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A rapid method to quantify left atrial contractile function: Doppler tissue imaging of the mitral annulus during atrial systole

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Abstract **Aims** Assess the value of peak atrial systolic mitral annular velocity (A_{ann}) measured by Doppler tissue echocardiography to quantify left atrial systolic function.
Methods We studied a total of 61 adults; 10 subjects without history of heart disease and 51 patients with a history of atrial fibrillation or undergoing evaluation for left ventricular systolic or diastolic dysfunction. A_{ann} was obtained by averaging peak atrial systolic mitral annular velocities from the septal, lateral, anterior, and inferior annulus. Left atrial fractional area change (FAC) and fractional volume change (FVC) during atrial systole were calculated. The correlation between peak atrial systolic mitral annular velocity (A_{ann}) and left atrial systolic FAC and FVC was determined.
Results Mean FAC and FVC were 27±12 and 40±14%, respectively; mean A_{ann} was 11.2±3.2 cm/s. Linear regression analysis showed correlation between A_{ann} and FAC ($r = 0.71$; $p < 0.001$) and between A_{ann} and FVC ($r = 0.74$; $p < 0.001$).
Conclusions Peak systolic mitral annular velocity correlates well with left atrial systolic FAC and FVC, thus providing an easy means to assess left atrial systolic function.

Introduction

The importance of the contribution of atrial contraction to ventricular filling has been known since William Harvey.[1] It has been suggested that normal atrial systole can keep the mean atrial pressure significantly lower than left ventricular end diastolic pressure and therefore, 'protect' the patient from pulmonary congestion. Experimental and clinical data have characterized the determinants of atrial function, but quantitative assessment is difficult, requiring invasive pressure–volume loops, thus precluding routine clinical use.[2–4]

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Estimation of left atrial ejection fraction by two-dimensional (2D) echo has been used to assess left atrial function in patients with dilated cardiomyopathy, but this method is tedious and requires accurate measurements from multiple views.

Doppler tissue imaging (DTI) is a relatively new technology, allowing measurement of myocardial velocities. Although numerous studies have been published using DTI for assessing left ventricular relaxation, little is known about the significance of myocardial velocities during atrial contraction.[5] The purpose of this study was to:

1. Evaluate in a larger group of patients the relation between peak mitral annular systolic velocity during atrial contraction and left atrial ejection fraction, measured as left atrial systolic fractional area and volume change (FAC and FVC).
2. Assess the correlation of peak mitral annular systolic velocity with other non-invasive indices of atrial function.

Methods

Patient population sample

We examined 61 consecutive patients, aged 55 ± 16 years, who underwent 2D echocardiography including DTI of the mitral annulus at the Cleveland Clinic Foundation, Cleveland, OH. These patients underwent echocardiography including DTI for evaluation of left ventricular systolic or diastolic function, or follow-up examinations for a history of paroxysmal atrial fibrillation. Of these 61 patients, 10 had no echocardiographic evidence of heart disease. Left ventricular systolic dysfunction, isolated diastolic dysfunction, and a history of atrial fibrillation were present in 16, 9, and 26 patients, respectively. Mitral regurgitation (MR) was found in 44 of these patients. All patients were in normal sinus rhythm at the time of the examination. The Cleveland Clinic Foundation Institutional Review Board has approved performing research on the routine and tissue Doppler imaging data obtained from the echocardiographic laboratory.

Echocardiography

Echocardiograms were obtained with the patient placed in the left lateral decubitus position by an Acuson 128 XP/10 Sequoia (Mountain View, CA) with a multifrequency transducer equipped with DTI technology. A simultaneous electrocardiogram was recorded in all subjects. Mitral inflow velocities were recorded by standard pulsed-wave Doppler at the tips of the mitral valve leaflets. Left atrial outlines and diameters were obtained from the apical two-chamber view and the four-chamber view at maximal atrial dimension, pre-atrial systole and end-atrial systole, as determined by the onset of the P-wave on the electrocardiogram and at the point of mitral valve closure before left ventricular systole.

