinal strain/strain rate were measured in the apical 4-chamber, 2-chamber, and long-axis views and averaged frame-by-frame to construct a time-global strain curve as well as a time-global strain rate curve (Figure 1). Next, the absolute value of peak longitudinal strain (LS), peak longitudinal strain rate in the early-diastolic phase (LSR_E), and during the IVR period (LSR_{IVR}) in the inner layer were measured (Figure 1). The ratios of E to LS (E/LS), E to LSR_E (E/LSR_E), and E to LSR_{IVR} (E/LSR_{IVR}) were calculated. Similarly, circumferential strain and strain rate were measured in the short-axis views at the basal, middle, and apical ventricular levels. The absolute value of peak circumferential strain (CS), peak circumferential strain rate in the early-diastolic phase (CSR_E) and during the IVR (CSR_{IVR}) in the inner layer were measured, and the ratios of E to CS (E/CS), E to CSR_E (E/CSR_E), and E to CSR_{IVR} (E/CSR_{IVR}) were calculated.

Data Collection

The study protocol was written by the investigators from Hokkaido University (S.Y. and H.I.), and reviewed and modified by the members of the steering committee (S.Y., H.Y., K.D., Y.S., and N.O.), including an echocardiographic measurement manual that was followed by each institution to ensure consistent measurements. Echocardiographic tracking was performed in each institution and all STE data were exported to a spreadsheet. The data sets including clinical data, LV pressure measurements, conventional echocardiographic measurements, and the STE analysis spreadsheets were sent to the investigators at Hokkaido University for analysis (T.H., S.Y., H.I., and M.N.).

Statistical Analysis

Data are presented as mean $\pm$ standard deviation. Linear regres-

Table 1. Characteristics of the Study Patients Undergoing Cardiac Catheterization for Diagnosis of Cardiac Disease

Age, years	59 $\pm$ 14
Sex, M/F	58/19
Body surface area, m ²	1.68 $\pm$ 0.20
Heart rate, beats/min	66 $\pm$ 10
Systolic blood pressure, mmHg	122 $\pm$ 24
Diastolic blood pressure, mmHg	70 $\pm$ 14
NYHA class, n (%)	
I	51 (66)
II	21 (27)
III	5 (6)
IV	0 (0)
Heart disease, n (%)	
Angina pectoris	20 (26)
Prior MI	15 (19)
DCM	12 (16)
HCM	8 (10)
Hypertensive heart disease	8 (10)
None	14 (18)
Complications, n (%)	
Hypertension	44 (57)
Diabetes mellitus	27 (35)
Dyslipidemia	45 (58)
Medications, n (%)	
ARBs and/or ACEIs	43 (56)
β -blockers	39 (51)
CCBs	22 (29)
Diuretics	19 (25)
Digitalis	2 (3)
Statin	35 (45)
Antiplatelet agents	38 (49)

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor-blocker; CCB, calcium-channel blocker; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; MI, myocardial infarction; NYHA, New York Heart Association.

Table 2. Basic Echocardiographic Parameters and Hemodynamic Data of Study Patients Undergoing Cardiac Catheterization for Diagnosis of Cardiac Disease

LV end-diastolic dimension, mm	51 $\pm$ 8
LV mass index, g/m ²	122 $\pm$ 43
LV hypertrophy, n (%)	41 (53)
LVEF, %	58 $\pm$ 17
Reduced LVEF ($<50\%$), n (%)	30 (39)
E/A	0.99 $\pm$ 0.65
e' , cm/s	7.4 $\pm$ 2.1
E/ e'	9.2 $\pm$ 4.2
τ , ms	49 $\pm$ 13
Prolonged τ (≥ 48 ms), n (%)	38 (49)
LVMDP, mmHg	8.3 $\pm$ 6.1
Elevated LVMDP (≥ 12 mmHg), n (%)	18 (23)

E/A, ratio of early-diastolic LV inflow velocity (E) to atrial-systolic velocity (A); e' , early-diastolic mitral annular velocity; E/ e' , ratio of E to e' ; EF, ejection fraction; LV, left ventricular; MDP, mean diastolic pressure.

