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Cardiac Image

Comparisons of Left Atrial Functional Parameters with Left Ventricular Diastolic Dysfunction in a Large Taiwanese Population with Normal Left Ventricular Ejection Fraction According to Age

Kai-Chieh Hsu,[1,2] Mei-Chun Chou,[3,4] Hsiao-Ching Chu,[4,5] Kuan-Rau Chiou,[6,7] Feng-You Kuo,[1] Wei-Chun Huang,[1,8] Wei-Tien Chang[9,10] and Wen-Yee Chen[1,11]

Background: Recent studies have shown that left atrial (LA) volume is a sensitive morphophysiological indicator of the severity of LV dysfunction and may also be a useful index of cardiovascular risk. In this study, we performed comparisons among left atrial (LA) functional parameters for predicting age-related diastolic dysfunction.

Methods: Echocardiography was performed in 2248 healthy participants with a low possibility of heart disease according to the decennium of age, and reference values were established. Progressive diastolic dysfunction paralleled increasing age and could be well identified by traditional and advanced echocardiographic parameters, including mitral inflow pattern, tissue Doppler parameters, and LA volume.

Results: Regarding LA functional parameters analyzed based on the decennium of age, left atrial ejection fraction (LAEF) and emptying fraction could not represent aging diastolic dysfunction well, but LA expansion index ((Vol_{max} − Vol_{min}) × 100% / Vol_{min}) could. Vol_{max} indicated maximal LA volume and Vol_{min} indicated minimal LA volume. In assessments of diastolic dysfunction with receiver operating characteristic curve analysis, the best cut-off value of LA expansion index was < 100%, with an area under the curve (AUC) of 0.86, sensitivity of 80%, and specificity of 74%. LAEF < 30% (AUC 0.76, sensitivity 67%, specificity 70%) and LA emptying fraction < 50% (AUC 0.80, sensitivity 72%, specificity 71%) were also useful but performed less well.

***Conclusions**:* Compared with other LA functional parameters, LA expansion index can well represent age-related diastolic dysfunction.

Key Words: Age-related diastolic dysfunction • Left atrial ejection fraction • Left atrial emptying fraction • Left atrial expansion index

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[1]Division of Cardiology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung; [2]Tzu Hui Institute of Technology, Pingtong; [3]Department of Radiology, E-Da Hospital; [4]College of Medicine, I-Shou University; [5]Department of Radiology, E-Da Cancer Hospital, Kaohsiung; [6]Division of Cardiology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City; [7]School of Medicine, Taipei Medical University, Taipei; [8]Department of Critical Care Medicine, Kaohsiung Veterans General Hospital, Kaohsiung; [9]Department of Emergency Medicine; [10]Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital and College of Medicine, Taipei; [11]Department of Emergency Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.
Corresponding author: Dr. Wen-Yee Chen, Department of Emergency Medicine, Kaohsiung Veterans General Hospital, No. 386, Da-Chung 1st Road, Kaohsiung 813, Taiwan. Tel: 886-7-342-2121 ext. 8342; Fax: 886-7-346-8343; E-mail: chenwenyee@yahoo.com

INTRODUCTION

As a marker of increased left ventricular (LV) filling pressure, recent studies have shown that left atrial (LA) volume is a sensitive morphophysiological indicator of the severity of LV dysfunction and may also be a useful index of cardiovascular risk.[1-6] Although LA volume indicates the chronicity and severity of diastolic dysfunction, no studies have determined the exact relationship between LA volume and LV filling pressure. We recently showed that the LA expansion index, which accurately reflects instantaneous LV filling pressure (logarithmic correlation) in many disease entities, including stable angina, acute myocardial infarction, and severe mitral regurgitation, is useful for predicting atrial fibrillation after coronary artery bypass graft surgery, heart failure (HF) rehospitalization, and both short- and long-term mortality in ischemic heart disease and relatively low-risk populations.[7-12] However, diverse LA volume parameters including phasic LA volumes, LA ejection fraction (LAEF), LA emptying fraction, and LA expansion index, can be used for assessing a patient's prognosis, and comprehensive studies analyzing their advantages and disadvantages are lacking. For example, Russo et al. reported minimal indexed LA volume, rather than maximal LA volume, was better correlated with LV diastolic function.[13] In addition, which LA functional parameter provides the best performance for predicting outcomes regarding accuracy and prognostic power is unknown. Thus, we conducted this study to compare all well-known LA functional parameters to evaluate their performance in representing diastolic dysfunction. Additionally, we discuss possible reasons for insufficient performance.