Left atrial volumes were calculated using the biplane area–length modified Simpson formula: $V\ (\mathrm{cm}^3) = 8A_1A_2/3\pi l$; where A_1 and A_2 represent the enclosed area of the atrial chamber from the two orthogonal views, and l is the common diameter directed from apex to base.[6]

Besides the routine 2D-echocardiographic evaluation, the following specific indices of left atrial function were directly measured or calculated:

1. A_{ann}—septal and lateral (from the apical four-chamber view), and anterior and inferior (from the apical two-chamber view) peak atrial systolic mitral annular velocities were measured during atrial contraction. Data from all four measurements were averaged to obtain A_{ann}.
2. FAC during atrial systole, calculated as $\mathrm{FAC}\ (\%) = (A_{pre-a} - A_{min})/A_{pre-a}$, where $A_{pre\text{-}a}$ is the left atrial area (cm^2) prior to atrial systole, and A_{min} is the minimal left atrial area (cm^2) at the end of atrial systole.
3. FVC during atrial systole, calculated as $\mathrm{FVC}\ (\%) = (V_{pre-a} - V_{min})/V_{pre-a}$, where $V_{pre\text{-}a}$ is the left atrial volume (ml) prior to atrial systole and V_{min} is the minimal left atrial volume (ml) at the end of atrial systole.
4. Peak transmitral *A* wave velocity.
5. Atrial ejection force (AEF), using the previously[6,7] described formula: $\mathrm{AEF} = 0.5\times\rho\times \mathrm{MOA}\times \mathrm{p}A^2$ ($\mathrm{gcm/s^2}$ = dynes), where ρ is the specific gravity of blood ($1.06\ \mathrm{g/cm^3}$), MOA the mitral valve opening area (cm^2), and p*A* is the peak transmitral *A* wave velocity (cm/s).

Statistical analysis

The indices of left atrial function were described as mean$\pm$SD, and differences between the groups were assessed using one-way ANOVA. We used uni- and multilinear regression analysis to relate A_{ann} to the following parameters: transmitral peak *E* and peak *A* wave velocity; *E*/*A* ratio; transmitral flow deceleration time; AEF; left atrial end-diastolic, pre-systolic and end-systolic areas and volumes; left atrial systolic FAC and FVC; heart rate; and left ventricular ejection fraction. Patients with MR were stratified according to the degree of its severity (none, mild, moderate, and severe) and their mean A_{ann} was compared using one-way ANOVA.

Interobserver variation

To assess interobserver variation, 10 echocardiograms were read by two independent investigators. Interobserver variability for each parameter was calculated as the difference between the two measurements divided by the average of the two, and expressed in percent ±SD (%).

Results

Baseline characteristics

We examined 35 men and 26 women with a mean age of 55±16 years (see Table 1). Of these 61 patients, 26 had a history of atrial fibrillation, 16 had evidence of left ventricular systolic dysfunction, and nine had evidence of left ventricular diastolic dysfunction; 10 had no heart disease. At the time of echocardiography all patients were in sinus rhythm. MR was found in 44 of these patients: trivial to mild in 24 patients, moderate in 15 patients, and severe in five patients. Mean age, heart rate, and left ventricular ejection fraction at the time of the echocardiographic examination are listed in Table 1. Subjects with no history of heart disease were younger. Patients with a history of atrial fibrillation had a lower heart rate than patients with left ventricular systolic or diastolic dysfunction. Compared with the other groups, left ventricular ejection fraction was lower in the group with known systolic heart failure.

Atrial dimensions

Mean left atrial pre-systolic and end-systolic areas (related to the atrial cycle) as measured from the apical four-chamber view, as well as the corresponding calculated left atrial volumes were greatest in the heart failure group, and smallest in the group without known heart disease (see Table 1).

Atrial function

Doppler tissue and 2D-echocardiographic imaging
Mean A_{ann} was greatest in the normal group and smallest in the heart failure group (see Table 1). Mean FAC and FVC during left atrial systole were lowest in the heart failure group. The SD was larger in the group with diastolic dysfunction and likely reflects the broad range of left atrial systolic function in this group.

