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Original Article

Is mitral annular ascent useful in studying left ventricular function through left atrio-ventricular interactions?

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ABSTRACT

Background: The mitral annulus (MA) is a crucial structure that is in constant motion throughout the cardiac cycle. The main purpose of this study was to determine if M-mode evaluation of the longitudinal motion of the MA could be useful to examine atrio-ventricular interactions.
Methods: Echocardiographic data obtained from 150 patients (mean age 56 ± 16; 82 males) from the University of Cincinnati College of Medicine was evaluated to examine if any relationship exists between MA motion and measures of atrio-ventricular interactions.
Results: Even though left atrial size, left ventricular (LV) mass index, LV ejection fraction (LVEF) and degree of LV diastolic dysfunction (LVDD) were significant echocardiographic variables affecting MA motion; LVEF and the degree of LVDD were the main determinants of MA excursion during systole (MAPSE) and after atrial contraction (MAa). Our results confirm the surrogate value of MAPSE with regards to LVEF and also show that the extent of MA excursion during systole is the main determinant of MAa. The effect of LV diastolic function applies more strongly to MAPSE than to MAa. However, the maximal MAa amplitude varies in accordance to the type of LVDD.
Conclusions: We have shown for the first time that M-mode interrogation of the MA longitudinal motion appears useful to assess atrio-ventricular interactions. Since LV systolic and diastolic functions are so closely related; additional studies are now required to examine how this longitudinal measure correlates with known circumferential rotational data obtained with other imaging modalities.

1. Introduction

The mitral annulus (MA) is a crucial structure that plays an important role in mitral leaflet coaptation, unloading mitral valve closing forces, and promoting left atrial (LA) as well as left ventricular (LV) filling and emptying.[1] The three-dimensional saddle shape of the MA is well characterized in both animals and humans.[2] In fact, the systolic excursion of the MA has been correlated to LV systolic function.[3–7] During the cardiac cycle not only the MA is in constant motion, but also its excursion encompasses a volume that is part of the total LV volume change during both filling and emptying.[8]

Longitudinal myocardial function has attracted interest in recent years. Specifically, this interest was greatly advanced by the work of Torrent-Guasp that introduced the concept of the myocardial band, which explained the architecture of all cardiac chambers.[9] In addition, a 180° twist in the middle portion of this band has been implied as the responsible element for the twisting-untwisting motion of the LV.[10,11] This twisting-untwisting movement of LV myofibers from base and apex rotating in opposite directions, and their spatial and directional orientation changes during the cardiac cycle, have shown a close relationship between LV systolic and early diastolic function.[12,13] In fact impairment of this long-axis LV contraction and relaxation has been reported in experimental and clinical studies in the setting of coronary artery disease, myocardial infarction, LV hypertrophy, dilated cardiomyopathy, and hypertrophic cardiomyopathy.[14]

Our laboratory has previously shown that both mitral annular plane systolic excursion (MAPSE) and the mitral annular ascent

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(MAa) component, occurring during late ventricular diastole, were useful in identifying serial activation differences between the right and left heart.[4,5] We now hypothesized that closer inspection of the MA M-mode signal, with its excellent temporal resolution,[15,16] might be useful to examine atrio-ventricular interactions between the LA and LV.

2. Methods

2.1. Population studied

The University of Cincinnati IRB office approved the study (protocol number 12061302) and no written consent was needed since this was a retrospective study.

The echocardiographic database at the University of Cincinnati College of Medicine Main University Hospital Echocardiography Laboratory was queried for patients who had a complete transthoracic echocardiogram performed between July 1, 2013 and July 31, 2014 for any clinical indication meeting all of the following inclusion criteria.

Inclusion criteria for this study required that all patients at the time of the echocardiographic study were in normal sinus rhythm during the examination. In addition, there had to be good visualization of the LA and LV endocardium with complete M-mode tracing interrogation as well as tissue Doppler signal of the lateral portion of the MA. Furthermore, a complete spectral Doppler study to examine LV diastolic function had to be acquired as recommended by published guidelines.[17–19] Since interpretation of multiple echocardiographic parameters that vary with loading conditions might provide conflicting diagnostic information that could limit LV diastolic function characterization[20–22]; only echocardiographic studies with non-conflicting LVDD diagnostic criteria were included into the final analysis.