Figure 2. Correlations of echocardiographic parameters with τ and left ventricular mean diastolic pressure (LVMDP). E/A, ratio of early-diastolic LV inflow velocity (E) to atrial-systolic velocity (A); e' , early-diastolic mitral annular velocity; E/e' , ratio of E to e' ; E/LS, ratio of E to LS; LS, absolute value of peak longitudinal strain.

sion analysis was performed to determine the correlation between parameters. Two correlation coefficients drawn from the same sample were compared following Cohen et al's method.¹⁷ In patients who had a peak strain rate during the IVR period (SR_{IVR}) of approximately zero, E/SR_{IVR} was corrected to a normal distribution. We set the upper limit of $1/SR_{IVR}$ as the 3rd quartile plus $1.5 \times (\text{interquartile range})$: 20 s in $1/LSR_{IVR}$ and 6.7 s in $1/CSR_{IVR}$. We regarded $1/LSR_{IVR}$ as 20 s and $1/CSR_{IVR}$ as 6.7 s in patients with $1/SR_{IVR}$ over the limit. To assess the diagnostic ability of the echocardiographic parameters, we performed receiver-operating characteristic (ROC) analysis. Significant differences between the areas under the ROC curves were tested using Hanley and McNeil's method.¹⁸ Also, to investigate the incremental diagnostic value of the parameters, we conducted interactive stepwise procedures. The incremental value of the added variables was determined by comparing the global chi-square value, which was calculated from the log likelihood ratio. The reproducibility of the STE analysis was assessed in 17 patients; 2 independent, blinded observers analyzed the same 2D cine-loops and 1 of them repeated the analysis on a separate day. SPSS Statistics software (version 19.0.0, SPSS Inc, Chicago, IL, USA), R software (version 3.0.1, R Foundation for Statistical Computing, Vienna, Austria), and JMP software (version 11.0.0, SAS Institute Inc, Cary, NC, USA) were used for the statistical calculations. The results were considered statistically significant with $P < 0.05$.

Results

Of the 84 patients who were eligible for study enrollment, 1 patient was excluded from the study because atrial fibrillation occurred during catheterization, 1 patient because of inability to measure LV pressure, 3 patients because of moderate mitral regurgitation, and 2 patients because of inadequate LV wall tracking in the STE analysis. All data from the remaining 77 patients were analyzed in this study.

Patients' Characteristics

Patients' characteristics are summarized in [Table 1](#). Of 34 patients who were suspected of having angina pectoris, 20 were diagnosed as having angina pectoris by coronary angiography. In the remaining 14 patients, coronary angiography and echocardiography revealed no coronary artery disease or other cardiac diseases. Echocardiographic and hemodynamic parameters are presented in [Table 2](#); 30 patients (39%) had reduced LVEF and 47 (61%) had preserved LVEF; 38 patients (49%) had abnormal LV relaxation and 18 (23%) had elevated LV filling pressure.

Correlations Between τ and Echocardiographic Parameters

There was a weak, but significant, correlation between τ and e' ([Figure 2A](#)). The correlations between τ and the STE-derived parameters are summarized in [Table 3](#). There were weak correlations between τ and the STE-derived parameters

Table 3. STE-Derived Parameters and Their Correlations With τ and LVMDP in Study Patients Undergoing Cardiac Catheterization for Diagnosis of Cardiac Disease							
	Mean $\pm$ SD	Correlation with τ			Mean $\pm$ SD	Correlation with LVMDP	
		r	P value			r	P value
LS, %	11.5 $\pm$ 3.8	−0.45	<0.001	E/LS, [$\times 10^2$] cm/s	6.2 $\pm$ 3.4	0.70	<0.001
LSR _E , s ^{−1}	0.50 $\pm$ 0.25	−0.29	<0.05	E/LSR _E , cm	153 $\pm$ 83	0.51	<0.05
LSR _{IVR} , s ^{−1}	0.17 $\pm$ 0.14	−0.40	<0.001	E/LSR _{IVR} , cm	699 $\pm$ 755	0.37	<0.001
CS, %	19.8 $\pm$ 7.8	−0.30	<0.01	E/CS, [$\times 10^2$] cm/s	3.9 $\pm$ 2.7	0.63	<0.01
CSR _E , s ^{−1}	0.88 $\pm$ 0.47	−0.20	0.08	E/CSR _E , cm	103 $\pm$ 90	0.41	0.08
CSR _{IVR} , s ^{−1}	0.49 $\pm$ 0.36	−0.29	<0.05	E/CSR _{IVR} , cm	133 $\pm$ 479	0.39	<0.05

