ORIGINAL ARTICLE

Left Ventricular Diastolic Function Assessment using the Timing of Mitral Annular and Transmitral Flow Velocities

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ABSTRACT

Background and aims: Evaluation of left ventricular (LV) diastolic function plays an important role in clinical echocardiography. The relationship between mitral annular velocities from tissue Doppler imaging (TDI) (E′ and A′) and mitral inflow velocities (E and A) from Doppler echocardiography (DE) provide additional information about LV filling and diastolic function. The aims of this study are to i) assess the time differences between peak E and peak E′, peak A and peak A′, peak Ar and peak A, and ii) examine the effects of age and gender on these time intervals parameters in normal subjects.

Methods: A total of 117 healthy subjects (age ranging from 22- to 78-years-old) were recruited for a standard of echocardiogram (ECHO). During early diastole, the time intervals from the peak of R-wave on the ECG to the peak of E-wave (R-pE), to the peak of E wave to peak of E′-wave (R-pE′) were measured. During late diastole, the time intervals from the onset of P-wave on the ECG to the peak A-wave (P-pA), to the peak Ar-wave on the pulmonary valve flow (P-pAr), to the peak A′-wave (P-pA′) were measured. Early-diastolic temporal discordance (EDTD) and late-diastolic temporal discordance (LDTD) were calculated as the differences between (R-pE) and (R-pE′), and (P-pA) and (P-pA′), respectively.

Results: The mean EDTD and LDTD were 28.7 ± 10.6 ms and 21.2 ± 15.9 ms, respectively. Similarly, the mean time difference [(P-pA) - (P-pAr)] was 21.5 ± 14.1 ms. EDTD was not associated with age (r=0.15, *p*=NS), while LDTD was inversely correlated with age (r=-0.65, *p*<0.01). No significant differences were found for both EDTD and LDTD between genders.

Conclusion: EDTD and LDTD, the temporal discordances between mitral annulus motion and trans-mitral flow, embody one of the earliest events at early- and late-diastole. Age is not associated with EDTD, but is accompanied by a decline in LDTD. With respect to gender, both EDTD and LDTD are not influenced.

Keywords: LV relaxation, Doppler echocardiography, Pulsed tissue Doppler imaging, Time interval

INTRODUCTION

Evaluation of LV diastolic function plays an important role in patients with heart diseases, particularly in those with heart failure. Echocardiography plays a central role in the assessment of LV diastolic function and filling pressure[1]. Trans-mitral flow (TMF) velocities (early [E] and late [A] diastolic velocities, E/A ratio), pulmonary venous reversal flow velocity (Ar), isovolumic relaxation time (IVRT), flow propagation velocity (Vp), and mitral annular velocities via tissue Doppler imaging (TDI) (early [E′] and late [A′] diastolic myocardial velocities) are commonly used to assess LV diastolic function. The resultant E/E′ ratio and E/Vp ratio are used to estimate left atrial (LA)- and LV-filling pressure[1]. Some studies have found that E′ is a potential marker of LV recoil[2–4]. Recently, some investigators proposed a new method for the assessment of LV diastolic function in terms of time difference between mitral annulus and transmitral flow velocities[2,5,6]. EDTD was defined as the time difference between peak E and E′. Likewise, LDTD was defined as the time difference between peak A and A′.

Peak Ar has previously been shown to coincide with

Table 1. Characteristics of the Population.

Age (years)	43.6 ± 13.4
Male / Female	54 / 63
Height (cm)	164.0 ± 8.61
Weight (kg)	63.7 ± 13.1
Heart rate (beat / min)	73.3 ± 10.6
BSA (m^2)	1.7 ± 0.2
SBP (mmHg)	120.9 ± 12.3
DBP (mmHg)	73.8 ± 8.6

BSA= body surface area; SBP= systolic blood pressure; DBP: diastolic blood pressure