Finally, studies were excluded if patients had atrial fibrillation or rhythm abnormalities at the time of the study, mitral annular calcification, mitral valve stenosis, previous mitral valve repair or valvular replacement surgery.

Since our laboratory had previously shown significant differences with regards to LV systolic function and MAa using 75 patients,[5] for this study we targeted a total of 150 patients to analyze atrio-ventricular (LA and LV) interactions with an α value of 0.05 and desired power of 0.80.

Therefore, from a total number of 425 echocardiograms performed during that time frame, the first 150 consecutive echocardiograms that met all inclusion and none of the exclusion criteria were included in to the final analysis.

Calculation of body surface area was performed as previously described by Mosteller as follows[23]:

$$\text{BSA } (m^2) = ([\text{Height (cm)} \times \text{Weight (kg)}]/3600)^{1/2}$$

2.2. Echocardiographic studies

We utilized commercially available systems (Vivid 7 and 9; GE Medical Systems, Milwaukee, WI, USA) to perform two-dimensional echocardiographic studies. Images were obtained in the parasternal and apical views with the patient in the left lateral decubitus position and in the subcostal view with the patient in the supine position using a 3.5 MHz transducer. Standard two-dimensional, color, pulsed, and continuous-wave Doppler data were digitally acquired in gently held end-expiration, and saved in regular cine loop format for subsequent offline analysis.

Left ventricular end-diastolic and end-systolic volumes were traced from the apical 4-chamber view in accordance to published data; while ejection fraction calculations were done using the Simpson's rule algorithm.[6]

Calculation of LV mass was performed according to the American Society of Echocardiography (ASE) recommended formula using LV linear dimensions based on modeling the LV as a prolate ellipse of revolution using the following formula [6]:

$$\text{LV mass} = 0.8 \times \{1.04[(\text{LVIDd} + \text{PWTd} + \text{SWTd})3 - (\text{LVIDd})3]\} + 0.6\,\text{g}$$

Specifically, in this formula PWTd and SWTd correspond to posterior wall thickness at end diastole and septal wall thickness at end diastole, respectively.[6] Since this formula is appropriate for evaluating patients without major distortions of LV geometry such as patients with hypertension, it was appropriate for utilization in this study. Correction for BSA was then performed to express LV mass as LV mass index (LVMI) as g/m^2.

Measurement of LA volume was performed following the ASE guidelines using the area-length method from the apical 4-chamber and apical 2-chamber views at ventricular end systole (where LA size is largest) using the following formula [6,17]:

$$\text{LA Volume} = 8/3\pi\ [(A1) \times (A2)/(L)]$$

In this formula, L is measured from back wall to line across hinge points of mitral valve and is the shortest length from either the 4-chamber (A1) or 2-chamber (A2). To accurately correct for the effect of body habitus, LA volumes were corrected for BSA and consequently LA volumes were expressed as LAVI (mL/m^2).

Mitral inflow velocity was obtained using pulsed-wave Doppler examination at a sweep speed of 100 mm/s from the apical four-chamber view by placing the sample volume at the tips of the mitral leaflets.[17–19] Peak velocity in early diastole (E-wave, LV relaxation) and late diastole (A-wave, LA contraction) and deceleration time of the E-wave were measured as previously described.[17–19]

Since our laboratory has previously described that maximal MA excursion and MA ascent are better assessed when the lateral portion of the MA is interrogated,[4,5] pulsed-wave tissue Doppler imaging (TDI) was only performed on the lateral portion of the MA in order to perform direct ipsilateral correlations.