CS, absolute value of peak circumferential strain; CSR_E, peak circumferential strain rate in the early-diastolic phase; CSR_{IVR}, peak circumferential strain rate during the IVR period; E/CS, ratio of E to CS; E/CSR_E, ratio of E to CSR_E; E/CSR_{IVR}, ratio of E to CSR_{IVR}; E/LSR_E, ratio of E to LSR_E; E/LSR_{IVR}, ratio of E to LSR_{IVR}; IVR, isovolumic relaxation; LS, absolute value of peak longitudinal strain; SD, standard deviation; STE, speckle-tracking echocardiography.

Figure 3. Receiver-operating characteristic curves for E/LS, E/e', and E/A for distinguishing patients with elevated left ventricular filling pressure. *P<0.05 vs. E/A. AUC, area under the curve; E/A, ratio of early-diastolic LV inflow velocity (E) to atrial-systolic velocity (A); e', early-diastolic mitral annular velocity; E/e', ratio of E to e'; E/LS, ratio of E to LS; LS, absolute value of peak longitudinal strain.

in which LS showed the strongest correlation with τ (Figure 2B). There was, however, no statistically significant difference between the correlation of e' with τ and that of LS (P=0.21).

Correlations Between LVMDP and Echocardiographic Parameters

There was a significant correlation between LVMDP and E/A as well as between LVMDP and E/e' (Figures 2C,D). The correlations between LVMDP and STE-derived parameters are summarized in Table 3. Strain rate parameters during the IVR period significantly but weakly correlated with LVMDP. Strain rate parameters in the early-diastolic phase correlated modestly with LVMDP. In contrast, E/LS and E/CS correlated well with LVMDP. E/LS showed the strongest correlation with LVMDP (Figure 2E). The correlation of E/LS was significantly better than that of E/A (P<0.05) and E/e' (P<0.01).

Figure 4. Incremental diagnostic value for elevated left ventricular filling pressure by multivariate logistic regression models. E/A, ratio of early-diastolic LV inflow velocity (E) to atrial-systolic velocity (A); e', early-diastolic mitral annular velocity; E/e', ratio of E to e'; E/LS, ratio of E to LS; LS, absolute value of peak longitudinal strain.

Prediction of Elevated LV Filling Pressure

The area under the ROC curve of E/LS for distinguishing elevated LV filling pressure was significantly larger than that of E/A, and tended to be larger than that of E/e' (Figure 3). E/LS distinguished the patients with a sensitivity of 72% and a specificity of 88% using the best cutoff value of 680 cm/s. The additional benefit of E/e' and E/LS to identify patients with elevated LV filling pressure is shown in Figure 4. A significant improvement was obtained by the addition of E/e' (P<0.01). Also, the addition of E/LS improved the diagnostic utility of the model containing E/A and E/e' (P<0.001).

Analysis in Subgroups According to LVEF

The e' did not significantly correlate with τ (r=−0.12, P=0.52) in the subgroup with reduced LVEF (n=30, LVEF: 39 $\pm$ 8%), whereas e' significantly, but weakly, correlated with τ (r=−0.32, P<0.05) in the subgroup with preserved LVEF (n=47, LVEF: 70 $\pm$ 9%). LS significantly correlated with τ in both subgroups with reduced LVEF (r=−0.40, P<0.05) and with preserved LVEF (r=−0.32, P<0.05). In both subgroups with reduced LVEF and with preserved LVEF, there were modest correlations between LVMDP and E/A (r=0.58, P<0.01; r=0.49,

Figure 5. Receiver-operating characteristic curves for E/LS, E/e', and E/A for distinguishing patients with elevated LV filling pressure in patients with reduced LVEF and those with preserved LVEF. AUC, area under the curve; E/A, ratio of early-diastolic LV inflow velocity (E) to atrial-systolic velocity (A); e', early-diastolic mitral annular velocity; E/e', ratio of E to e'; E/LS, ratio of E to LS; LS, absolute value of peak longitudinal strain; LVEF, left ventricular ejection fraction.