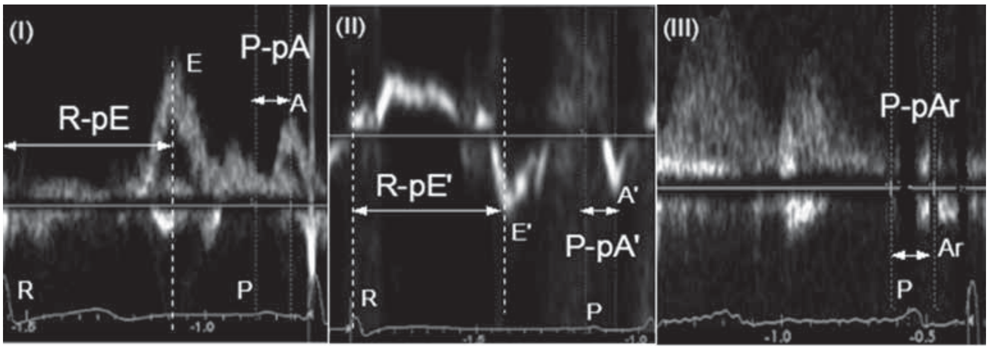

Fig. 1. Transmitral and pulmonary venous pulsed wave echo-Doppler tracings, and tissue Doppler imaging at the basal left ventricular septal wall. (I) R-wave on ECG to the peak E and P-wave on ECG to the peak A for transmitral flow; (II) R-wave on ECG to the peak E′ and P-wave on ECG to the peak A′ for mitral annulus velocities via tissue Doppler imaging; (III) P-wave on ECG to the peak of Ar of pulmonary vein flow.

the peak A′ during late diastole[7], and both peak A′ and Ar precede peak TMF A[8]. As a result, LDTD was diminished with age in normal healthy population. Furthermore, it was also reported that the timing of regional atrial contraction by TDI could be used to accurately estimate corresponding measurements of pulmonary flow reversal Ar in subjects with normal left atrial pressure[9]. Although conventional LV diastolic function parameters (E/A and E/E′) have been shown to change with age, the effects of age and gender on EDTD and LDTD have not been fully studied. We sought to investigate age- and gender-specific changes in EDTD and LDTD in healthy subjects.

METHODS

Subject

A total of 117 healthy volunteers (ranging in age from 22- to 78-years-old; male/female: 54/63) were included in this study. Part of the data of participants has been published recently[34,35]. The baseline characteristics of the population are shown in Table 1. All subjects did not have any history of cardiovascular disease and were not on any cardiovascular medicine. All were in sinus rhythm and distinct P-waves on ECG. The subjects were then divided into five age groups (group 1, 20–30 years; group 2, 31–40 years; group 3, 41–50 years; group 4, 51–60 years, and group 5, > 60 years). This study was approved by the Singhealth Centralised Institutional Review Board and written informed consent was obtained from study participants.

Echocardiography

Echocardiography was performed using IE33, Philips with a 4MHz probe. In each subject, the TMF E- and A-wave (i.e. the sample volume was positioned at the tip of the mitral valve leaflets) on the LV four-chamber view, and pulmonary venous flow reversals (Ar) (i.e. sample volume was positioned in the right superior pulmonary vein) were recorded by pulsed-wave DE. Pulsed-wave TDI was performed (i.e. the sample volume was positioned at the septal mitral annulus from the apical four-chamber view) and the velocity patterns were recorded and peak E′ and A′ were measured. As shown in Figure 1, during early diastole, the time interval from the R on the ECG to peak TMF E-wave (R-pE) and TDI E′ (R-pE′) were measured, and hence EDTD was computed. Likewise, during late-diastole, the time interval from the onset of P-wave on the ECG to the peak TMF A-wave (P-pA), and TDI A′ (P-pA′) were measured, and hence LDTD was computed. Each parameter was measured three times and expressed as an average value.

Statistic Analysis

All data was analysed by SPSS 16.0. Data are expressed as the mean ± standard deviation. The statistical significance of the differences in echocardiographic measurements among age groups was assessed by ANOVA. Linear regression analysis was performed to assess the correlations between EDTD, LDTD, and age. Unpaired student's *t*-tests were used to compare the differences between men and women. A *p*-value less than 0.05 is accepted as statistical significance.

RESULTS

The mean values of R-pE, R-pE′, P-pA, P-pAr, P-pA′ among different age groups are shown in Table 2. The mean differences between R-pE and R-pE′, P-pA and P-pAr, and P-pA and P-pA′ in all subjects were 28.7 ± 10.6 ms, 21.9 ± 14.1 ms, and 21.2 ± 15.9 ms, respectively. The peak E′ preceded peak E in all age groups. R-pE and R-pE′ slightly increased from group 1 to group 4, and decreased in group 5, but not significantly (both ANOVA $p>0.05$). Compared to group 1, EDTD in group 5 significantly decreased (group 1: 32.1 ± 17.8 ms versus group 5: 18.1 ± 24.3 ms, $p<0.05$). EDTD was not significantly associated with age (r=0.15, *p*=NS).

