Determinants of Enhanced Left Atrial Active Emptying with Aging: Left Atrial Preload, Contractility or Both?

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Abstract

Objective Senile persons have reduced left ventricular (LV) relaxation and increased late diastolic filling. However, the determinant factor of the enhanced active emptying of the left atrium has not been well established.

Methods Subjects were 62 healthy individuals with a mean age of 58±19 (21-85) years. The biplane modified Simpson's rule was applied to measure left atrial (LA) volume at pre-atrial contraction (LAVpre) as an index of LA preload and LA volume change during atrial contraction (LASV) as an index of active LA emptying. These values were divided by the body surface area and represented as LAVpreI and LASVI, respectively. Postero-basal (dorsal cranial) left atrial wall velocity (LAWV) during atrial contraction as an index of LA contractility was measured in the apical three-chamber view by two-dimensional tissue Doppler echocardiography.

Results Age significantly correlated with mitral flow velocity (TMA), velocity-time integral during atrial contraction (TMAVTI) and LASVI ($r=0.63$, $p<0.001$ and $r=0.71$, $p<0.001$, $r=0.21$, $p=0.049$, respectively). LAVpreI was significantly correlated with age ($r=0.44$, $p<0.001$), LASVI ($r=0.71$, $p<0.001$), TMA ($r=0.31$, $p=0.008$) and TMAVTI ($r=0.40$, $p<0.001$). LAWV remained unchanged with aging and had no correlation with TMA, TMAVTI or LASVI.

Conclusion The enlargement of the LA in senile persons may be a major determinant of enhanced active LA emptying and the increased LA contractility may be less contributory.

Key words: left atrial volume, tissue Doppler echocardiography, left atrial function, left atrial contractility, aging

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Introduction

The left atrial (LA) pump function (active emptying) during the late left ventricular (LV) diastole plays an important role in LV filling, such as in patients with hypertension or myocardial infarction, etc (1, 2). Senile persons also have reduced early diastolic LV filling and augmented late diastolic filling (3, 4). However, the determinant factors responsible for augmentation of atrial active emptying with aging have not been well established. Some investigators have de-

scribed LA volume or LA dimension increase in the older age group, which means an increase in preload before LA contraction (5, 6). However, others described no increase in LA volume and suggested an increased atrial force in the older group (7, 8). The contribution of LA wall contractility has not been adequately clarified, because there are few noninvasive methods for estimating LA contractility. Myocardial contraction velocity has been demonstrated as one of the indices of myocardial contractility (9-11). Similar to LV wall contraction velocity, the LA wall contraction velocity (LAWV) may also serve as an indicative variable of LA

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Table 1. Characteristics of Healthy Individuals

Variables	Normal subjects
Number of patients	62
Age (years)	58 ± 19
Males	34
BSA (m ²)	1.6 ± 0.2
HR (bpm)	73 ± 10
LVDd (mm)	45 ± 3
LAD (mm) (M-mode)	32 ± 4
LVEF (%)	68 ± 5
TMA (cm/s)	70 ± 17
TMAVTI (cm)	6.8 ± 1.7
TME (cm/s)	76 ± 17
TMEVTI (cm)	11 ± 3
A' (cm/s)	9.8 ± 2.4
E' (cm/s)	11.1 ± 3.3
LAWV (cm/s)	3.3 ± 0.8
LASVI (mL/m ²)	7 ± 3
LAVprel (mL/m ²)	16 ± 6
LAVpostl (mL/m ²)	9 ± 4

BSA, Body surface area.