METHODS

Study population

Between August 2015 and April 2016, this prospective study recruited patients who received echocardiographic examinations on their first visit to the cardiovascular outpatient clinic of Kaohsiung Veterans General Hospital in Kaohsiung, Taiwan. The exclusion criteria were any history of the following: 1) LV ejection fraction less than 50%; 2) valvular heart disease with more than a mild degree of severity or any prosthetic valves; 3) atrial septal abnormalities (e.g., atrial septal defect or aneurysm); 4) rhythm other than sinus rhythm; 5) history of hospitalization for any heart problems; and 6) lung disease confirmed by chest image, pulmonary function test, or diagnosis by a chest specialist. The analysis also excluded patients with inadequate image quality and those who did not provide informed consent to participate. The study protocol has been described previously.[12] Diastolic dysfunction was defined according to the 2016 ASE/EACVI recommendations, and included a normal ejection fraction and four items including average E/e′ > 14, septal e′ < 7 cm/s or lateral e′ < 10 cm/s, tricuspid regurgitation velocity > 2.8 m/s, and LA volume index > 34 ml/m^2.[14] A total of 2248 patients were enrolled for final analysis. The study protocol was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital. Patients were invited to participate in this study only after giving written informed consent.

Echocardiographic measurements

Conventional echocardiographic and tissue Doppler measurements

Pulmonary artery systolic pressure was estimated using Doppler echocardiography by calculating the right ventricular to right atrial pressure gradient during systole. Right atrial pressure, estimated on the basis of echocardiographic characteristics of the inferior vena cava,[15] was then added to the calculated gradient. The pulmonary venous flow velocity waves were obtained from apical four-chamber view by using a 2-mm sample volume placed 0.5 to 1 cm into the right superior pulmonary vein. In each patient, the velocity waves of three cardiac cycles obtained during end-expiratory apnea were averaged. The LV mass was calculated using the formula described by Devereux and Reichek.[16] The LV mass was indexed to body surface area (BSA). Pulsed-wave tissue Doppler (TDI) was performed in apical views and a pulsed-wave Doppler sample volume was placed at the level of the mitral annulus over the septal and lateral borders. Pulsed-wave TDI tracing recorded over five cardiac cycles at a sweep speed of 100 mm/s was used for offline calculations. The average early-diastolic velocity (e′) of the septal and lateral mitral annuli was used to estimate LV diastolic filling using the E/e′ method.[17]

LA volume parameter measurements

All volume measurements were calculated using the biplane area-length method in apical four- and two-chamber views.[18] The LA volumes were measured at three points, immediately before mitral valve opening (maximal LA volume or Vol_{max}), at the onset of the P-wave on electrocardiography (pre-atrial contraction volume or Vol_p), and at mitral valve closure (minimal LA volume or Vol_{min}). The LA expansion index was calculated as $(Vol_{max} - Vol_{min}) \times 100\% / Vol_{min}$. $(Vol_p - Vol_{min}) \times 100\% / Vol_p$ and $(Vol_{max} - Vol_{min}) \times 100\% / Vol_{max}$ were defined as LAEF and LA emptying fraction, respectively. In all patients, LA volumes were indexed to BSA.

Interobserver variability

In the first 150 enrolled cases, Vol_{max} and Vol_{min} were measured by two independent observers. Interobserver variability was calculated as the difference between the values obtained by the two observers divided by the mean. The interobserver differences and variabilities were 2.9 ± 4.7 ml/m^2 and 4.9 ± 8.1% for Vol_{max}, 3.1 ± 4.5 ml/m^2 and 5.7 ± 8.1% for Vol_p, and 2.7 ± 4.3 ml/m^2 and 6.1 ± 8.6% for Vol_{min}, respectively. Therefore, interobserver variabilities in LAEF, LA emptying fraction, and LA expansion index measurements were 6.2 ± 8.9%, 5.9 ± 8.3%, and 5.9 ± 7.7%, respectively. The intraobserver variabilities in LAEF, LA emptying fraction and LA expansion index were 5.8 ± 6.7%, 5.1 ± 6.0%, and 5.0 ± 5.2%, respectively.