In terms of the lateral MA TDI, peak velocity in systole (S′), early diastole (E′), and late diastole (A′) were measured by placing the sample volume at the junction were the mitral valve plane intersects the left ventricular free wall using images obtained from the apical 4-chamber view. As previously explained, for the purpose of this study LV diastolic pressure was estimated only using the E/E′ ratio obtained from the lateral MA E' velocity.[18,19] Finally, LV diastolic function was classified as normal, impaired relaxation, pseudonormal and restrictive pattern following published recommendations.[17]

Overall MA motion was examined by M-mode by placing the cursor in the same orientation as previously described for TDI. The resulting M-mode tracing generated a signal containing both MAPSE and MAa. Specifically, MAa was measured as the distance traveled by the lateral portion of the MA from the end of diastasis until the end of atrial contraction.[4,5] MAPSE was measured as the total excursion of the mitral annulus from the end of atrial ascent until the end of ventricular systole. A representative MA M-mode tracing showing both MAPSE and the MAa component is shown in Fig. 1.

2.3. Statistical analysis

The commercially available software Merge Cardio Workstation (Merge Healthcare) was used to calculate all echocardiographic measurements. All continuous data are presented as mean and standard deviation. Comparison between groups' baseline

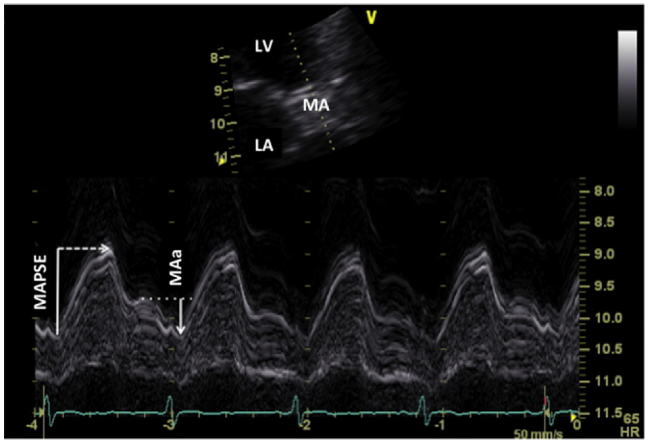

Fig. 1. Representative, MA M-mode image with a corresponding to MA motion showing MAPSE (straight line and dashed arrows) and MAa (dotted line and straight arrow) that is measured after atrial contraction. The location of the lateral mitral annulus (MA) is shown in relation to both LV and LA in the superior portion of the image.

characteristics was performed using analysis of variance (ANOVA) for continuous data and Fisher's exact test for categorical data. Multivariate logistic regression analysis was performed to detect significances to identify with accuracy abnormalities with both MAPSE and MAa.

Intra-class correlation coefficient was utilized to assess reliability of MAa. In order to compare reproducibility of a single reader, ten patients were randomly selected from each group and variables of interest were re-measured after a 6-month span. For comparison among different readers, 10 patients were randomly selected from each group and a trained and blinded reader measured variables of interest. Intra-class correlation coefficients were calculated using one- and two-way agreement models for comparison between single and multiple readers, respectively.[24] All statistics were calculated in MedCalc Software bvba Version 14.12.0 (Belgium). P-values of <0.05 were considered to be statistically significant.

3. Results

A total of 150 patients (mean age 56 ± 16; 82 males) that met all the inclusion and none of the exclusion criteria comprised the study population. The main indication for obtaining the echocardiogram is listed in Table 1. Furthermore, all recorded echocardiographic data can be found on Table 2.

Table 1
Main indication to obtain an echocardiogram on the studied population.

Indication	Number of studies
Syncope	2
Hepatitis	4
Abnormal ECG	3
COPD	5
Diabetes mellitus	6
Malignancy	8
History of PAF	9
Chest pain	9
CVA	10
Aortic valve disease	11
CAD	13
Shortness of breath	14
Renal disease	17
CM/HF	18
Hypertension	21

Table 2
Main echocardiographic findings for the entire studied population.