$P < 0.001$) and between LVMDP and E/e' ($r = 0.39$, $P < 0.05$; $r = 0.56$, $P < 0.001$). In contrast, E/LS correlated modestly with LVMDP in the preserved LVEF group ($r = 0.55$, $P < 0.001$) and correlated strongly in the reduced LVEF group ($r = 0.73$, $P < 0.001$). The ROC curves for distinguishing elevated LV filling pressure are shown in **Figure 5**. In both groups, the area under the ROC curve for E/LS tended to be larger than those for E/A and E/e'.

Reproducibility

Mean intraobserver differences for LS, LSRE, LSRIVR, CS, CSRE, and CSRIVR were 6%, 10%, 17%, 6%, 8%, and 20%, respectively. Mean interobserver differences for LS, LSRE, LSRIVR, CS, CSRE, and CSRIVR were 7%, 13%, 19%, 7%, 11%, and 23%, respectively.

Discussion

One of the major findings in the present study was that e' significantly but weakly correlated with τ , and E/e' modestly correlated with LVMDP. E/LS correlated well with LVMDP, which distinguished patients with elevated LV filling pressure better than E/A or E/e'.

Conventional Echocardiographic Parameters

Several Doppler measurements are currently used to evaluate LV relaxation and filling pressure. Mitral annular velocity is reported to be less affected by loading conditions and better reflects LV relaxation than inflow E/A.^{19–21} E is influenced by filling pressure as well as inversely altered by changes in relaxation, and correcting E by e' for the influence of relaxation improves its relation with filling pressure.²⁰ E/e' is thus considered to accurately estimate filling pressure in a broad spectrum of patients with preserved or reduced LVEF. According to the results of several studies,^{22–24} the American Society of Echocardiography recommended not to use e' and E/e' in

patients with significant mitral annular calcification, surgical rings, mitral stenosis, prosthetic mitral valves, moderate to severe primary mitral regurgitation, and constrictive pericarditis.¹ Subsequently, Geske et al found no correlation between mean left atrial pressure and E/e' in patients with symptomatic hypertrophic cardiomyopathy.² Mullens et al also reported no significant correlation between pulmonary artery wedge pressure and E/e' in decompensated patients with advanced systolic heart failure.³ Based on those results, it is widely believed that taking patient characteristics into consideration is necessary when e' and E/e' are used. Also, almost all studies that validated e' and E/e' were performed in a single center. Therefore, we assessed these parameters against invasively measured LV relaxation and filling pressure in a multicenter study in which the Doppler echocardiographic measurements were standardized. We examined 77 patients with various cardiac diseases after excluding patients with the known restrictions mentioned earlier. As a result, e' significantly but only very weakly correlated with τ , and E/e' correlated modestly with LVMDP, which differed from the results of some previous studies possibly because of the differences in patients' characteristics. These findings suggest that these parameters should not be used as single quantitative parameters to estimate relaxation and filling pressure.

Estimation of LV Relaxation Using STE-Derived Parameters

It was previously considered that strain rate during the IVR period and in the early-diastolic phase correlated with τ . However, in our study LV peak global strain tended to better correlate with τ than did these early-diastolic parameters. The myocardial wall stores energy in the form of elastic recoil during systole and this energy is released when the myocardium relaxes.²⁵ Although τ is widely accepted as a gold standard measure of LV relaxation, it can be affected by contractile properties. In fact, several researchers reported an inverse correlation between τ and LV contractility.^{12,26} Contraction

and relaxation are thus physiologically coupled. Although early-diastolic wall deformation may reflect a pure relaxation property, it can be associated with τ through contractility more strongly than through relaxation. If so, because contractility has a closer relationship with peak strain, peak global strain could correlate better with τ than would the early-diastolic parameters.

In addition to the underlying physiology, there may be a methodological reason for the advantage of peak global strain over the strain rate during early diastole. Because STE directly extracts a time-strain curve by tracking the echo-dense speckles frame-by-frame and because strain rate is calculated by differentiating the strain by time, peak global strain is a more robust parameter than strain rate when measured by STE. Although global strain rate during the IVR period is theoretically a suitable marker to estimate LV relaxation, because relaxation and the resulting LV pressure decay occur during the IVR period,⁶ accurate measurement of strain rate during the relatively short duration requires an adequate image with high temporal resolution, which is sometimes difficult to obtain during a clinical examination.