Statistical analysis

SPSS software was used for all statistical analyses. Baseline characteristics and echocardiographic parameters were assessed. The analyses of diastolic echocardiographic parameters were performed according to the decennium of age, and reference values were established. For assessing age-related diastolic dysfunction, the trends of LAEF, LA emptying fraction and LA expansion index were analyzed accordance to age, and the chi-square test was used to compare differences among decennial groups. Pearson's correlation test was performed to assess correlations among E/e′, LA parameters, and age. Since diabetes and hypertension could also affect diastolic function and confound the interpretation of the final results, we also performed subgroup analyses after excluding these two diseases.

RESULTS

In total, 2248 participants were enrolled for final analysis. The basic characteristics and echocardiographic parameters are shown in Table 1. The participants were enrolled from our outpatient clinic but not from a community base. Although a certain number of participants had hypertension, diabetes, renal dysfunction, coronary artery disease and were current smokers, the study cohort was close to a low-risk normal population, and LVEF was within normal range. The values of mitral inflow pattern, pulmonary arterial systolic pressure (PASP), LV mass index, phasic LA volume, and E/e′ were also within normal ranges, which indicated that the study cohort lacked obvious heart or lung problems.

Table 1. Basic characteristics of participants.

Variable	N = 2248
Age (years)	56 ± 17
Gender (M/F)	1144/1104
Hypertension (%)	684 (30.4%)
Diabetes (%)	255 (11.3%)
Current smoker (%)	391 (17.4%)
Coronary artery disease (%)	135 (6.0%)
Renal dysfunction (%)	249 (11.1%)
Heart rate (BPM)	71 ± 12
Diastolic function according to mitral inflow	
Normal	1213 (54.0%)
Impaired relaxation	879 (39.1%)
Pseudonormal	106 (4.7%)
Restrictive	50 (2.2%)
E velocity (cm/s)	74 ± 22
A velocity (cm/s)	71 ± 22
E/A ratio	1.2 ± 0.6
E-deceleration time (ms)	221 ± 63
LV mass index (g/m^2)	115 ± 36
PASP (mmHg)	28 ± 10
LVEF (%)	60 ± 8
Max indexed LAV (ml/m^2)	25.1 ± 13.3
Pre-P indexed LAV (ml/m^2)	18.3 ± 10.6
Min indexed LAV (ml/m^2)	12.2 ± 8.6
E/e′	10.0 ± 4.3
LA ejection fraction (%)	35.2 ± 13.0
LA emptying fraction (%)	54.3 ± 17.0
LA expansion index (%)	142 ± 85
Septal e′ < 7 cm/s or lateral e′ < 10 cm/s	401 (17.8%)
Average E/e′ > 14	332 (14.8%)
LAVI > 34 ml/m^2	386 (17.2%)
TR velocity > 2.8 m/s	354 (15.7%)
Diastolic function according to 2016 ASE guideline	
Normal diastolic function	1169 (52.0%)
Indeterminate	315 (14.0%)
Diastolic dysfunction	764 (34.0%)

A, late-diastolic mitral inflow velocity; ASE, American Society of Echocardiography; BPM, beats per minute; E, late-diastolic mitral inflow velocity; e′, peak velocity of mitral annulus; LAV, left atrial volume; LAVI, indexed left atrial volume; LVEF, left ventricular ejection fraction; PASP, pulmonary arterial systolic pressure; TR, tricuspid regurgitation.

Age-related diastolic dysfunction

According to the decennium of age, the means and standard deviations of echocardiographic parameters are shown in Table 2. Regardless of gender, the trends of diastolic dysfunction clearly followed the aging process. Compared to younger groups, older groups had lower values of mitral E/A ratio, LA emptying fraction and LA expansion index, and higher values of LV mass index, E/e′, and phasic LA volumes. The distributions of TDI parameters and LA volume are shown in Figure 1A and 1B, respectively. Chi-square tests for each TDI parameter and each phasic LA volume among decennial groups reached statistical significance. All indicated that diastolic function declined with age.

