

Evaluation of Left Ventricular Diastolic Function in Atrial Fibrillation Using Dual Doppler System

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Left ventricular (LV) diastolic function is closely related to the symptoms, exercise tolerance, and prognosis of patients with heart failure. Evaluation of LV diastolic function is also needed in patients with atrial fibrillation (AF); however, it is extremely challenging because of the lack of atrial systolic transmitral flow wave and the irregularity of Doppler parameters caused by irregular R-R intervals. A newly developed ultrasound machine (HI VISION Preirus*) has the capability of simultaneous recording of pulsed Doppler waveforms at 2 different locations (Dual-Doppler System). We evaluated the usefulness of the ratio of the early diastolic transmitral flow velocity (E) to the mitral annular velocity (e') calculated from simultaneously recorded E and e' in AF¹⁾.

Key Words: Atrial fibrillation, Diastolic function, Dual Doppler system

1. Left ventricular diastolic function in patients with atrial fibrillation

Atrial fibrillation (AF) is the most frequent form of arrhythmia encountered in the clinical practice of cardiovascular medicine. The prevalence of AF markedly increases with age, affecting more than 5% of patients aged 65 years and older²⁾. Since AF is a significant factor that increases the risk of heart failure and cardiogenic cerebral embolism, and these conditions influence the prognosis of patients, its management is extremely important. For these reasons, evaluation of left ventricular (LV) function in AF patients is clinically important. However, since AF produces ventricular irregular arrhythmia, and preload and post extrasystolic potentiation vary beat by beat, it is difficult to accurately evaluate LV function. In the presence of sinus rhythm, LV diastolic function can be examined by evaluating the atrial contribution to left ventricular filling, but such evaluation is difficult in AF patients because of the absence of mechanical atrial contraction. The use of tissue Doppler echocardiography has been proposed as a non-invasive method for assessing LV diastolic function in AF patients. Sohn et al.³⁾ reported that E/e' , the ratio of early diastolic transmitral flow velocity (E) to early diastolic mitral annular velocity (e'), correlated well with the LV filling pressure in AF patients, and Okura et al.⁴⁾ reported that E/e' was a strong predictor for heart failure in AF patients. However, these studies measured E and e' during different heartbeats and calculated the mean values for analysis, which is a limitation of these studies.

Recently, a Dual-Doppler system (incorporated in the HI VISION Preirus*, a diagnostic ultrasound system

manufactured by Hitachi Medical Corporation) has been developed which allows simultaneous recording of pulsed Doppler waveforms in two locations. This system can measure transmitral flow velocity (E) and mitral annular velocity (e') simultaneously, and thus E and e' during the same heartbeat. Therefore, single-beat E/e' can be calculated, overcoming the limitation of the above studies (Figure 1).

2. Methods

The purpose of this study was to evaluate the usefulness of E/e' in AF patients by comparing echocardiographic variables obtained using the Dual-Doppler system with the brain natriuretic peptide (BNP) level—a blood biochemical marker for heart failure—and with pulmonary capillary wedge pressure (PCWP) measured by heart catheterization.

The study subjects consisted of 56 patients with chronic AF (40 male, mean age 66 ± 11 years). The BNP level was measured in all patients, 21 of whom (mean age 72 ± 6 years) underwent right heart catheterization to measure PCWP together with echocardiographic examination. Patients were excluded if they had severe valvular heart disease, congenital heart disease, LV systolic dysfunction (LV ejection fraction $<50\%$), renal dysfunction, or LV regional wall motion abnormality at the basal lateral or septal segment. As echocardiographic variables, LV dimensions, LV mass index, LA volume index, LV ejection fraction (LVEF), the deceleration time of E-wave (DT), E, e' (lateral

and septal), and E/e' were determined. The E/e' value was calculated by three different methods: 1) mean E/e' was the average calculated from simultaneously recorded E and e' in 30 sec; 2) single-beat E/e' was calculated from simultaneously recorded E and e' when the preceding R-R interval (RRp)/pre-preceding R-R interval (RRpp) was nearly equal to 1; and 3) conventional E/e' was calculated from the average of E and e' in three randomly selected consecutive cardiac cycles. The echocardiographic variables were examined for the relationships with the BNP level and PCWP.

3. Results

Regarding clinical characteristics, 21 patients had hypertensive heart disease and 19 patients had lone AF. In the NYHA functional classification, no patients were classified as Class IV, but many were classified as Class I or II. The mean heart rate was 74 beats/min. The heart rate was fairly controlled in most of the patients. The mean BNP level was 295 pg/ml. Regarding echocardiographic variables, the mean LV mass index was slightly high (120 g/m²). The LA volume index was 43 ml/m², indicating that many patients had an enlarged left atrium. The LV ejection fraction, which was 60%, was preserved (Table 1).