Table 1 Descriptive statistics—all values expressed as mean±SD

Patient group	ALL ($n=61$)	NL ($n=10$)	AFIB ($n=26$)	CHF ($n=16$)	DIAST ($n=9$)
Baseline characteristics					
Age (years)	55 ± 16	37 ± 5*	59 ± 16**	58 ± 12**	55 ± 15**
Heart rate (bpm)	68 ± 14	69 ± 9	60 ± 12*	72 ± 12**	80 ± 16**
LV EF (%)	48 ± 18	56 ± 7*	59 ± 8*	21 ± 6**	53 ± 11*
Left atrial areas (A)/volumes (V), related to atrial cycle					
Pre-systolic A (cm^2)	19.9 ± 5.4	16.6 ± 2.7*	19.6 ± 4.3	22.6 ± 6.8**	19.9 ± 5.9
End-systolic A (cm^2)	16.0 ± 5.3	12.3 ± 3.6*	15.4 ± 4.2	19.2 ± 6.2**	16.3 ± 3.6
Pre-systolic V (cm^3)	54.5 ± 25.4	42.5 ± 11.8*	50.3 ± 18.7	67.1 ± 35.9**	57.4 ± 24.7
End-systolic V (cm^3)	39.2 ± 21.4	26.3 ± 9.6*	33.9 ± 14.9*	53.3 ± 26.4**	44.0 ± 24.9
Left atrial functional parameters					
A_{ann} (cm/s)	11.2 ± 3.2	13.4 ± 1.7*	12.0 ± 1.8*	9.1 ± 2.9**	10.2 ± 5.3
FVC (%)	40 ± 14	39.5 ± 4.5	47.5 ± 8.5*	31.0 ± 15.0**	35.1 ± 22.2
FAC (%)	27 ± 12	25.4 ± 5.5	34.0 ± 8.0*	18.1 ± 12.5**	22.2 ± 5.4**
Peak E wave (m/s)	0.76 ± 0.19	0.63 ± 0.17*	0.76 ± 0.14	0.77 ± 0.19	0.87 ± 0.28**
Peak A wave (m/s)	0.65 ± 0.23	0.56 ± 0.12	0.63 ± 0.24	0.71 ± 0.24	0.71 ± 0.27
AEF (kdynes)	15.9 ± 11.9	11.5 ± 6.5	15.4 ± 13.1	19.0 ± 10.6	16.6 ± 14.9
E/A ratio	1.3 ± 0.6	1.2 ± 0.4	1.4 ± 0.5	1.3 ± 0.9	1.4 ± 0.8
DT (ms)	206 ± 48	215 ± 22	221 ± 44	188 ± 57	184 ± 49

*/** = Difference between group * compared to ** statistically significant at $p<0.05$. A, area; ALL, all patients; AFIB, patient group with history of atrial fibrillation; CHF, patient group with history of congestive heart failure; DIAST, patient group with left ventricular diastolic dysfunction (all stages); DT, mitral deceleration time; FAC, left atrial systolic fractional area change; FVC, left atrial systolic fractional volume change; NL, patient group without heart disease; and V, volume.

Doppler flow derived parameters
Mean transmitral peak E and A wave velocity, deceleration time, as well as the calculated E/A ratio are listed in Table 1. There was no statistically significant difference between the groups.