Comparison of LA functional parameters for assessing diastolic dysfunction

The distributions of LA functional parameters including LAEF, LA emptying fraction, and LA expansion index according to age are shown in Figure 2 and Table 1. Chi-square tests for differences among decennial groups showed that only LA expansion index reached statistical significance, although LA emptying fraction also showed a borderline difference among groups (p = 0.056). Regarding LAEF, the decennial difference was small and did not show statistical significance (p = 0.092). Contrary to LA expansion index, LAEF was relatively constant and was not obviously affected by the aging process. According to ROC curve analysis for assessing diastolic dysfunction based on the American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) commendations (Figure 3), the best cut-off value of LA expansion index was < 100% with an area under the curve (AUC) of 0.86, sensitivity of 80%, and specificity of 74%. LAEF < 30% (AUC 0.76, sensitivity 67%, specificity 70%) and LA emptying fraction < 50% (AUC 0.80, sensitivity 72%, specificity 71%) were also useful but performed less well.

Correlations between age and diastolic parameters

Table 3 shows the correlations between age and di-

Table 2. The means and standard deviations of diastolic parameters in males and females of different ages

	Mitral E (cm/s)	Mitral A (cm/s)	E/A ratio	LV mass index (g/m^2)	E/e'	Max indexed LAV (ml/m^2)	Pre-P indexed LAV (ml/m^2)	Min indexed LAV (ml/m^2)	LAEF (%)	LA emptying fraction (%)	LA expansion index (%)
Age (year)											
Male (N = 1144)											
15-20 (N = 43)	87 ± 20	43 ± 10	2.17 ± 0.95	78 ± 16	7.0 ± 2.1	20.0 ± 5.2	12.1 ± 6.8	7.4 ± 3.4	32 ± 7	58 ± 7	164 ± 36
21-30 (N = 73)	76 ± 20	50 ± 11	1.60 ± 0.47	80 ± 27	6.7 ± 2.1	19.5 ± 12.9	11.9 ± 9.5	7.1 ± 5.3	36 ± 15	58 ± 15	179 ± 107
