Concordance between M-mode, pulsed Tissue Doppler, and colour Tissue Doppler in the assessment of mitral annulus systolic excursion in normal subjects

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Aims M-mode left atrioventricular plane displacement (AVPD) correlates with Tissue Doppler (TD) peak systolic annular velocity in healthy individuals. This approach is biased by several interacting factors related to the structural complexity of mitral annulus physiology, including the different dimensional values of measures, the confounding effect of isovolumic motions, and the spectral thickness of pulsed TD envelope. We sought to analyze the effective concordance between techniques in the assessment of systolic annular excursion.

Methods and results In 92 healthy subjects (age 60.5 ± 18.6, 43.5% women), systolic AVPD was measured after exclusion of isovolumic components using three techniques: (i) M-mode; (ii) temporal integration of pulsed TD systolic wave; and (iii) colour TD-derived tissue tracking. Close correlations of M-mode AVPD with pulsed TD velocity-time integral (VTI) (R = 0.90, P < 0.0001) and colour TD AVPD (R = 0.86, P < 0.0001) were found. However, M-mode AVPD underestimated pulsed TD VTI (mean error 2.5 ± 1.7 mm) and overestimated colour TD AVPD (mean error 3.4 ± 1.3 mm). The concordance between M-mode and pulsed TD increased after adjustment for spectral dispersion of pulsed TD instantaneous velocities (mean error 0.1 ± 1.1 mm).

Conclusion Despite strict correlations exist between M-mode and TD in the assessment of mitral annulus systolic excursion, the effective concordance between techniques is sub-optimal.

KEYWORDS
Doppler Tissue imaging; M-mode; Mitral annular systolic motion

Introduction

M-mode imaging and Tissue Doppler (TD) are commonly used echocardiographic techniques for the assessment of left ventricular (LV) long-axis function. We have recently shown that total left atrioventricular plane systolic displacement (AVPD) evaluated by M-mode significantly correlates with pulsed TD-derived mitral annulus peak systolic velocity (Sm) in healthy middle-aged individuals, suggesting that a good concordance between the two techniques exists in the evaluation of long-axis systolic LV function.1 However, this approach is characterized by a number of conceptual mismatches related to the structural complexity of mitral annulus physiology. First, the analysis of the simple correlation between AVPD and Sm—i.e. an excursion measure and a velocity measure—precludes an assessment of the effective concordance between the two techniques, which by definition requires dimensional homogeneity of variables.

Second, the standard measurement of total AVPD as the distance between the nadir of the annular motion profile and the point of maximal excursion towards LV apex provides an index that reflects a contractile phenomenon occurring throughout the whole systole—with inclusion of the displacement component related to LV isovolumic contraction phase2—whereas Sm represents an instantaneous level of maximal velocity that characterizes the ejection phase of LV systolic contraction. Third, total AVPD may sometimes be affected by the presence of post-ejection shortening components occurring during LV isovolumic relaxation period.3 Fourth, the spectral envelope thickness of pulsed TD signal—reflecting non-uniform velocities within the sample volume—may act as an adjunctive confounding factor.4 These considerations could explain the presence of only a moderate degree of correlation between AVPD and Sm.1

A comparison between the M-mode annular displacement effectively occurring during the ejection period of systolic LV contraction and the velocity-time integral (VTI) of
signals recorded by pulsed and colour TD during this phase may allow more direct evaluation of the concordance between M-mode and TD techniques in the assessment of long-axis LV systolic function, avoiding the confounding effects of isovolumic intervals. Considering that systolic VTI is a mathematical equivalent of displacement (i.e. displacement = velocity x time), this approach may also overcome the drawback due to variables with different dimensional value. Additionally, such a comparison might in theory help to better understand the relation between annular excursion amplitude, velocity, and time — i.e. the three main components of annular motion. To our knowledge, this comparison has never been performed.

For pulsed TD analysis, determination of systolic VTI requires tracing of systolic wave contour, whereas for colour TD an instantaneous calculation of VTI at any given instant of cardiac cycle can be obtained using tissue tracking imaging, a modality that automatically generates displacement curves by integration of colour TD velocity data over time. The aim of this study was to compare mitral annulus systolic excursion assessed by standard M-mode, pulsed TD, and colour TD-derived tissue tracking in a population of healthy subjects.

Methods

Study population
The study population was selected among consecutive normal subjects aged > 16 years, referred to our Echo Laboratory for a diagnostic examination between 2 January 2007 and 18 June 2007. All patients gave their consent to participate in the study. Inclusion criteria were: no history of cardiovascular and/or pulmonary disease, diabetes mellitus, arterial hypertension, or systemic disease; and normal findings on physical examination, electrocardiogram, and echocardiography. Subjects taking cardiovascular medications or with inadequate quality of echocardiograms were excluded from the study. A total of 92 patients met the selection criteria during the period of enrolment. In the large majority of cases (n = 78), patients were referred by their general practitioner for a general evaluation of cardiovascular risk. Among the remaining subjects, main reasons for referral included pre-participation sports examination (n = 6), pre-operative assessment of risk in subjects undergoing minor non-cardiovascular surgery (n = 3), atypical chest discomfort (n = 3; all with evidence of maximal negative stress test), and hemicrania (n = 2; both with evidence of negative contrast transcranial Doppler).