LVDd, Left ventricular end-diastolic dimension. LAD, Left atrial dimension, LVEF, Left ventricle ejection fraction by echocardiography,

TMA, Peak transmitral flow velocity during atrial contraction, MAVTI, Peak transmitral flow velocity-time integral during atrial contraction

TME, Peak transmitral flow velocity during early diastole, MAVTI, Peak transmitral flow velocity-time integral during early diastole

A', mitral annular motion velocity during atrial contraction, E', mitral annular motion velocity during early diastole

LAWV, Left atrial wall velocity during atrial contraction, *, Statistically significant. NS, Not significant,

LA, Left atrium, LASVI, LA stroke volume during atrial contraction/body surface area,

LAVprel, LA volume in pre-atrial contraction/body surface area, LAVpostl, LA volume in post-atrial contraction/body surface area.

contractility during atrial contraction. We have previously demonstrated that the LAWV correlated with the LA appendage flow velocity or fractional shortening, suggesting that the LAWV presents LA contractile function (12). Thomas L et al described that LA contraction velocity measured by tissue Doppler echocardiography is increased in the old age group (7, 8). However, we cannot readily understand why LA contractility increases in elderly persons. In the present study, we attempted to restudy the responsible factors for augmented LA active emptying function with aging in healthy subjects.

Methods

Study population

The study population comprised 62 (34 men and 28 women) healthy individuals with a mean age of 58±19 (21-85) years (Table 1). They visited our laboratory for examination of some chest discomfort or for screening of cardiovascular disease prior to surgical treatment. They had no remarkable findings on routine physical examinations, chest X-ray, electrocardiography, and echocardiography. They had no history of treatment for angina pectoris, hypertension or diabetes mellitus.

Standard transthoracic echocardiography

A Vivid 7 ultrasound system (GE Yokogawa Medical Systems, Hino City, Tokyo, Japan) was used for transthoracic echocardiographic examinations. We used the probe type of M3S, and the probe frequency of 1.7/3.4 MHz. The transmitral flow velocity was conventionally recorded in the 2-chamber view by pulsed Doppler echocardiography and mi-

tral flow velocity in early diastole (TME) and during atrial contraction (TMA), and velocity-time integral (TMEVTI, TMAVTI) were obtained. The mitral annular motion velocity of the free wall side was recorded in the 4-chamber view by pulsed tissue Doppler echocardiography and early diastolic peak velocity (E') and late diastolic peak velocity (A') were determined.

Tissue Doppler echocardiography and measurement of LA wall contraction velocity

The LA wall velocity was obtained by the apical 3-chamber view by pulsed tissue Doppler echocardiography, which was shown as a velocity profile. We used the probe type of M3S; the probe frequency of 1.7/3.4 MHz, acoustic pressure setting of 0 dB, frame rate of 142 frames/s and sampling volume of 8-mm high and 4-mm wide (12, 13).

When the region of interest (ROI) for measurement of LA wall velocity by tissue Doppler echocardiography was placed at the postero-basal (dorsal cranial) wall away from the mitral valve, a positive peak wave during atrial contraction was obtained. We considered the ROI as a proper area, because the posterobasal LA wall motion could not be affected by the adjacent structures, such as the aortic root or pulmonary veins. Moreover, the wall motion vector of this area was nearly perpendicular to the ultrasonic beam from the apical view. The positive peak during atrial contraction did not change considerably when the sampling volume was moved by 3 to 5 mm at the posterior LA wall away from the mitral valve. The positive peak velocity during atrial contraction (LAWV) was used as an index of LA wall contractility (Fig. 1) (12, 13).

Figure 1. The measurement of left atrial (LA) wall velocity (LAWV) during atrial contraction by tissue Doppler echocardiography (velocity profile method). The region of interest (ROI) for measuring LAWV was placed at the posterobasal wall of the LA in the apical 3-chamber view. The peak wave during the atrial contraction phase was designated as LAWV. LA, left atrium; LV, left ventricle; ROI, region of interest.

LA volumes

The biplane modified Simpson's rule was applied to measure the LA volumes on apical 4-chamber and 2-chamber views. The LA volumes in the beginning of the P wave: (LAVpre) and in the beginning of the QRS complexes (LAVpost), were obtained by the Simpson's method from two-dimensional echocardiography. The LA stroke volume (LASV), that is, active emptying volume was calculated as LAVpre-LAVpost. These values were divided by the body surface area (BSA) and represented as LAVpreI, LAVpostI, and LASV index (LASVI), respectively.