31-40 (N = 97)	71 ± 17	54 ± 13	1.39 ± 0.41	87 ± 27	7.0 ± 2.1	19.4 ± 12.1	12.9 ± 11.8	7.4 ± 7.2	39 ± 11	59 ± 11	162 ± 79
41-50 (N = 169)	71 ± 19	62 ± 16	1.20 ± 0.45	93 ± 31	8.6 ± 4.1	22.0 ± 14.0	14.8 ± 10.1	7.9 ± 5.1	37 ± 14	57 ± 13	162 ± 99
51-60 (N = 243)	71 ± 24	69 ± 21	1.12 ± 0.63	93 ± 37	9.9 ± 4.4	24.9 ± 17.3	14.9 ± 14.5	9.1 ± 10.6	37 ± 14	55 ± 14	146 ± 87
61-70 (N = 176)	68 ± 21	76 ± 20	0.98 ± 0.56	103 ± 36	11.1 ± 5.1	24.6 ± 13.4	17.2 ± 13.1	11.7 ± 11.2	33 ± 14	50 ± 21	129 ± 63
71-80 (N = 177)	70 ± 22	84 ± 22	0.93 ± 0.59	104 ± 33	11.4 ± 4.7	26.7 ± 14.4	17.1 ± 12.6	11.1 ± 10.5	33 ± 13	50 ± 13	126 ± 74
81-90 (N = 129)	71 ± 21	88 ± 21	0.88 ± 0.51	112 ± 44	12.3 ± 4.2	27.0 ± 12.0	20.2 ± 10.3	12.1 ± 9.1	32 ± 13	49 ± 16	113 ± 59
91-100 (N = 37)	74 ± 19	90 ± 20	0.68 ± 0.33	113 ± 20	12.9 ± 2.6	26.1 ± 14.4	21.9 ± 10.1	12.0 ± 8.6	35 ± 10	49 ± 8	100 ± 25
Female (N = 1104)											
15-20 (N = 45)	89 ± 13	49 ± 13	1.88 ± 0.37	73 ± 18	6.8 ± 1.3	20.3 ± 8.2	11.8 ± 6.6	7.4 ± 4.2	38 ± 10	63 ± 9	170 ± 72
21-30 (N = 77)	85 ± 19	50 ± 14	1.77 ± 0.49	76 ± 22	7.0 ± 2.4	19.8 ± 9.5	11.9 ± 6.9	7.3 ± 5.0	35 ± 11	62 ± 11	188 ± 98
31-40 (N = 131)	79 ± 18	56 ± 16	1.49 ± 0.45	83 ± 27	7.7 ± 2.1	19.3 ± 7.8	12.5 ± 6.1	7.2 ± 4.1	37 ± 12	58 ± 10	160 ± 78
41-50 (N = 217)	80 ± 21	66 ± 18	1.28 ± 0.41	92 ± 27	9.4 ± 3.4	20.6 ± 11.3	13.6 ± 9.1	8.1 ± 5.6	38 ± 12	59 ± 11	166 ± 92
51-60 (N = 240)	73 ± 20	70 ± 17	1.09 ± 0.36	94 ± 27	9.8 ± 3.6	23.0 ± 9.5	14.7 ± 8.9	9.0 ± 6.7	35 ± 12	54 ± 12	149 ± 84
61-70 (N = 199)	72 ± 19	82 ± 19	0.93 ± 0.42	96 ± 35	11.8 ± 4.1	25.1 ± 14.5	17.4 ± 11.7	10.9 ± 9.2	34 ± 12	49 ± 34	125 ± 65
71-80 (N = 116)	74 ± 26	86 ± 23	0.94 ± 0.61	98 ± 34	12.5 ± 4.5	25.3 ± 12.8	17.3 ± 11.4	10.7 ± 9.6	32 ± 13	50 ± 15	122 ± 72
81-90 (N = 57)	72 ± 31	99 ± 22	0.86 ± 0.38	101 ± 28	13.2 ± 4.5	26.7 ± 16.7	20.8 ± 14.4	12.1 ± 13.0	31 ± 13	48 ± 13	112 ± 58
91-100 (N = 32)	71 ± 18	98 ± 33	0.77 ± 0.36	114 ± 33	13.0 ± 4.6	26.3 ± 16.1	22.1 ± 16.2	12.3 ± 11.7	34 ± 14	48 ± 16	98 ± 39