Variables	Mean ± SD	Range
BSA	2.0 ± 0.3	1.2–3.2 m^2
LVMI	113 ± 42	38–275 g/m^2
LAVI	31 ± 15	12–100 ml/m^2
LV end systolic volume	58 ± 60	10–378 ml
LV end diastolic volume	133 ± 60	38–415 ml
LVEF	63 ± 20	10–85%
MAPSE	1.2 ± 0.4	0.2–2.6 cm
MAa	0.5 ± 0.2	0.1–0.9 cm
MV deceleration time	182 ± 53	69–366 ms
MV E velocity	79 ± 34	0.4–186 cm/s
MV A velocity	68 ± 35	0.4–168 cm/s
MV E/A ratio	1.5 ± 1.1	0.4–11
MA S' velocity	8 ± 3	2–19 cm/s
MA E' velocity	9 ± 4	2–21 cm/s
MA A' velocity	8 ± 3	1–21 cm/s
MV E/MA E' ratio	12 ± 9	0.1–53

We found no difference in either MAPSE or MAa measurements with regards to age, gender and body surface as seen on Table 3. However, we noted significant differences in MAPSE and MAa measures when examined against known variables that affect atrio-ventricular interactions such as LAVI, LVMI and LVEF.[25] To simplify these assessments, we utilized recently published reference values suggested by the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[6]

First, the relationship with regards to LAVI was investigated. We noted that MAPSE values were significantly higher in patients with a normal LAVI value ($<34\ ml/m^2$) when compared to patients with abnormally high LAVI ($\geq 34\ ml/m^2$) values (1.3 ± 0.3 cm versus 1.1 ± 0.5 cm; $p < 0.001$). Similarly, differences were also noted for MAa values (0.5 ± 0.2 cm versus 0.4 ± 0.2 cm; $p = 0.0001$).

Second, a similar analysis was then performed after adjusting for gender specific values. In this analysis, MAPSE values were also significantly higher for patients with normal LVMI ($<95\ g/m^2$ for females and $<115\ g/m^2$ for males) values (1.4 ± 0.3 cm) when compared to MAPSE values in patients with abnormally higher LVMI values (1.1 ± 0.4 cm; $p < 0.0001$). However, the impact of LVMI on MAa values, though still significant, was less robust (0.5 ± 0.2 cm versus 0.4 ± 0.1 cm; $p < 0.04$).

Third, when we examined the effect of LV systolic function on both MAPSE (1.4 ± 0.3 cm) and MAa (0.5 ± 0.2 cm), these were significantly higher in patients with an LVEF $\geq 55\%$ when compared to patients with an LVEF $<55\%$ (0.7 ± 0.2 cm and 0.3 ± 0.1 cm; $p < 0.0001$, respectively).

Finally, significant differences in terms of both MAPSE and MAa were identified as seen in Fig. 2A and B when the study population was divided in terms of their LV diastolic function according to published guidelines.[17–19] Interestingly, MAPSE was progressively smaller with worsening LV diastolic function. In contrast, MAa was the highest among LVDD stage 1 patients and then progressively smaller as LV diastolic function deteriorated.

Table 3
Examination of age, gender and body surface area on MAPSE and MAa.

Variables	MAPSE	p value	MAa	p value
Patients <55 years of age	1.3 ± 0.4 cm	$p = 0.2$	0.5 ± 0.2 cm	$p = 0.8$
Patients ≥55 years of age	1.2 ± 0.4 cm		0.5 ± 0.2 cm	
Females	1.2 ± 0.4 cm	$p = 0.3$	0.5 ± 0.2 cm	$p = 0.5$
Males	1.3 ± 0.4 cm		0.5 ± 0.2 cm	
Normal BSA adjusted for gender	1.2 ± 0.4 cm	$p = 0.5$	0.4 ± 0.2 cm	$p = 0.5$
High BSA adjusted for gender	1.2 ± 0.4 cm		0.5 ± 0.2 cm	