Statistical analysis

The variables were measured in 5 cardiac cycles. The values were expressed as mean $\pm$ SD. Simple linear regression analysis was used to correlate 2 parameters. The Statistical Package for the Social Sciences (SPSS version 11.0J; SPSS Japan Inc, Tokyo, Japan) software was used for statistical analysis. $p < 0.05$ was considered statistically significant.

Results

Mitral flow velocity (TME), mitral flow-velocity-time integral (TMEVTI) or mitral annular motion velocity (E') during early diastole had significant negative correlations with age ($r = -0.54$, $p < 0.001$, $r = -0.35$, $p = 0.003$ or $r = -0.67$, $p < 0.001$, respectively) (Table 2). Mitral flow velocity (TMA), mitral flow velocity-time integral (TMAVTI) and mitral annular motion velocity (A') during atrial contraction had significantly positive correlations with age ($r = 0.63$, $p < 0.001$, $r =$

Table 2. Pearson Correlation Coefficients between Age and Other Parameters

Variables	Normal subjects	
	Correlation coefficient	p value
LAWV (cm/s)	-0.02	0.437
LASVI (mL)	0.21	0.049*
TMA (cm/s)	0.63	$< 0.001^*$
TMAVTI (cm)	0.71	$< 0.001^*$
TME (cm/s)	-0.54	$< 0.001^*$
TMEVTI (cm)	-0.35	0.003*
A' (cm/s)	0.45	$< 0.001^*$
E' (cm/s)	-0.67	$< 0.001^*$
LAVpreI (mL/m ²)	0.44	$< 0.001^*$
LAVpostI (mL/m ²)	0.42	$< 0.001^*$

See Table 1

0.71, $p < 0.001$ or $r = 0.45$, $p < 0.001$, respectively) (Fig. 2) (Table 2). LASVI (LA emptying volume) had a weak but significant correlation with age ($r = 0.21$, $p = 0.049$). LAVpreI was significantly increased with aging ($r = 0.44$, $p < 0.001$) and was significantly correlated with LASVI ($r = 0.71$, $p < 0.001$) (Fig. 3), TMA ($r = 0.31$, $p = 0.008$) and TMAVTI ($r = 0.40$, $p < 0.001$). LAWV remained unchanged with age (Fig. 4) and had no correlation with TMA, TMAVTI and LASVI. The intraobserver and interobserver variabilities were low for LAWV (5.3% and 8.2%, respectively).

Discussion

Several studies on mitral flow velocity by Doppler echocardiography demonstrated reduced early diastolic LV filling and augmented late diastolic filling during atrial contraction in several diseases (14, 15). Senile persons also have re-

Figure 2. Age plotted against peak transmitral flow velocity-time integral during atrial contraction (TMAVTI). TMAVTI increases with aging.

Figure 3. LA volume in pre-atrial contraction index (LAVpreI) plotted against LA stroke volume during atrial contraction index (LASVI). Their correlation indicates that LA preload is responsible for the LA emptying volume.

Figure 4. Age plotted against left atrial wall velocity during atrial contraction (LAWV). There is no significant correlation between them.

duced early diastolic LV filling and increased late diastolic filling (3, 4). The present study on LV filling with aging also supported these previous works. However, the determinant factor of the augmented late diastolic filling by atrial active contraction in elderly persons has not been adequately established. Gardin et al described that LA dimension in the oldest group (over 70 years) was larger by 16% compared with the youngest group (21-30 years) (6). On the other hand, Thomas et al described that in healthy subjects, when divided into two groups (young group <50 years and old group ≥ 50 years), normal aging did not increase maximum atrial size (8). In the study of Gardin et al (6) and in the present study, the subjects included higher age persons than in the study of Thomas et al. The discrepancy of the above data concerning LA volume changes with aging might result from the differences in age and other backgrounds of the studied subjects. An increase in LA size means an increase in the preload of atrial contraction. According to the Frank-Starling rule, an increased preload may result in enhanced LA active emptying and late diastolic LV filling. We showed in the present study that LAVpreI was significantly increased with aging and significantly correlated with LASVI ($r=0.71$, $p<0.001$). However, LAVpreI had significant but weak correlations with age ($r=0.44$, $p<0.001$) and TMAVTI ($r=0.40$, $p<0.001$), while TMAVTI had a better correlation with age ($r=0.71$, $p<0.001$). These findings may suggest that enhancement of TMA or TMAVTI in senile persons may depend on other factors, other than the increase in LA preload.

