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Determination of Diastolic Dysfunction Cut-Off Value by Tissue Doppler Imaging in Adults 70 Years of Age or Older: A Comparative Analysis of Pulsed-Wave and Color-Coded Tissue Doppler Imaging

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ABSTRACT

Background and Objectives: The cut-off value of diastolic dysfunction by tissue Doppler imaging (TDI) is affected by aging and modalities used (pulsed-wave vs. color-coded). The purpose of this study was to investigate the diastolic function of healthy elderly people and to determine the appropriate cut-off value of diastolic dysfunction in elderly individuals. **Subjects and Methods:** Healthy volunteers (n=76) and patients with hypertension (n=51) aged ≥ 70 years underwent 2-dimensional and Doppler echocardiography. Mitral annulus velocities of TDI were measured at septal and lateral sites using the pulsed-wave and color-coded modalities. The appropriate cut-off value of diastolic dysfunction for healthy elderly individuals was defined as the lower limit of the 95% confidence interval for early diastolic mitral annulus velocity (Ea). **Results:** The mean septal and lateral Ea were 6.5 ± 1.5 and 8.3 ± 1.7 cm/s, respectively, by pulsed-wave TDI, and 6.1 ± 1.4 and 7.9 ± 1.7 cm/s, respectively, by color-coded TDI. The cut-off values for diastolic dysfunction were as follows: septal and lateral Ea were 6.1 and 7.9 cm/s by pulsed-wave TDI, and 5.7 and 7.5 cm/s by color-coded TDI, respectively. When the group was stratified by gender, Ea was significantly lower in women than men. **Conclusion:** When interpreting diastolic function as measured by TDI in elderly subjects, different cut-off values should be considered based on the TDI modality, annulus site, and gender. (**Korean Circ J 2011;41:137-142**)

KEY WORDS: Heart failure, diastolic; Echocardiography; Aging.

Introduction

It is important to assess diastolic function in the elderly population because diastolic dysfunction is responsible for heart failure, especially heart failure with preserved left ventricular

ejection fraction.¹⁾

The differentiation of pathologic diastolic dysfunction is more difficult in the context of the physiologically decreased diastolic function in elderly subjects because impairment of left ventricular diastolic function is related to the normal aging process as well as pathologic disorders.²⁻⁸⁾ Hence, appropriate cut-off values of diastolic function in the elderly population are needed to discriminate normal healthy diastolic function from true pathologic diastolic dysfunction.

Although there are many reports suggesting a reference range for tissue Doppler imaging (TDI) velocities of the mitral annulus, the difference between pulsed and color tissue Doppler-derived velocities for the mitral annulus has not been systematically investigated. By measuring both pulsed-wave and color-coded TDI in the same individual, we evaluated the difference in left ventricular mitral annulus velocity between the two TDI modalities.

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Subjects and Methods

Subjects

We prospectively enrolled healthy elderly subjects and patients with hypertension who were all aged ≥ 70 years. The healthy subjects were recruited from volunteers among relatives of hospital personnel or referrals for consultation in preoperative evaluation. Inclusion criteria were the presence of normal findings on 2-dimensional echocardiography for cardiac chamber dimension, left ventricular wall thickness, left ventricular ejection fraction, and left ventricular wall motion. The presence of hypertension, known congestive heart failure or symptoms, diabetes mellitus, coronary artery disease, cardiac arrhythmia, valvular heart disease, and obesity were exclusion criteria for healthy subjects. Fifty-one patients who had an evidence of hypertrophy by electrocardiography while taking concomitant anti-hypertension medication were enrolled in the hypertension group.

Systemic blood pressure, heart rate, height and weight were measured at the time of echocardiographic examination. A 12-lead electrocardiogram was obtained for each subject before or at the time of echocardiographic examination to exclude arrhythmia and to detect ST-segment changes, Q waves, or abnormal T waves that represent ischemic heart disease. Informed consent was obtained from each subject.

Echocardiography

Echocardiography was performed by one experienced investigator using a Hewlett-Packard Sonos 7500 (Hewlett Packard, Palo Alto, CA, USA) and IE 33 ultrasound system with a 2.5-MHz transducer. The investigator was blinded to the subjects' clinical information, including blood pressure.