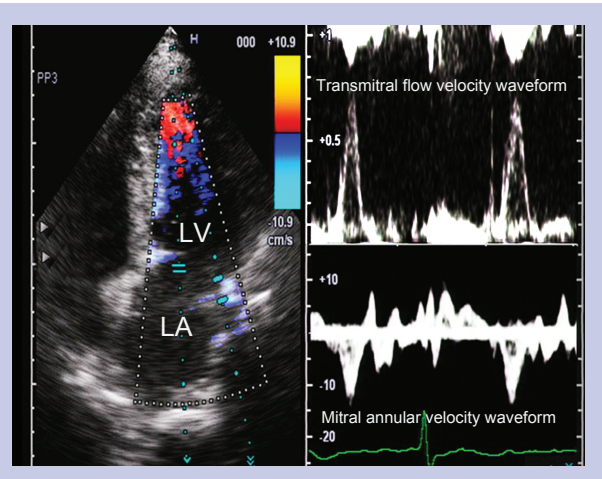


Figure 1
Simultaneous recording of E and e' using a Dual-Doppler system

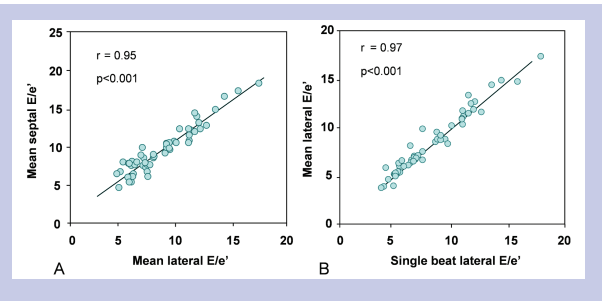


Figure 2
Relationships between mean lateral E/e' and mean septal E/e' or single-beat lateral E/e'
(Extracted and modified from 1))

Firstly, we examined the difference in E/e' when e' was measured at different sites. As shown in Figure 2A, there was a good correlation between the septal E/e' and the lateral E/e' . As shown in Figure 2B, there also was a good correlation between the mean lateral E/e' and the single-beat lateral E/e' .

Secondly, we examined the relationship of the BNP level—a biochemical marker of heart failure—with echocardiographic variables. The BNP level was affected by age, LV mass index, E , DT , E/e' , and pulmonary artery systolic pressure estimated from tricuspid regurgitation. A multivariate regression analysis identified the LV mass index and E/e' as significant factors, of which E/e' correlated the best with the plasma BNP level. Then we examined which method of e' measurement could predict a BNP level of ≥ 200 pg/ml with high sensitivity and specificity by the receiver–operating characteristic (ROC) curve. The areas under the curves (AUCs) for the mean septal E/e' , mean lateral E/e' and single-beat E/e' exceeded 0.9, but the AUC for the mean conventional E/e' measured during different beats was slightly low (0.84). A single-beat E/e' of ≥ 9.3 predicted a plasma BNP level of ≥ 200 pg/ml with a sensitivity of 85% and a specificity of 87%, indicating that the single-beat E/e' may be a useful index comparable to the mean E/e' (Figure 3). Finally, we examined the relationships of PCWP with

n = 56	
Diagnosis	
Hypertensive heart disease	21
Ischemic heart disease	8
Cardiomyopathy	8
Lone atrial fibrillation	19
NYHA functional class	
I	28
II	18
III	10
IV	0
Age (yrs)	66±11
Sex (male/female)	40/16
Heart rate (beats/min)	74±10
Systolic blood pressure (mm Hg)	129±15
Diastolic blood pressure (mm Hg)	72±10
BNP (pg/ml)	295±243
Echocardiographic data	
End-diastolic LV dimension (mm)	51±6
End-systolic LV dimension (mm)	34±7
Interventricular septal thickness (mm)	10±3
LV posterior wall thickness (mm)	10±2
LV mass index (g/m ²)	120±43
LA volume index (ml/m ²)	43±17
Pulmonary artery systolic pressure (mm Hg)	28±8
IVC dimension (mm)	14±4
LV ejection fraction (%)	60±6
E (cm/s)	79.9±12.5
DT (ms)	129.6±30.3
Mean lateral e' (cm/s)	9.2±2.6
Mean lateral E/e'	8.9± 3.1
Conventional lateral E/e'	8.4±3.4
Single-beat lateral E/e'	8.8±3.2
BNP = brain natriuretic peptide; DT = deceleration time of E wave; E = early diastolic transmitral flow velocity; e' = early diastolic mitral annular velocity; IVC = inferior vena cava; LA = left atrium; LV = left ventricle; NYHA = New York Heart Association.	