Table 2. Time Differences and EDTD and LDTD in Different Age Groups.

	Group 1 (20–30 years old; n=23)	Group 2 (31–40 years old; n=25)	Group 3 (41–50 years old; n=24)	Group 4 (51–60 years old; n=26)	Group 5 (> 60 years old; n=19)	p-value
R-pE (ms)	520.5 ± 20.9	533.9 ± 27.7	538.7 ± 24.1	539.6 ± 23.2	525.6 ± 18.6	> 0.05
R-pE′ (ms)	488.4 ± 15.4	499.4 ± 21.8	505.0 ± 28.9	510.0 ± 21.8	507.5 ± 35.3	> 0.05
P-pA (ms)	154.7 ± 10.7	152.5 ± 11.1	147.9 ± 10.8	146.2 ± 12.0	139.8 ± 15.9*	< 0.05
P-pA′ (ms)	123.1 ± 10.7	121.1 ± 13.0	129.4 ± 10.6*	130.8 ± 9.8*	131.2 ± 12.8*	< 0.05
P-pAr (ms)	123.3 ± 12.2	122.5 ± 14.4	127.2 ± 10.9*	131.2 ± 11.4*	131.7 ± 11.9*	< 0.05
EDTD= (R-pE) – (R-pE′) (ms)	32.1 ± 17.8	34.5 ± 22.3	33.7 ± 23.1	29.6 ± 16.4	18.1 ± 24.3*	< 0.05
LDTD= (P-pA) – (P-pA′) (ms)	31.6 ± 13.0	31.4 ± 10.9	18.5 ± 12.0*	15.4 ± 11.1*	8.6 ± 10.3*	< 0.05
(P-pA) – (P-pAr) (ms)	31.4 ± 13.9	30.0 ± 10.2	20.7 ± 11.7*	15.0 ± 8.6*	8.1 ± 11.1*	< 0.05

R-pE: peak R-wave on the ECG to the peak of E-wave on the transmitral flow; R-pE′: peak R-wave on the ECG to the peak of E′-wave on the LV septal wall of tissue Doppler imaging; P-pA: the onset of P-wave on the ECG to the peak of A-wave on the transmitral flow; P-pA′: the onset of P-wave on the ECG to the peak of A′-wave on the LV septal wall of tissue Doppler imaging; P-pAr: the onset of P-wave on the ECG to the peak of Ar-wave on the pulmonary venous flow reversal.
[1]Statistic significant difference among group; p< 0.05; *p< 0.05 versus group 1

Table 3. Time Differences and EDTD and LDTD between Men and Women.

	Men (n=54)	Women (n=63)	p-value
R-pE (ms)	533.0 ± 25.0	533.3 ± 23.6	0.944
R-pE′ (ms)	503.5 ± 29.1	505.4 ± 26.7	0.170
P-pA (ms)	146.5 ± 13.4	146.5 ± 12.3	0.999
P-pA′ (ms)	125.1 ± 12.8	126.0 ± 12.1	0.752
P-pAr (ms)	123.8 ± 14.9	125.8 ± 11.3	0.463
EDTD= (R-pE) – (R-pE′) (ms)	29.5 ± 22.3	27.9 ± 22.0	0.088
LDTD= (P-pA) – (P-pA′) (ms)	21.4 ± 15.8	20.5 ± 16.2	0.808
(P-pA) – (P-pAr) (ms)	22.7 ± 15.2	20.7 ± 14.1	0.517

R-pE: peak R-wave on the ECG to the peak of E-wave on the transmitral flow; R-pE′: peak R-wave on the ECG to the peak of E′-wave on the LV septal wall of tissue Doppler imaging; P-pA: the onset of P-wave on the ECG to the peak of A-wave on the transmitral flow; P-pA′: the onset of P-wave on the ECG to the peak of A′-wave on the LV septal wall of tissue Doppler imaging; P-pAr: the onset of P-wave on the ECG to the peak of Ar-wave on the pulmonary venous flow reversal.