e′, peak early-diastolic velocity of mitral annulus; LAEF, left atrial ejection fraction; LAV, left atrial volume; LV, left ventricle; Mitral A, peak late-diastolic velocity of mitral inflow; Mitral E, peak early-diastolic velocity of mitral inflow.

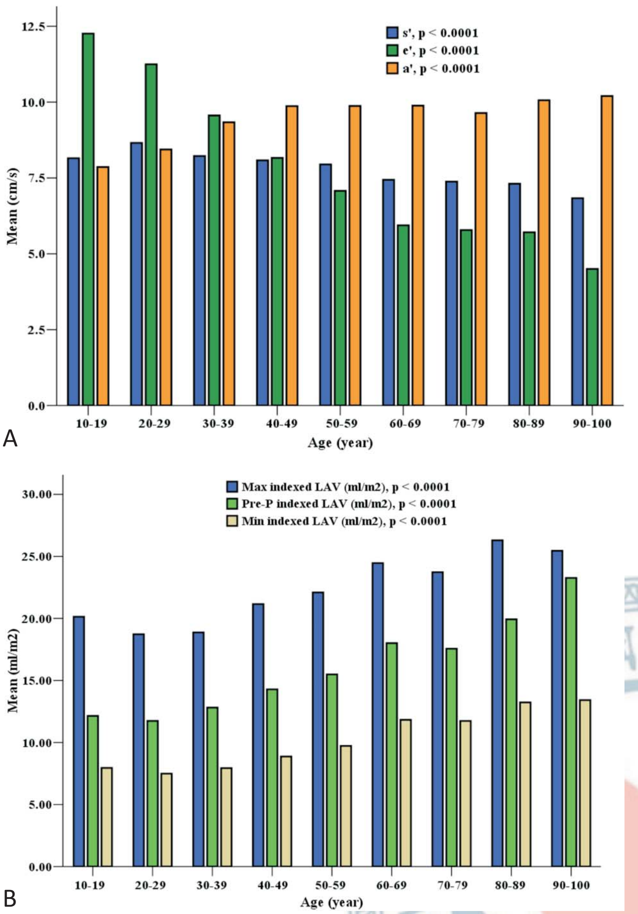

Figure 1. *(A) The decennial distributions of tissue Doppler parameters; (B) The decennial distributions of left atrial (LA) volumes; s′ = peak systolic velocity of mitral annulus, e′ = peak early-diastolic velocity of mitral annulus, a′ = peak late-diastolic velocity of mitral annulus.*

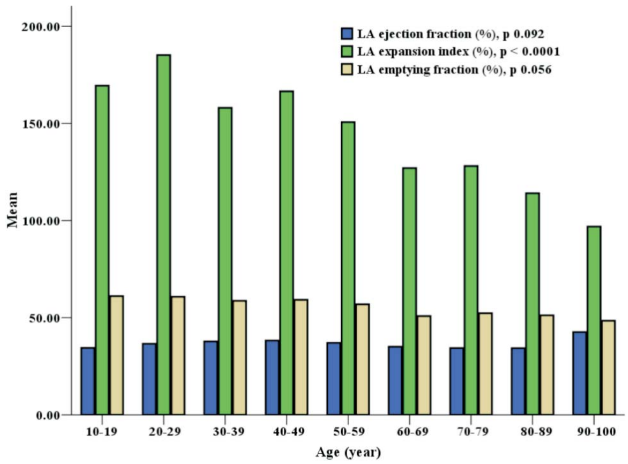

Figure 2. *The decennial distributions of left atrial (LA) function parameters.*

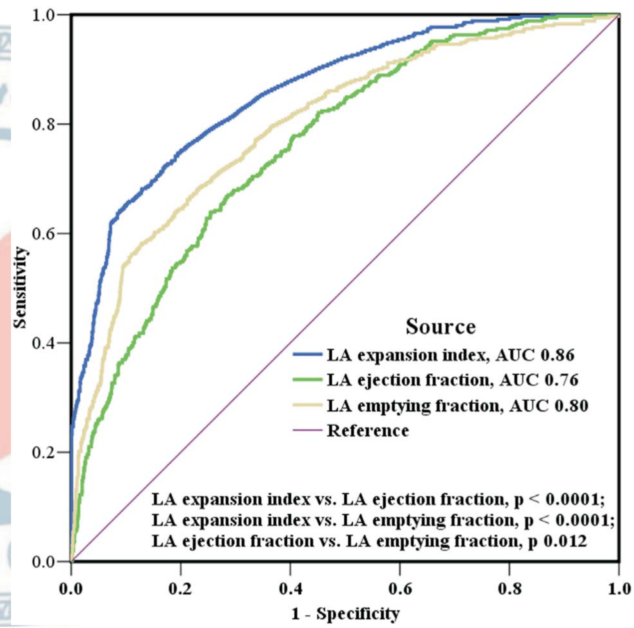

Figure 3. *ROC curves of LA function parameters for predicting diastolic dysfunction according to ASE/EACVI recommendations. ASE/EACVI, American Society of Echocardiography/European Association of Cardiovascular Imaging; AUC, area under the curve; LA, left atrial; ROC, receiver operating characteristic.*

astolic parameters including E/e′, LAEF, LA emptying fraction, and LA expansion index. In analysis of the whole group, the correlation between age and LA expansion index was more evident (β -0.415, $p < 0.0001$), although the other parameters also correlated significantly to age. Subgroup analyses after excluding diabetes and hypertension showed similar results. According to the 2016 ASE and EACVI guidelines, the ratios of diastolic dysfunction according to age are shown in Figure 4.