Left ventricular ejection fraction was estimated by the quantitative biplane Simpson's method.⁹ Left ventricular mass and left atrial volume were calculated from M-mode and 2-dimensional measurements, respectively, as previously described.¹⁰ Left ventricular internal dimension, interventricular septum, and posterior wall thickness were measured in end-diastole and end-systole according to the recommendations of the American Society of Echocardiography.¹⁰

Pulsed-wave Doppler transmitral velocities were recorded from the apical 4-chamber view by placing the sample volume between the leaflet tips in the center of the flow stream. Early diastolic mitral flow velocity (E), late diastolic mitral flow velocity (A), the ratio of early to late diastolic mitral flow velocity (E/A), and deceleration time were measured. From the apical 4-chamber view, the pulmonary venous flow velocities were recorded by placing the sample volume approximately 1 cm into the right upper pulmonary vein. The pulmonary venous peak systolic (PVs) and peak diastolic (PVd) flow velocities, the ratio of peak systolic-to-diastolic flow velocities (PVs/PVd), and peak reversal flow velocity due to left atrial con-

traction (PVa) were recorded.

All patients underwent repeated echocardiography on the same day to obtain pulsed-wave and color-coded TDI. In pulsed-wave TDI, velocities were obtained by placing the TDI cursor at the mitral annulus. In color-coded TDI, velocities were measured at the mitral annulus by superimposition of wall motion velocity on the 2-dimensional echocardiographic imaging using velocity color coding. Mitral annulus velocities were measured at septal and lateral sites of the mitral annulus. The peak systolic (Sa), early (Ea), and late (Aa) diastolic velocities were measured on-line at a sweep speed of 100 mm/s. To obtain the best quality recordings, the filter settings and gains were adjusted at the minimal optimal level to minimize noise and to eliminate the signals produced by the transmitral flow. The echocardiograms were stored digitally and analyzed off-line. A mean of 3 consecutive cycles was used to calculate all echocardiography Doppler parameters.

Statistics

Statistical Package for the Social Sciences (SPSS, version 17, SPSS Inc., Chicago, IL, USA) was used for data management and statistical analysis. Results are presented as mean \pm SD. Comparisons of mitral annulus velocities (Sa, Ea, Aa) between pulsed-wave and color-coded TDI were analyzed with the paired t-test. The relationship of transmitral annulus velocities (Sa, Ea, Aa) between pulsed-wave and color-coded TDI were shown using Pearson's correlation coefficients. Comparisons of mitral annulus velocities according to gender were performed by the student t-test.

To determine the appropriate cut-off value of diastolic dysfunction for healthy elderly individuals, the lower limit of the 95% confidence interval (CI) for Ea was used. A p of < 0.05 was considered as statistically significant. We also evaluated whether these cut-off values were applicable to the detection of hypertensive patients who have diastolic dysfunction.

Results

Clinical and echocardiographic characteristics

We enrolled a total 127 subjects (76 healthy volunteers and 51 patients with hypertension). All subjects had adequate echocardiographic images for analysis. Table 1 summarizes demographic data along with 2-dimensional and conventional Doppler echocardiographic characteristics.

Tissue Doppler echocardiographic characteristics

All values of mitral annulus velocities measured by color-coded TDI were lower than those measured by pulsed-wave TDI at both the septal and lateral sites (Table 2). The relationship of each Sa, Ea, and Aa between pulsed-wave and color-coded TDI showed a positively strong and statistically significant correlation (septal Sa, $r=0.653$; lateral Sa, $r=0.682$; septal

Table 1. Clinical and echocardiographic characteristics of the two groups

	Normal (n=76)	Hypertension (n=51)	P
Clinical baseline characteristics			
Age (years)	74±4	73±3	0.083
Male sex (n, %)	34 (44.7)	21 (41.2)	0.691
BMI (kg/m ²)	22.5±2.8	24.4±3.0	<0.001
SBP (mmHg)	119±11	134±11	<0.001
DBP (mmHg)	76±7	81±6	<0.001
Heart rate (beats/min)	69±13	64±11	0.018
2-dimensional echocardiographic characteristics			
LV EF (%)	66±2	65±3	0.258
LVIDd (mm)	44.4±3.8	45.8±4.2	0.050
IVSd (mm)	8.5±1.1	10.2±1.2	<0.001
LVPWd (mm)	8.7±0.9	10.2±1.1	<0.001
LA volume (mL)	45.1±11.6	55.1±16.0	<0.001
LV mass index (g/m ²)	78.0±14.8	93.3±17.6	<0.001
Conventional Doppler echocardiographic characteristics			
Mitral inflow parameters			
E (cm/s)	62.5±15.1	57.9±12.7	0.076
A (cm/s)	81.9±17.2	86.6±14.4	0.112
E/A	0.8±0.2	0.7±0.2	0.004
DT (m/s)	224.7±49.2	278.9±64.4	<0.001
Pulmonary vein flow parameters			
PVs (cm/s)	63.2±14.5	61.0±13.2	0.394
PVd (cm/s)	38.6±10.2	37.7±9.3	0.604
PVs/d (cm/s)	1.8±1.3	1.7±0.4	0.503
PVa (cm/s)	30.4±10.5	28.0±11.7	0.230

BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, EF: ejection fraction, LVIDd: left ventricular internal diameter in diastole, IVSd: interventricular septal diameter in diastole, LVPWd: left ventricular posterior wall diameter in diastole, LA: left atrium, LV: left ventricular, E: early diastolic mitral flow velocity, A: late diastolic mitral flow velocity, E/A: ratio of early to late diastolic mitral flow velocity, DT: deceleration time, PVs: systolic pulmonary vein flow velocity, PVd: diastolic pulmonary vein flow velocity, PVa: atrial reversal pulmonary vein flow velocity

Ea, r=0.841; lateral Ea, r=0.826; septal Aa, r=0.612; lateral Aa, r=0.629, all p<0.001).

Cut-off value for diastolic dysfunction in elderly subjects

Median values of septal Ea and lateral Ea measured by pulsed-wave TDI were 6.5 cm/s (95% CI, 6.1-6.8) and 8.3 cm/s (95% CI, 7.9-8.7), respectively. Median values of septal Ea and lateral Ea measured by color-coded TDI were 6.0 cm/s (95% CI, 5.7-6.4) and 8.0 cm/s (95% CI, 7.5-8.2), respectively (Fig. 1).

Using the lower limit of the 95% CI for Ea, the appropriate cut-off value of diastolic dysfunction in elderly people was determined. In pulsed-wave TDI, the cut-off values of septal Ea and lateral Ea were 6.1 cm/s and 7.9 cm/s, respectively. In

Table 2. Tissue Doppler echocardiographic characteristics in two groups measured by the pulsed-wave and color-coded modalities

		Normal (n=76)	Hypertension (n = 51)	P
Pulsed-wave tissue Doppler image				
Sa (cm/s)	Septal	7.6±1.8	6.4±1.4	<0.001
	Lateral	9.1±2.1	7.6±1.4	<0.001
Ea (cm/s)	Septal	6.5±1.5	4.6±1.2	<0.001
	Lateral	8.3±1.7	6.4±1.7	<0.001
Aa (cm/s)	Septal	9.6±1.8	9.0±1.5	0.098
	Lateral	11.1±2.2	10.6±1.9	0.150
Color-coded tissue Doppler image				
Sa (cm/s)	Septal	7.4±1.5	6.4±1.1	<0.001
	Lateral	8.8±2.0	7.6±1.3	<0.001
Ea (cm/s)	Septal	6.1±1.4	4.6±1.2	<0.001
	Lateral	7.9±1.7	6.1±1.6	<0.001
Aa (cm/s)	Septal	8.9±1.5	8.7±1.5	0.566
	Lateral	10.4±2.4	9.7±1.8	0.080

Sa: systolic mitral annulus velocity, Ea: early diastolic mitral annulus velocity, Aa: late diastolic mitral annulus velocity

color-coded TDI, the cut-off values of septal Ea and lateral Ea were 5.7 cm/s and 7.5 cm/s, respectively. The sensitivity of cut-off values of septal Ea and lateral Ea by pulsed-wave TDI, and septal Ea and lateral Ea by color-coded TDI were 68% and 62%, and 59% and 59%. The specificity of cut-off values of septal Ea and lateral Ea by pulsed-wave TDI, and septal Ea and lateral Ea by color-coded TDI were 90% and 79%, and 81% and 83%. Of the 4 cut-off values, septal Ea by pulse-wave TDI (68% sensitivity, 86% specificity, 0.841 area under the curve) was the useful value to diagnose diastolic dysfunction in the current study, but it did not reach statistical significance (Fig. 2).

Transmitral annulus velocities stratified by gender

When the subjects were stratified by gender, the values of Sa, Ea, and Aa in men showed a trend toward being higher than those in women. This pattern remained regardless of whether color-coded or pulsed-wave TDI was used or of annulus site measured (Table 3).