Regression analysis

Univariate linear regression analysis
There was a good correlation between A_{ann} and left atrial systolic FVC ($y = 4.7 + 0.2x$; $r = 0.74$; $p<0.001$, see Fig. 1), and between A_{ann} and left atrial systolic FAC ($y = 6.3 + 0.2x$; $r = 0.71$; $p<0.001$) (see Table 2). A_{ann} showed better correlation with FAC or FVC than the individual (septal, lateral, inferior, and anterior) annular velocities. Peak transmitral A wave velocity, deceleration time, AEF, and left ventricular ejection fraction correlated weakly positively with A_{ann}; a weak negative correlation was noted between A_{ann} and peak transmitral E wave velocity, E/A ratio, left atrial areas, and left atrial volumes. There was no correlation between A_{ann} and heart rate or age. Comparing the different patient groups, A_{ann} correlated best with left atrial systolic FVC in the group with left ventricular diastolic dysfunction ($r = 0.93$; $p<0.001$), followed by patients with a history of atrial fibrillation ($r = 0.68$; $p<0.001$) and left ventricular systolic dysfunction ($r = 0.66$; $p = 0.005$). There was no correlation for the group without heart disease ($r = 0.10$; $p = 0.78$), which is most likely related to the narrow scatter of values in this relatively small patient group. Values were similar for the correlation between A_{ann} and left atrial systolic FAC.

Multivariate linear regression analysis
We examined two different models including either left atrial systolic FAC or FVC. In the model including area parameters, the following variables were independently predictive of A_{ann} and were included in a stepwise forward fashion in the multilinear regression model: left atrial systolic FAC, age, peak transmitral A wave velocity, and deceleration time (F-ratio 22.9; $r = 0.79$; $p<0.001$). In the volumetric model, the predictive variables were: left atrial systolic FVC, age, left ventricular ejection fraction, and transmitral peak E and A wave velocities (F-ratio 18.5; $r = 0.80$; $p<0.001$). The most powerful predictors of A_{ann} in each model were left atrial systolic FAC and FVC, respectively.

Peak atrial systolic mitral annular velocity in mitral regurgitation

Mean A_{ann} in the patients with no or mild MR was 11.4 ± 3.6 and 12.6 ± 2.2 m/s, respectively. Compared to the group with mild MR, A_{ann} was decreased in patients with moderate (9.6 ± 3.2 m/s) or severe (8.7 ± 2.9 m/s) MR (see Fig. 2).

Interobserver variation

The mean interobserver variation (in % $\pm$SD) was 8.9 ± 6.1% for measurement of 2D indices,

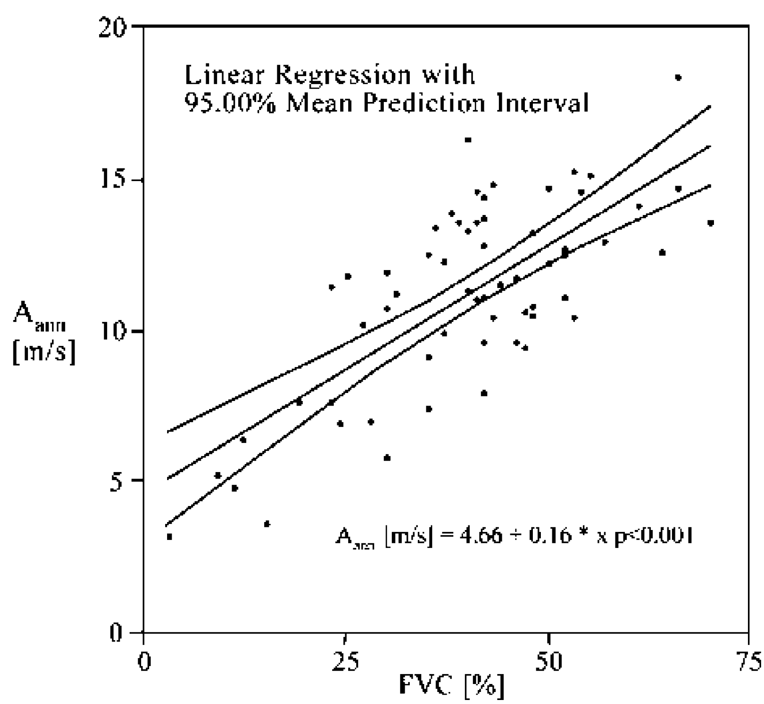

Figure 1 Correlation of left A_{ann} (in m/s) with left atrial systolic FAC (in %).