Table 1
Clinical characteristics (Extracted and modified from 1))

echocardiographic variables and with the BNP level. The PCWP did not correlate with the LV mass index, LA volume index, E, or DT, but correlated well with E/e' and BNP. Compared with the conventional E/e', the single-beat E/e' correlated better with PCWP (Table 3). The single-beat E/e' of ≥ 11 could predict PCWP of ≥ 15 mmHg with a sensitivity of 90% and a specificity of 90%.

4. Discussion

We used a newly developed Dual-Doppler system to simultaneously record transmitral flow velocity (E) and mitral annular velocity (e') in chronic AF patients to calculate the single-beat E/e', and reported its usefulness for the first time in the world.

It is known that the beat-to-beat variation in LV systolic function of AF patients is associated with the Frank-Starling mechanism during the preceding R-R interval and with the interval-force relationship during the pre-preceding R-R interval. However, few studies have reported on the beat-to-beat variation in LV diastolic function. In an experiment using dogs that underwent thoracotomy under anesthesia⁵⁾, it was reported that LV relaxation depended on the systolic LV pressure during the preceding heartbeat and was determined by the filling time of the preceding beat. This finding suggests that LV diastolic function is also influenced by the preceding R-R interval in AF patients. Furthermore, atrial systolic waves are lost in AF patients; therefore it is difficult to evaluate LV diastolic function based on transmitral flow velocity. In comparison, mitral annular velocity (e') is less influenced by preload; therefore an increase in E/e' could reflect an elevation of the LV filling pressure, and this parameter may be useful for evaluating LV diastolic function in AF patients. Sohn et al.³⁾ has shown that E/e' correlates well with LV filling pressure even in AF patients, and Okura et al.⁴⁾ has reported that E/e' could be a prognostic factor in patients with nonvalvular AF. However, these studies measured E and e'

during different heartbeats, and calculated the E/e' value from two values recorded under different loading conditions because the R-R interval was irregular in AF patients. Theoretically, this method is not accurate, which is a limitation of these studies. In the present study, we overcome this limitation by using a Dual-Doppler system to record transmitral flow velocity and mitral annular velocity simultaneously.

During sinus rhythm, the plasma BNP level correlates with the end-diastolic LV pressure⁶⁾, and reflects the prognosis of patients with heart failure. Therefore, this parameter is often used for managing patients with various heart diseases. The results of the present study showed that the mean value of simultaneously measured E/e' in chronic AF patients correlated well with the plasma BNP level. This finding indicates that the E/e' value measured in AF patients by this procedure reflects the plasma BNP level and that this parameter is useful for evaluating heart failure and may predict not only the severity of LV diastolic function but also the prognosis of AF patients.

Previous studies examining E/e' used e' values, or the mean of the e' values measured on the lateral or septal sides of the mitral annulus. However, few studies have examined which side of the annulus should be used to measure e' to evaluate LV diastolic function. Some researchers recommend that e' be measured on the lateral side rather than the septal side in patients after thoracotomy⁷⁾. Lateral e' was generally higher than the septal e'; therefore changes are more sensitively detected

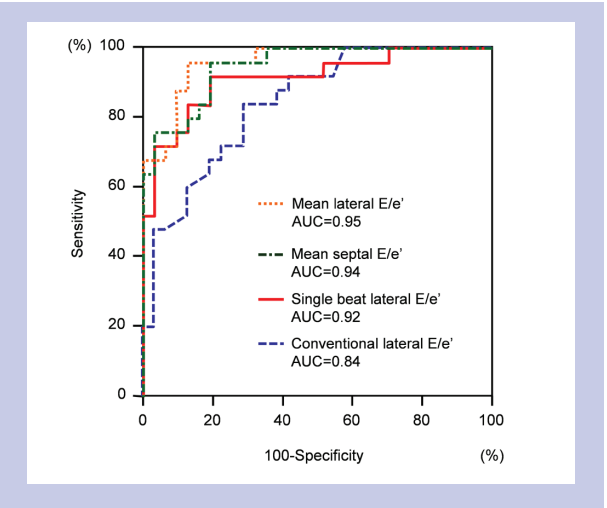


Figure 3: Receiver-operator characteristic (ROC) analysis of various E/e' values for differentiating plasma BNP

	Univariate Regression Analysis		Multivariate Regression Analysis	
	r	p Value	t	p Value
Age	0.39	0.01	—	NS
Heart rate	—	NS	—	NS
LV ejection fraction	—	NS	—	NS
LV mass index	0.40	<0.01	2.6	<0.01
LA volume index	—	NS	—	NS
E	0.37	<0.01	—	NS
DT	-0.28	0.035	—	NS
Single-beat lateral E/e'	0.84	<0.001	10.8	<0.001
PASP	0.39	<0.01	—	NS
IVC dimension	—	NS	—	NS

PASP = pulmonary artery systolic pressure; other abbreviations as in Table 1.