Discussion

Diastolic dysfunction in healthy elderly people

Heart failure with normal left ventricular ejection fraction is currently accepted as a disease entity, and diastolic dysfunction has a critical role in the clinical presentation of heart failure.¹¹⁾ Moreover, asymptomatic diastolic dysfunction is predictive of future occurrence of heart failure and is related to an increase in all-cause mortality.¹²⁾¹³⁾

Echocardiography has been used for the noninvasive evaluation of diastolic function.¹⁴⁾ Mitral inflow and pulmonary vein

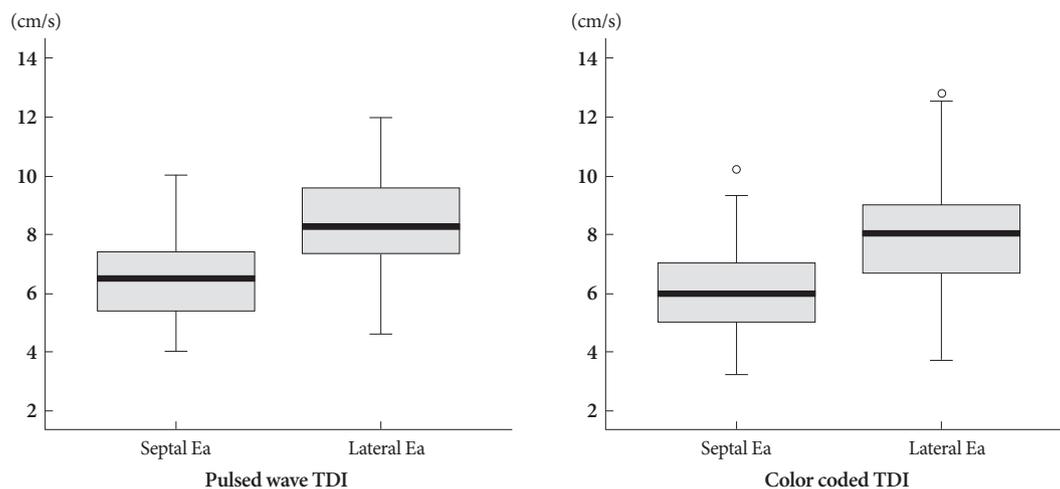


Fig. 1. Box plots showing distributions of septal and lateral Ea measured by pulsed-wave TDI and color-coded TDI, respectively. Box heights reflect interquartile ranges (IQRs). Vertical capped lines (whiskers) extend to most extreme data points within 1.5 IQRs of boxes. Data beyond 1.5 IQRs from boxes are plotted individually. Ea: early diastolic mitral annulus velocity, TDI: tissue Doppler imaging.

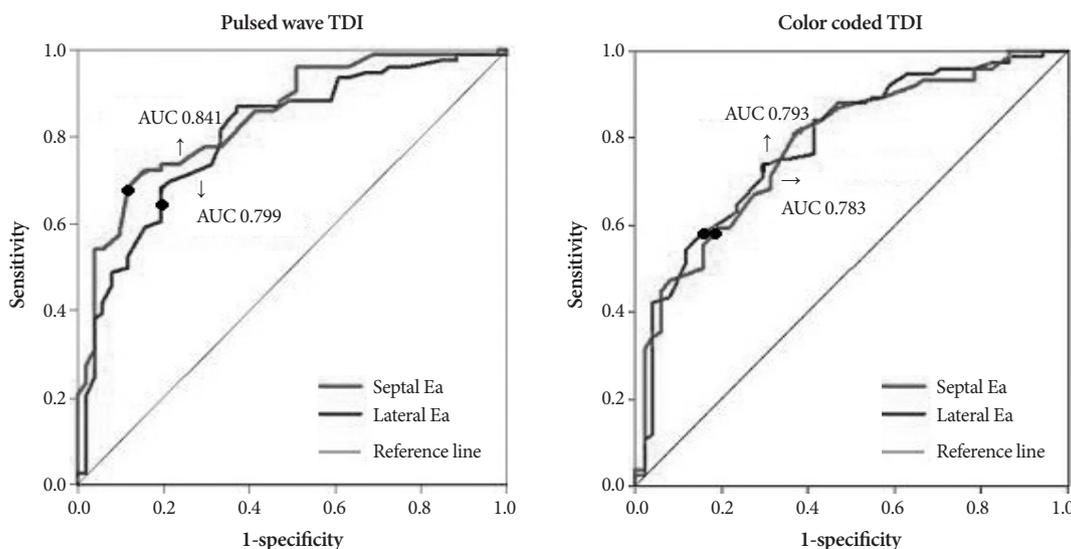


Fig. 2. Receiver-operator characteristic curve of Ea. The point (●) is the sensitivity and specificity of cut-off value, which is defined by the lower limit of the 95% CI for Ea to detect hypertensive patients who have diastolic dysfunction. TDI: tissue Doppler imaging