There have been very few studies concerning LA contractility in relation to aging. In the present study, we used LAWV as an index of LA contractility. We have previously demonstrated that the LAWV correlates with the flow velocity in the LA appendage or the fractional area shortening of the LA appendage (12). Therefore, LAWV may be used as a tool for evaluating the characteristics of active LA contraction. In the present study, LAWV remained unchanged with aging and had no correlation with TMA, TMAVTI and LASVI. In contrast, Thomas et al described that old group (≥ 50 years) had higher LA contraction velocity than young group (<50 years) using pulsed tissue Doppler and color tissue Doppler and postulated the increased contractility of LA in old age (6). Zhang et al also indicated increased contraction velocity of LA in the older age patients (16). The difference of the values in their studies between young and old groups was significant but very modest, and there was no clear explanation for the increased LA contractility in the old group. It is known that pathohistology of the LA muscle exhibits fibrosis and fat or amyloid deposits in elderly persons (17). These pathological changes may not be compatible with augmented LA wall contractility. Unchanged or rather reduced LA contractility might be possible in elderly persons from this pathological viewpoint. However, if the sympathetic nervous system is augmented in elderly persons, a subtle increase in LA contractility will be possible. The force-velocity relationship in the isolated mus-

cle has shown that increased afterload results in a decrease in contraction velocity (20-22). If aged persons have increased left ventricular diastolic pressure, LA contraction velocity may decrease according to the above force-velocity theory. However, the subjects in our study had neither left ventricular hypertrophy nor ischemic heart disease. Therefore, we speculated that the left ventricular diastolic pressure would not be so high so as to affect contraction velocity. However, the LA dilatation with aging may accompany mild elevation of diastolic left ventricular pressure resulting from the increased stiffness of the left ventricle due to elderly pathological changes of the muscle. If the LAWV is constant despite a slight increase in afterload with aging, LA contractility should be slightly enhanced with aging according to the force-velocity relationship. Moreover, the LAWV in the present study might not be a sensitive parameter for detecting the subtle changes in LA contractility with aging. Therefore, it should be considered that the LA contractility may in part be responsible for enhanced LA emptying with aging.

Limitations

LAWV in this study was analyzed at a single point in the posterior base of the LA. Di Salvo et al have reported that the regional LA wall contractile function may be different among septum, middle and annular areas (18). Moreover, LA wall function may be affected anatomically by the surrounding structures, such as the aortic root, pulmonary veins and left ventricle. However, our sampling point of LAWV was in the LA posterior base away from the left ventricle and positioned between the bilateral pulmonary veins, so the tethering effect of the left ventricle and pulmonary veins may be small. Really, the changes of the value, when the ROI was moved within several mm, were minimal and the intraobserver and interobserver variabilities were low. Strain and strain rate imaging of the LA wall may provide more accurate information about global and regional LA contractility. Telagh et al reported that the systolic strain rate is significantly reduced in the LA wall in the annular ($p=0.007$) and middle ($p=0.001$) segments and in the IAS middle segment ($p=0.007$) in patients with hypertrophic cardiomyopathy (19). The reduction of LA contraction was similar among the LA segments. Accordingly, LAWV at the posterobasal area in the present study may allow some information about LA contractility. Another weakness of our study might be the ultrasonic beam angle to the LA wall motion vector. However, the ultrasonic beam we used was nearly perpendicular to the wall motion vector, because we measured the motion of the posterobasal area of the LA not the area near the mitral valve. Therefore, the error due to the ultrasonic beam angle may be less.

Conclusion

The increase in preload due to compensatory enlargement of the LA may be a major determinant of enhanced active

LA emptying in elderly persons and the contribution of the increased LA contractility may be less.

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