DISCUSSION

The current study is based on a large-scale observation and the number of participants is large enough to establish reference values according to the decennium of age (Table 2). Our results demonstrate the background of myocardial diastolic dysfunction from the young to the elderly. This study may be a useful base for further studies of diastolic dysfunction and the development of devices or medications. Additionally, it shows the progressive decline in diastolic function with age according to conventional and advanced echocardiographic parameters. This is the strength of

Table 3. Pearson correlations among age, E/e′ and left atrial (LA) parameters

	E/e'	LA ejection fraction	LA emptying fraction	LA expansion index
Total cases (N = 2248)				
Age				
Pearson correlations	0.251	-0.121	-0.233	-0.415
p values	< 0.0001	< 0.0001	< 0.0001	< 0.0001
E/e′				
Pearson correlations		-0.233	-0.293	-0.246
p values		< 0.0001	< 0.0001	< 0.0001
Cases after excluding DM and HT (N = 1309)				
Age				
Pearson correlations	0.21	-0.103	-0.227	-0.424
p values	< 0.0001	< 0.0001	< 0.0001	< 0.0001
E/e′				
Pearson correlations		-0.153	-0.265	-0.221
p values		< 0.0001	< 0.0001	< 0.0001

Abbreviations as shown in Table 1.

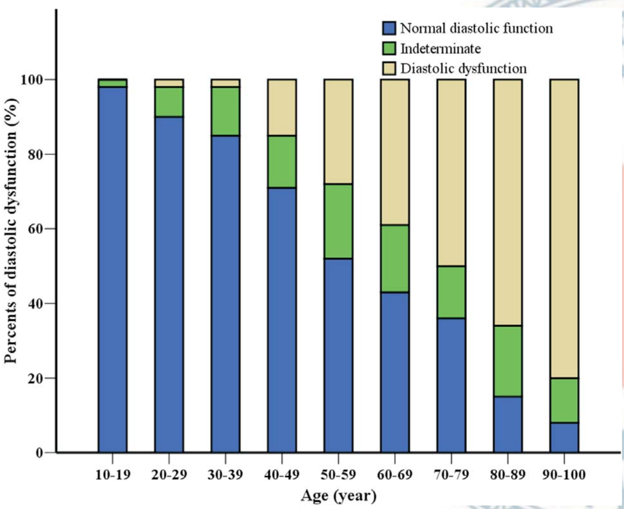

Figure 4. *The ratios of diastolic dysfunction according to age.*

the current study. In addition, it provides a broad view of how LA functional parameters are well associated with age-related diastolic dysfunction. Our results showed that LA expansion index is the potentially best parameter of LA function for assessing diastolic function, because it can reflect subtle changes of diastolic function according to the aging process. Its potential application is to identify the elderly with more advanced diastolic dysfunction to allow for early interventions such as aggressive hypertension control, coronary artery disease risk factor control, and prevention of atrial fibrillation. These interventions would decrease further diastolic heart failure.

The causes of age-related diastolic dysfunction

For the elderly, vascular stiffness due to collagen accumulation, calcification, and fragmentation of elastin erodes vascular compliance.[19] Myocardial hypertrophy modulates ventricular wall tension as afterload increases, which is associated with an age-related reduction of LV compliance leading to pulmonary congestion or edema during myocardial ischemia, uncontrolled hypertension, and atrial fibrillation.[20] Changes in diastolic function are also thought to account for an increase in LA size and pressure with advancing age. In line with prior studies, incremental LV mass index with elevation of E/e′ and phasic LA volumes during the aging process indicated age-related diastolic dysfunction. Regarding LA functional parameters, the reduction of LA expansion index also confirmed it, although LAEF seemed to be relatively constant.