Table 2 Univariate linear regression analysis—correlation of A_{ann} with other left atrial parameters

Parameter (x)	A_{ann} (y) equation	r	p
LA fractional volume change	$y = 4.7 + 0.2x$	0.74	<0.001
LA fractional area change	$y = 6.3 + 0.2x$	0.71	<0.001
LA end-systolic volume	$y = 13.7 - 0.1x$	0.60	<0.001
LA end-systolic area	$y = 15.1 - 0.4x$	0.59	<0.001
E/A ratio	$y = 14.6 - 2.6x$	0.52	<0.001
Deceleration time	$y = 5.1 + 0.03x$	0.45	<0.001
LA pre-systolic volume	$y = 13.8 - 0.1x$	0.45	<0.001
LA pre-systolic area	$y = 15.0 - 0.3x$	0.44	<0.001
LV ejection fraction	$y = 7.7 + 0.1x$	0.41	<0.001
Transmitral peak E wave velocity	$y = 16.0 - 6.5x$	0.40	0.002
LA end-diastolic area	$y = 15.9 - 0.2x$	0.40	0.002
LA end-diastolic volume	$y = 14.0 - 0.1x$	0.40	0.001
Transmitral peak A wave velocity	$y = 8.3 + 4.4x$	0.32	0.015
Atrial ejection force	$y = 10.0 + 0.1x$	0.27	0.036
Patient age		0.22	NS
Heart rate		0.19	NS

r, Regression coefficient; p, p-value; NS, non-significant; LA, left atrium; and LV, left ventricle.

7.1±6.2% for transmitral Doppler parameters, and 4.5±4.3% for assessment of peak left atrial systolic mitral annular velocity.

Discussion

The major finding of this study is that A_{ann} measured by DTI correlates with left atrial systolic FAC and FVC, thus providing an easy means to assess left atrial systolic function. While DTI has been more widely assessed for its ability to evaluate ventricular function, this study supports the additional role of DTI in quantitating atrial systolic function.

Multiple studies have examined left atrial systolic function using a variety of parameters, namely left atrial emptying volume or left atrial emptying volume fraction;[8–10] left atrial fractional shortening or FAC;[11–13] Doppler transmitral flow parameters such as peak A wave velocity and its time—velocity integral, or the E/A ratio;[14–16] left atrial work load;[17,18] left atrial appendage flow velocities;[19–21] AEF;[6,14,22] and left atrial kinetic energy.[22] However, some of these require cumbersome invasive procedures[15,22] while others are highly sensitive to changes in cardiac loading conditions, left ventricular systolic function, and autonomic state.[2,6,11,23,24] The assessment of left atrial function is thus complex and the accuracy of these parameters to measure atrial contractility is limited.