The peak A′ coincided with peak Ar in all age groups, but both preceded peak A. P-pA decreased significantly, while P-pA′ and P-pAr increased with age (all ANOVA $p<0.05$). Both (P-pA) – (P-p A′) and (P-pA) – (P-pAr) were significantly smaller in the subjects aged >40 years (group 3, 4, and 5) than those aged <40 years (group 1 and group 2) (all $p<0.05$). LDTD correlated inversely with age (r=-0.65, $p<0.01$). With regard to gender, both EDTD and LDTD showed no differences (Table 3).

DISCUSSION

Early diastolic filling is mainly dependent on ventricular function, while late diastolic filling relies on atrial mechanical function. In this study, we found that EDTD was not changed significantly, while LDTD uniformly decreased significantly with age. Both EDTD and LDTD were not significantly different between genders.

Early Diastolic Phase

During early diastole, LV suction plays an important role on transmitral blood flow from the LA to the LV. The LV suction is determined by relaxation of the LV, LV elastic recoil and also untwisting of the LV[10–14]. With ageing, LV relaxation is prolonged and delayed, and LV early diastolic suction is reduced[15–21]. However, the effect on mitral annular motion are unknown.

Numerous studies have demonstrated that mitral annular motion velocity (E′) from TDI is associated with conventional transmitral flow velocity (E)[22–31] and LV recoil[32]. A study by Bukachi et al[8] showed both peak E and peak E′ prolonged, but EDTD did not change significantly in the elderly group compared to the young ones. In patients with impaired relaxation and pseudonormal filling pattern, R-pE′ was delayed more than those age-matched subjects[4,18,33]. Furthermore, in patients with LV hypertrophy, R-pE′ adversely preceded peak E[9]. In our present study, we found that during LV early diastole, the R-E and R-E′ had no changes, and the resultant EDTD (i.e. the time difference of R-E and R-E′) was not significantly associated with age (r=0.15, p=NS). However, interestingly, we found that in group 5, EDTD decreased substantially compared to other groups. These findings were in partial agreement with previous studies[4,8,23]. The substantial decrease in EDTD in group 5 might be caused by reduced LV relaxation (i.e. prolonged IVRT), delayed mitral annular motion (i.e. prolonged R-E′), and impaired LV recoil.

Late Diastolic Phase

When LV relaxation is impaired, LV filling is compensated by augmented LA contraction[34]. The E/A ratio, one of the most commonly used indexes for assessing LV filling dynamics, inverses with impaired relaxation in the elderly population. Numerous studies[3,4,12,31] have shown that mitral annular velocities (E′ and A′) correlate well with mitral flow velocities (E and A) and changed earlier than mitral inflow. In the elderly population, the pressure gradient between LA and LV decreases due to impaired LV relaxation. In order to maintain the required LV filling, LA contraction is augmented, as we have shown previously[34]. Augmented LA contraction would cause prolonged A′, as shown in our current study (i.e. P-pA′ increased from 123 ms in group 1 to 131 ms in group 5). On the other hand, P-pA decreased with age. As a result, LDTD, the time difference between P-pA and P-pA′, was reduced. This is in agreement with the findings from Bukachi et al[8]. Furthermore, we also found that the changes of A′ and Ar were almost at the same time so that A′ could be an alternative parameter to Ar if Ar is not available in some patients. We found no significant difference in both EDTD and LDTD between men and women.

Study Limitations

First, assessment of LV diastolic function by DE may be influenced by many factors like the changes of preload and afterload, although our study focused on a healthy population without any cardiovascular diseases, who were at rest minimising changes in blood pressure and heart rate. Second, the number of subjects in group 5 was relatively smaller than other age groups, which limits the power of statistical analysis. Third, E, E′, A, A′, and Ar were technically not measured at the same cardiac cycles; however, heart rate was not significantly different among cardiac cycles.

CONCLUSION

EDTD and LDTD, the temporal discordance between mitral annulus motion and trans-mitral flow, embodies one of the earliest events at early-diastole and late-diastole. Age is not associated with EDTD, but is accompanied by a decline in LDTD. This may explain the preservation of LV suction at early diastole and compensated LA contraction at late diastole in the elderly population. With respect to gender, both EDTD and LDTD are not influenced. Additional studies with a larger number of patients are warranted to explore their potential clinical impact.

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