Shortages of LAEF and LA emptying fraction

Viewing LA as a balloon, the internal pressure cannot be estimated by the size of the balloon. However, if a constant volume of air with constant pressure is put into the balloon and changes of balloon morphology are observed, the original pressure inside the balloon can be speculated. For these reasons, the original concept should be that LA functional parameters are superior to LA volume for assessing diastolic function. Regarding LA emptying fraction using Vol_{max} as the denominator, the increase in Vol_{min} with worsening diastolic function is more pronounced than that of Vol_{max}, and Vol_{min} is better correlated with E/e′ than Vol_{max} according to the report of Russo et al.[13] The relationship between Vol_{max} and LV diastole may be confounded by LV systolic function. On the other hand, the relationship between Vol_{min} and LV diastolic function appears to be more direct, as in end-diastole the mitral valve is open and the LA is directly exposed to the LV pressure. Therefore, the predictive power of LA expansion index is better than that of LA emptying fraction. According to Figure 2, LA emptying fraction was relatively constant, which means that the efficiency and accuracy of this parameter was insufficient to detect age-related changes of diastolic dysfunction. Since Vol_{max} is much larger than Vol_{min}, the ratio between total LA emptying volume ($Vol_{max} - Vol_{min}$) and Vol_{max}, namely LA emptying fraction, is much smaller than the ratio between total LA emptying volume and Vol_{min}, namely LA expansion index, which possibly makes LA emptying fraction not sufficiently sensitive to detect subtle changes of diastolic dysfunction. Based on these three reasons, LAEF is not well suited to assessing the prognosis. First, it cannot be measured in patients with atrial arrhythmia, particularly atrial flutter and atrial fibrillation. Second, tachycardia, particularly heart rate more than 110 beat per minute, causes T and P waves to merge in electrocardiography, which makes the measurement of LAEF impossible. Additionally, time-velocity integral of atrial reverse flow of pulmonary veins increases corresponding to aging diastolic dysfunction (Figure 5). As the model of mitral regurgitation which presents as backward flow coming into the preceding chamber (LA), LV ejection fraction should have a compensatory increase to provide adequate forward flow and cardiac output. Regarding increasing backward flow of LA during atrial kick with age, it is reasonable to assume that LA is similar, which causes a relatively hyperdynamic reaction. If LAEF progressively declines due to aging diastolic dysfunction, this compensatory process would mask the downhill trend. Therefore, LAEF offers the worst performance for predicting age-related diastolic dysfunction.

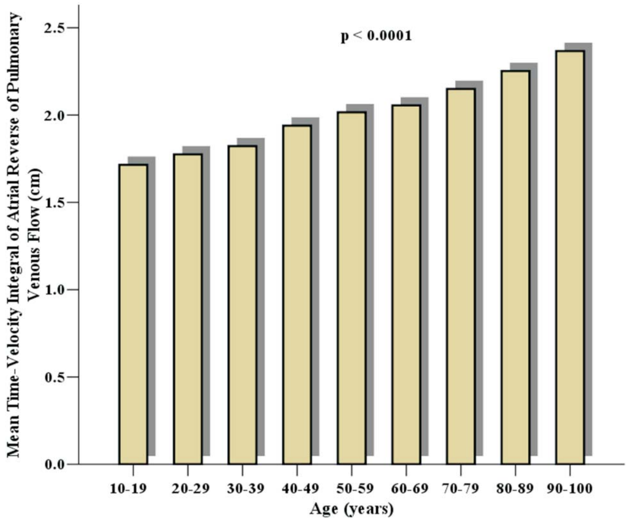

Figure 5. *The decennial distributions of atrial reverse of pulmonary venous flow.*

Limitations of the study

This study has several limitations. First, only single measurements of resting LA volume parameters were evaluated. Other echocardiographic measures of LA function, including segmental atrial function assessment, strain, strain rate, and atrial response to exercise, were not examined. Therefore, the superiority of LA expansion index and LA strain rate needs further studies to resolve. Second, the study cohort was enrolled from our outpatient clinic, and they cannot represent the normal decennial distribution of age-related changes of diastolic parameter completely, since the enrolled population was not community based. In other words, the trends of distribution could be confounded by many uncontrolled factors. However, we believe that, while the trends of E/A ratio, LV mass index, E/e′, and LA expansion index indeed reflected aging diastolic dysfunction even though the confounders were not well controlled in the current study cohort, the trends of no differences in LAEF and LA emptying fraction with age shows the insufficient efficiency of these two parameters for detecting diastolic dysfunction.

CONCLUSIONS

Age-related diastolic dysfunction exists and can be demonstrated by many echocardiographic parameters. Regarding LA functional parameters, LA expansion index is more strongly associated with age-related diastolic dysfunction. For assessing aging diastolic dysfunction, the performance of LAEF is obviously insufficient.

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CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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