Table 2: Determinants of BNP (Extracted and modified from 1))

	r	p Value
LV mass index	—	NS
LA volume index	—	NS
E	—	NS
DT	—	NS
Conventional lateral E/e'	0.57	<0.01
Single-beat lateral E/e'	0.74	<0.001
BNP	0.56	<0.01

Abbreviations as in Table 2.

Table 3: Determinants of PCWP (Extracted and modified from 1))

on the lateral side. However, mitral annular motion on the lateral side is greatly influenced by the swinging motion of the heart as a whole, and in this respect, mitral annular motion on the septal side is easier to align to the Doppler beam direction and is less affected by the motion of the heart as a whole. The E/e' value measured in this study correlated well with the plasma BNP level regardless of the site of e' measurement, but the correlation coefficient was higher for the lateral side than the septal side. The subjects in this study did not include patients with regional wall motion abnormalities on the lateral side or those with marked mitral annular calcification. In such patients, however, care should be taken as different results are expected⁸⁾.

In this study, we simultaneously recorded transmitral flow velocity and mitral annular velocity for 30 sec and performed statistical analysis using the mean E/e' calculated per heartbeat. However, 30-sec recording and calculation of the mean E/e' is unfeasible in clinical practice, unless automatic measurement becomes possible. Therefore, we conducted a similar analysis using single-beat E/e' when the RRp/RRpp (preceding R-R interval/pre-preceding R-R interval) was nearly equal to 1, which is reported to reflect the average LV function in AF patients. The E/e' value calculated by this method had an extremely good correlation with the mean E/e' over 30 sec, and a good correlation with PCWP and plasma BNP level.

*Preirus, HI VISION Preirus are registered trademarks or trademarks of Hitachi Medical Corporation in Japan and other countries.

5. Conclusion

Through the present study we have established echocardiographic parameters useful for assessing LV diastolic function in AF patients, which has been considered difficult so far. The Doppler echocardiographic parameters defined in this study could allow noninvasive, accurate evaluation of LV diastolic function in AF patients and provide critical information for decision-making on treatment strategies. The parameters could also be useful for evaluating treatment outcomes and predicting prognosis.

References

- 1) Kusunose K, et al. : Clinical utility of single-beat E/e' obtained by simultaneous recording of flow and tissue Doppler velocities in atrial fibrillation with preserved systolic function. *JACC Cardiovasc Imaging*, 2 : 1147-56, 2009.
- 2) Gersh BJ, et al. : The changing epidemiology and natural history of nonvalvular atrial fibrillation : clinical implications. *Trans Am Clin Climatol Assoc*, 115 :149-60, 2004.
- 3) Sohn DW, et al. : Mitral annulus velocity in the evaluation of left ventricular diastolic function in atrial fibrillation. : *J Am Soc Echocardiogr*, 12 : 927-31, 1999.
- 4) Okura H, et al. : Tissue Doppler-derived index of left

ventricular filling pressure, E/E', predicts survival of patients with non-valvular atrial fibrillation. *Heart*, 92 : 1248-52, 2006.

5) Tabata T, et al. : Determinants of LV diastolic function during atrial fibrillation : beat-to-beat analysis in acute dog experiments. *Am J Physiol Heart Circ Physiol*, 286 : H145-52, 2004.

6) Taylor JA, et al. : B-type natriuretic peptide and N-terminal pro B-type natriuretic peptide are depressed in obesity despite higher left ventricular end diastolic pressures. *Am Heart J*, 152 : 1071-6, 2006.

7) Hadano Y, et al. : Ratio of early transmitral velocity to lateral mitral annular early diastolic velocity has the best correlation with wedge pressure following cardiac surgery. *Circ J*, 71 : 1274-8, 2007.

8) Soeki T, et al. : Mitral inflow and mitral annular motion velocities in patients with mitral annular calcification : evaluation by pulsed Doppler echocardiography and pulsed Doppler tissue imaging. *Eur J Echocardiogr*, 3 : 128-34, 2002.