flow velocities are representative parameters that provide valuable information about diastolic function; however, these parameters are affected by the preload condition. In contrast, the TDI-derived mitral annulus velocity is relatively preload-independent and more accurate for the evaluation of diastolic dysfunction.¹⁵⁻¹⁸⁾ Previous studies have shown that TDI is more sensitive than conventional echocardiography in detecting early myocardial dysfunction before development of left ventricular structural changes.¹⁹⁾²⁰⁾ Munagala et al.²¹⁾ evaluated the age reference range of Doppler diastolic function parameters and from that study, the reference range for septal Ea was defined as 7 cm/s (5th to 95th percentile value=5-11 cm/s) and for lateral Ea as 8 cm/s (5th to 95th percentile value=5-11 cm/s) in normal adults ≥ 70 years. Sohn et al.¹⁶⁾ suggested that the mean septal Ea of the normal elderly group (age range=60-69 years, n=11) was 7.5 ± 1.6 cm/s. In contrast to most previous

studies which presented reference ranges of TDI, we focused on determining a cut-off value for diastolic dysfunction using 2 different TDI modalities and at both sites of the mitral annulus.

Difference between pulsed-wave and color-coded tissue Doppler imaging

In pulsed-wave TDI, the myocardial velocity is obtained from the peak value using the edge of the spectral pulsed Doppler envelopes, while in color-coded TDI, the value represents the mean velocity. Therefore, based on previously published data, it appeared that pulsed-wave TDI yielded higher velocities than color-coded TDI.²²⁾ We performed repeated pulsed-wave and color-coded tissue Doppler echocardiography in the same individual. The results of this study showed a clear difference in mitral annulus velocities according to the TDI modalities. Color-coded TDI derived velocities were lower than

Table 3. Tissue Doppler echocardiographic characteristics stratified by gender

		Men (n=34)	Women (n=42)	P
Pulsed-wave tissue Doppler image				
Sa (cm/s)	Septal	8.1±2.2	7.2±1.2	0.055
	Lateral	9.8±1.8	8.6±2.1	0.010
Ea (cm/s)	Septal	7.0±1.6	6.0±1.2	0.003
	Lateral	8.8±1.7	7.9±1.5	0.018
Aa (cm/s)	Septal	9.9±2.0	9.3±1.7	0.119
	Lateral	11.1±2.3	11.1±2.2	0.929
Color-coded tissue Doppler image				
Sa (cm/s)	Septal	7.9±1.5	6.9±1.5	0.004
	Lateral	8.9±1.8	8.6±2.1	0.524
Ea (cm/s)	Septal	6.6±1.5	5.6±1.2	0.002
	Lateral	8.4±1.8	7.4±1.4	0.006
Aa (cm/s)	Septal	9.2±1.7	8.6±1.4	0.073
	Lateral	10.4±2.3	10.4±2.5	0.915

Sa: systolic mitral annulus velocity, Ea: early diastolic mitral annulus velocity, Aa: late diastolic mitral annulus velocity

pulsed-wave TDI derived velocities with minimum 0.1 to maximum 0.8 cm/s differences. In septal Ea and lateral Ea, color coded TDI values were 0.21 and 0.4 cm/s lower than those of pulsed-wave TDI, respectively. Therefore, the TDI modality must be taken into consideration when interpreting results.

Effect of gender on diastolic function

In many previous studies, there were consistent reports that women were more vulnerable to heart failure with preserved left ventricular systolic function when compared with men, which may underlie the premise that diastolic dysfunction could be more prevalent in women than men.²³⁻²⁵ In Redfield's study, for example, women had higher vascular and left ventricular systolic and diastolic stiffness than men, which might explain the female predominance in heart failure with preserved left ventricular systolic function.²⁶ Considering this gender characteristic, we stratified the normal healthy group by gender. We did not find significant differences in clinical and 2-dimensional echocardiographic findings between men and women. However, we found that women had lower mitral annulus velocities; especially, the Ea of women was significantly lower than that of men. Although hormonal changes are a possible underlying factor for this difference, the mechanism underlying the gender difference in diastolic function is unknown. Thus, additional comparative studies are needed to examine the diastolic function difference between women and men.

Limitations of our study

First, although all the normal subjects in our study did not have any signs or symptoms of heart failure, and had normal

findings on electrocardiogram and on 2-dimensional and conventional Doppler echocardiography, we could not completely exclude asymptomatic coronary artery disease. Second, our study had relatively a small population size to determine the cut-off value for diastolic dysfunction.

Conclusion

Although mitral annular velocity is a valuable index of left ventricular diastolic function, before making interpretations of 'diastolic function,' the normal aging process and gender differences should be considered, and different cut-off values should be applied to the normal elderly population. Moreover, one should keep in mind that myocardial annulus velocities depend on the TDI modality used, whether pulsed-wave or color-coded.

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