We also consistently found that the strain/strain rate in the longitudinal direction tended to correlate with τ better than in the circumferential direction. This may have resulted in part from the vulnerability of the longitudinally-orientated inner myocardial fibers in the early stage of diastolic dysfunction.²⁷ Ishizu et al demonstrated in an animal study that LS, but not CS, significantly correlated with τ in the presence of LV hypertrophy induced by hypertension.²⁸ Because a large number of our patients had hypertension, not circumferential but longitudinal indices could detect subclinical abnormalities in LV relaxation.

Estimation of LV Filling Pressure Using STE-Derived Parameters

In the present study, E/LS correlated with LVMDP most strongly among E/A, E/e', and various STE-derived parameters. As is the case with E/e', the parameter that accurately reflects LV relaxation should be the most suitable denominator for this type of index. Therefore, LS correlated most strongly with τ , and E/LS correlated most strongly with LVMDP. Global LS is now widely used as a prognostic marker of various cardiac diseases,^{29–31} and E/LS can be easily evaluated in routine examinations as a parameter of LV filling pressure.

Together with SR_{IVR} as a parameter of LV relaxation, E/SR_{IVR} has been reported to be an accurate marker of LV filling pressure.⁶ However, we did not find strong correlations between the LVMDP and any E/SR_{IVR} measurements. In addition to the difficulty of accurately measuring SR_{IVR}, the low absolute value of SR_{IVR} is unsuitable as a denominator for indices such as E/e'. SR_{IVR} values were considerably low and it was necessary to correct the denominator of E/SR_{IVR} in patients with extremely low SR_{IVR} values as mentioned in the Methods section. Therefore, the instability of E/SR_{IVR} as an index would have decreased the correlations between LVMDP and E/SR_{IVR}.

Influence of LVEF on the Correlation Between LV Filling Pressure and STE-Derived Parameters

Because of the problem of pseudonormalization of LV inflow, E/A is the recommended indicator of elevated LV filling pressure only in patients with reduced LVEF, but not preserved LVEF.¹ In contrast, E/e' is considered a surrogate marker of LV filling pressure in patients with preserved LVEF.¹ Our results showed that the diagnostic ability of E/LS for distin-

guishing elevated LV filling pressure tended to be superior to E/A and E/e' in both groups. Therefore, E/LS could be a useful parameter for LV filling pressure regardless of LVEF.

Study Limitations and Clinical Implications

There are several limitations to be acknowledged in this study. First, echocardiographic studies were not performed simultaneously with cardiac catheterization, which may have created differences in loading conditions. However, a previous study showed little difference in the results of the subgroup simultaneously measured echocardiographic and invasive data, when compared with results for the entire population.² Second, although 49% of the 77 patients had impaired LV relaxation, only 33% had heart failure of New York Heart Association class II or more and only 23% had elevated LV filling pressure, partly because LV pressures were measured after stabilizing loading conditions in most of the heart failure patients, which could have weakened the correlation between filling pressure and the echocardiographic parameters. Therefore, the correlation coefficients for all echocardiographic parameters were relatively low in this study population as compared with previous studies. However, even in such a patient population as in the present study, E/e' modestly correlated whereas E/LS strongly correlated with LV filling pressure, and the correlation of E/LS was statistically significantly better than that of E/e'. Furthermore, the addition of E/LS improved the diagnostic utility of the model containing E/A and E/e' for estimating elevated LV filling pressure. In the clinical setting, echocardiography plays an important role in the estimation of LV filling pressure in patients with slightly elevated LV filling pressure who are suspected to have heart failure, but not in healthy subjects or in patients with obvious lung congestion. Therefore, our results might have important clinical implications in the diagnosis of heart failure in such a patient population. Accordingly, E/LS might have an incremental diagnostic value for estimating LV filling pressure in patients with intermediate filling pressure regardless of LVEF. However, we should avoid estimating the LV filling pressure with too much confidence using a single echocardiographic parameter such as E/e'. A larger study is needed to confirm the feasibility and clinical usefulness of E/LS in the future.

Conclusions

Tissue Doppler-derived e' weakly correlated with τ , whereas STE-derived longitudinal parameters tended to better correlate with τ than e'. Although E/e' only modestly correlated with LVMDP, STE-derived longitudinal parameters, especially E/LS, strongly correlated with LVMDP, which had an incremental diagnostic value for estimating LV filling pressure.

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Disclosures

None.

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