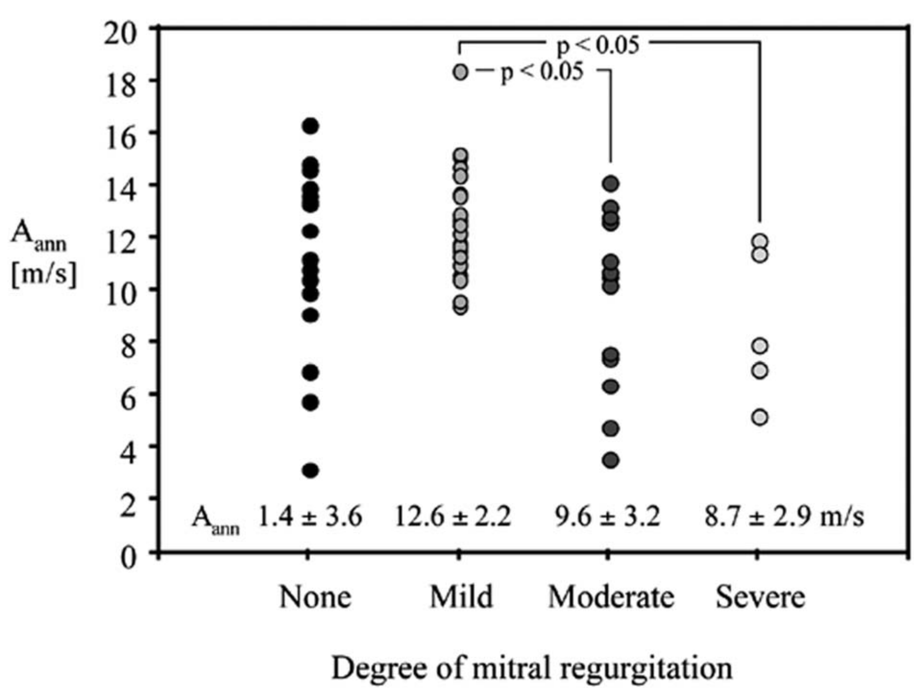

Figure 2 Left A_{ann} (in m/s) stratified according to the degree of MR. The values above the x-axis reflect the mean A_{ann} ± SD in patients with no MR, mild MR, moderate MR, and severe MR.

DTI is a relatively new technology that allows direct and non-invasive measurement of myocardial velocities.[5] To our knowledge, no previous attempt has been made to evaluate the utility of DTI to assess atrial systolic function in humans. In a recent animal experiment, Nagueh et al. found that A_{ann} was directly related to atrial contractility (left atrial d*P*/d*t*) and inversely related to left ventricular end-diastolic pressure.[25] In our study, A_{ann} was related to left atrial systolic FACs and FVCs. Furthermore, it correlated positively with traditional parameters reflecting atrial systolic function such as transmitral peak *A* wave velocity and AEF; and inversely with parameters going along with decreased myocardial contractility, such as impaired left ventricular ejection fraction. Although the subgroups with MR were small, there appears to be a decline in A_{ann} with worsening degrees of MR. The significance of these findings deserves further investigation in a larger number of patients with chronic MR.

Previous reports have yielded differing results concerning the relationship between left atrial function and left atrial size, patient age, heart rate, or underlying cardiac morbidity.[8,10,14,26] We could not confirm the previously described decline of left atrial function expressed as A_{ann} with age or heart rate, which has been previously noted.[10] Maximal atrial area or volume predicted A_{ann} in the univariate linear analysis, but not after including other atrial functional parameters. This indicates the possible importance of adjusting left atrial dimensions for body surface area.[26,27]

Given the simplicity of the measurement, left atrial peak mitral annular velocity was associated with a smaller interobserver variability than the measurement of traditional parameters; these often require several measurements and calculations which multiply the risk of error.

The major limitation of this study is the lack of a gold standard measurement of left atrial function. The measurement of atrial ejection fraction has limitations similar to the ventricular ejection fraction, and the annular motion itself may be influenced by other factors such as annular interdependence.[11,28,29] Left atrial appendage function was not assessed, and we performed only 2D-transthoracic echocardiographic measurement of the left atrium. Compared to angiographic data this has been shown to underestimate true left atrial volume.[27] Recent publications are proposing the use of echocardiographic atrial volume as parameter of atrial size.[30]

As can be depicted from Fig. 1, the standard error of the estimate is significant, and the application of this method may be problematic in an individual patient. Therefore, further evaluation of A_{ann} regarding its reproducibility and robustness is needed.[31] The individual patient groups were small and we included patients who were diagnosed at different stages of their disease, which limits the statistical significance of their comparison. This may explain the fact that the mitral inflow velocities did not significantly differ between patients with or without diastolic dysfunction (stages I—IV). However, the goal of this report was to establish the correlation between A_{ann} and various LA functional parameters in a group of patients with various clinical conditions.

In spite of these limitations, A_{ann} provides a potentially useful means to determine left atrial systolic function; it can easily be assessed echocardiographically by direct measurement and is valid in a variety of cardiac conditions. Further research is needed to apply this method in a larger group of patients with altered contractile patterns such as hypertrophic cardiomyopathy, and in the same individual patient after loading and inotropic conditions have changed.

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