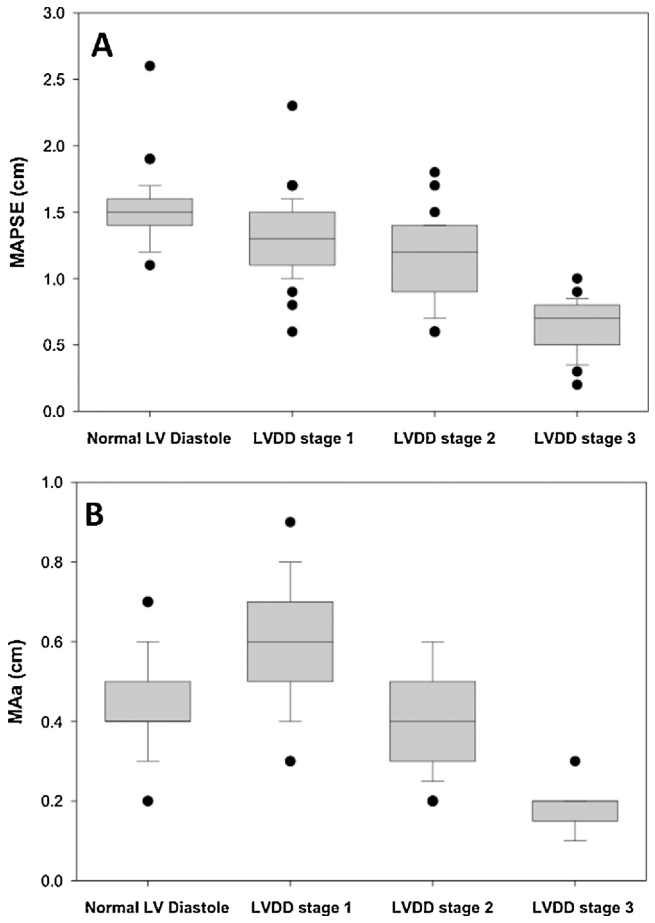

Fig. 2. Box plot representations of (A) MAPSE and (B) MAa according to LV diastolic function.

In a stepwise multiple regression analysis using echocardiographic parameters that were found statistically significant, LVEF and type of LVDD were the best predictors of both MAPSE and MAa as seen on Table 4.

Inter-rater agreement (K, Kappa) value assessment between MAa measurements was then utilized to determine variability. In general, the strength of the agreement was very good (K = 0.985, standard error = 0.094 and 95% confidence interval = 0.711–1.000) if a trained observer (intraobserver) was performing these measurements. The strength of the agreement was moderate (K = 0.546, standard error = 0.158 and 95% confidence interval = 0.237–0.855) when untrained observers (interobserver) were asked to reproduce MAa measurements. While their measurements improved with repeated measurements, the first recording was used for the purpose of the analysis.

Table 4
Stepwise multiple regression analysis individually performed for MAPSE and MAa.

Multiple regression analysis for MAPSE:				
Independent variables	Coefficient	Std. Error	r	P-value
LVAI	0.0007663	0.001651	0.03851	0.6433
LVMI	−0.0007844	0.0005385	−0.1201	0.1474
LVEF	0.007693	0.001228	0.4615	<0.0001
LVDD type	−0.1578	0.02905	−0.4112	<0.0001
Multiple regression analysis for MAa:				
Independent variables	Coefficient	Std. Error	r	P-value
LVAI	−0.0009532	0.001021	−0.07733	0.3518
LVMI	−0.0001156	0.0003328	−0.02884	0.7288
LVEF	0.003634	0.0007591	0.3695	<0.0001
LVDD type	−0.03973	0.01795	−0.1808	0.0020

4. Discussion

This study highlights that close examination of MA motion is useful to explain the relative importance of atrio-ventricular interactions. Even though LAVI, LVMI, LVEF and the degree of LVDD are the most important measured echocardiographic variables in this study that affect MA motion; LVEF and the degree of LVDD were found as main determinants of both MAPSE and MAa. Specifically, our results confirm the surrogate value of MAPSE with regards to LVEF and also show that the extent of MA excursion during systole is the main determinant of MAa. The effect of LV diastolic function applies more strongly to MAPSE than to MAa. However, the maximal MAa amplitude varies in accordance to the type of LVDD. Interestingly, even though LAVI and LVMI influence both MAPSE and MAa, the effect of both LVEF and type of LVDD was stronger in determining MA motion.

Even though numerous techniques have been applied to study cardiac rotation, both cardiac magnetic resonance imaging and speckle-tracking echocardiography are the most useful clinical tools for this assessment, with cardiac magnetic resonance imaging currently considered the reference standard.[12] The concept of cardiac rotation, signifying the wringing or twisting motion of the LV along its long-axis, has been anatomically and functionally described by the work of Torrent-Guasp after the introduction of the myocardial band.[9] The three-dimensional representation of this single strip of muscle arranged in a double-loop helical orientation extending from the pulmonary artery to the aorta helped explain the architecture of all cardiac chambers. Furthermore, 180° twist in the middle portion of this band has been implied as the responsible element for the twisting-untwisting motion of the LV.[10,11] It is now recognized that rotation of myocardial fibers from base and apex in opposite directions, as well as their change in spatial directional orientation that occurs dynamically during the cardiac cycle, might explain the close relationship existing between LV systolic and early diastolic function.[12,13] In this particular study, M-mode interrogation was used for the first time to examine axial MA motion in relation to atrio-ventricular interactions as a result of cardiac rotation.

From a mechanistic point of view, it is important to remember that in diastole, chamber wall relaxation unmasks stored elastic strain, allowing the LV to recoil and act as a suction pump by promptly aspirating blood into the LV favoring LV filling.[26] In this kinematic model,[27] the MA is seen as a piston located in between atria and ventricle. Our results are certainly in agreement with this kinematic model as we showed that the extent of MAPSE and MAa are mainly determined by LVEF and LVDD when assessed longitudinally. In addition, our MA motion data is also in agreement with work published by van Dalen et al. that demonstrated a close relationship existing between LV shape and twist angle.[28] As seen by our results, the highest MAa was seen in LVDD stage 1 patients and then progressively smaller as LV diastolic function deteriorated. These results are in agreement with current knowledge of LA contribution to LV filling is basically dependent on LV diastolic properties. Specifically, with abnormal relaxation (LVDD stage I), the relative contribution of LA contractile function to LV filling increases. As LV filling pressures progressively increase and LVD diastolic function worsens, the limits of atrial preload reserve are reached and the LA serves predominantly as a conduit.[29]

The following limitations need to be acknowledged. First, this was a retrospective study; however, the main goal was attained. Second, even though a small number of patients were included for

analysis, the main purpose of this study was to determine if a correlation existed between MA motion and measurements of atrio-ventricular interactions and this was demonstrated. Third, based on the pre-specified exclusion criteria, no assumptions can be made on how atrial fibrillation, frequent ectopy, or mitral valve abnormalities affect the studied relationship. However, most likely none of these measurements could be obtained in these patients. Finally, LV speckle-tracking analysis was not performed concurrently in this study to make any potential correlations between MA motion and twisting as well as untwisting variables.

Atrio ventricular interactions are important in determining LV function. The MA is anatomically located between the atria and ventricle; hence, it should be functionally linked with regards to cardiac performance. Even though the surrogate value of MAPSE with regards to LVEF is well documented; the potential utility of the MAa component has not been either well studied or characterized. Our results not only suggest that the overall excursion of the MA during systole is the main determinant of MAa; but also that maximal MAa amplitude varies in accordance to LV diastolic function. Moreover LV systole is coupled to LA systole. This is a relatively new concept in which even late diastolic events are dependent upon systole. Since LV systolic and early diastolic functions are closely related as a result of the twisting motion of the myocardial band, additional studies are now required to examine how this longitudinal measure of MAa correlates with circumferential rotational data obtained with other imaging modalities.

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Role of sponsors

There are no sponsor(s).

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We attest that the article is the Authors' original work, has not received prior publication and is not under consideration for publication elsewhere. We adhere to the statement of ethical publishing as appears in the work cited by Shewan and associates.[30]

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