Echocardiography

M-mode analysis
Echocardiography was performed using commercially available ultrasound diagnostic systems (Vivid 7, GE, USA) equipped with 2.5–4.0 MHz probes. Two-dimensionally guided M-mode imaging of mitral annular motion was performed from the apical 4-chamber view at the lateral site of the annulus using the zoom function. Briefly, the M-mode pattern of mitral annular motion during systole in normal subjects includes two sequential phases, which correspond to the isovolumic contraction phase and the ejection phase, respectively. The isovolumic contraction phase starts at the onset of QRS, at the end of late diastolic descent due to atrial contraction, and is characterized by an initial displacement of the annulus towards LV apex. This may be followed by either a short plateau or a transitory backward descent, in accordance with the presence of a monophasic or biphasic pattern of isovolumic longitudinal annular dynamics. The abrupt increase in the slope of M-mode annular profile at the end of the isovolumic contraction period identifies the beginning of the ejection phase, which is responsible for the major part of annular displacement and ends at peak shortening. In this study, systolic AVPD was determined from M-mode tracing by measuring the annular displacement towards cardiac apex during systole, after excluding the component of excursion due to isovolumic LV contraction (Figure 1, top panel). In subjects showing two distinct peaks of displacement in the M-mode annular profile, the former was used for the measurement—regardless of which was closer to LV apex—based on the assumption that the latter reflects the isovolumic relaxation phase.

Figure 1 (Top) Measurement of M-mode systolic left atrioventricular plane displacement (AVPD) after exclusion of the components of excursion occurring during the isovolumic phases of the cardiac cycle. Note the presence of a second peak shortening, corresponding to the end of the isovolumic relaxation period. (Middle) Measurement of the velocity-time integral (VTI) of S wave by pulsed Tissue Doppler (TD) imaging. (Bottom) Measurement of systolic AVPD from tissue tracking displacement waveform. As for M-mode imaging, the components of excursion occurring during the isovolumic contraction and relaxation periods were excluded. Also note that the biphasic patterns of motion detected by M-mode and tissue tracking during the two isovolumic phases were concordant with the velocity patterns recorded by pulsed TD. ICT, isovolumic contraction time; IRT, isovolumic relaxation time.
Pulsed TD analysis
Pulsed TD imaging of systolic annular velocity was performed from the apical 4-chamber view by placing a 5-mm sample volume at the junction between basal lateral myocardium and lateral mitral annulus, in accordance with current American Society of Echocardiography recommendations. Filters and gains were adjusted at the minimal level for optimum signal-to-noise ratio, and the image sector was kept as narrow as possible to optimize frame rate. The VTI of systolic TD signal was obtained by tracing the contour of systolic ejection wave ($S_2$), after exclusion of both isovolumic contraction wave and any post-systolic shortening from the measurement (Figure 1, middle panel). When a crossing point with the baseline was not clearly identifiable at either the beginning or end of $S_2$ wave profile, linear extrapolation to baseline was performed. The peak of $S_2$ wave ($S_{p2}$) was also measured.

In an attempt to adjust for spectral dispersion of instantaneous velocities, an alternative measurement of pulsed TD systolic VTI was performed, as recently described. Briefly, any pulsed Doppler signal is characterized by a definite spectral width that reflects the broadening of instantaneous velocities recorded within the sample volume. The larger is the envelope thickness, the more dispersed are the velocities. Assuming normality of velocity distribution at any instant, a rough adjustment for spectral dispersion can be obtained by estimating the mean between the maximal and minimal velocity identified by the signal in that instant. Extending this concept to whole systole by temporal integration, it follows that an adjusted systolic VTI of TD signal can be calculated as the mean between the areas obtained by tracing the outer and inner contour of systolic TD envelope (Figure 2).

Colour TD analysis
Colour TD imaging of systolic mitral annular motion was performed from the apical 4-chamber view by placing a square region of interest containing 9 pixels in a $3 \times 3$ array at the junction between basal lateral myocardium and lateral mitral annulus, in accordance with current American Society of Echocardiography recommendations. Particular care was given to achieve optimization of pulse repetition frequency, colour saturation, sector size, depth, and velocity range.

Figure 2. Adjustment for spectral dispersion of pulsed Tissue Doppler (TD) signal. The pulsed TD envelope is characterized by a definite thickness, representing the instantaneous dispersion of velocities recorded within the sample volume. At any given instant, the point identified by the outer contour (in this example, the A point) corresponds to the maximal instantaneous velocity, whereas that identified by the inner contour (the B point) corresponds to the minimal instantaneous velocity recorded within the sample volume. Assuming normality of instantaneous velocity distribution, an adjusted instantaneous velocity can be calculated as $(A + B)/2$, corresponding to the midpoint between A and B (the C point). Extending this concept to the whole systole by temporal integration, it follows that an adjusted systolic velocity-time integral (VTI) can be obtained as the mean between the outer and inner VTI.

Data collection and reproducibility analysis
Images and clips were digitally acquired, stored on magneto-optical disks, and analyzed using an off-line system (Echo Pac, GE, USA). All measurements were obtained as the average of three values obtained in consecutive beats during end-expiratory apnoea, accurately controlling for correct alignment of mitral annulus motion with the ultrasonic beam. M-mode systolic AVPD, pulsed TD systolic VTI, and colour TD systolic AVPD values were all expressed in millimeters. Intra- and inter-observer reproducibility, evaluated in a randomly selected subset of 40 subjects and expressed as coefficient of variation and intra-class correlation coefficient, were: M-mode systolic AVPD, 3.8%, $R = 0.95$, $P < 0.0001$, and 4.5%, $R = 0.92$, $P < 0.0001$; pulsed TD systolic VTI, 4.0%, $R = 0.94$, $P < 0.0001$, and 4.7%, $R = 0.92$, $P < 0.0001$; pulsed TD adjusted systolic VTI, 4.4%, $R = 0.93$, $P < 0.0001$, and 4.9%, $R = 0.91$, $P < 0.0001$; colour TD systolic AVPD, 4.6%, $R = 0.91$, $P < 0.0001$, and 5.6%, $R = 0.89$, $P < 0.0001$, respectively.

Statistical analysis
Data are presented as mean ± SD. Pearson's regression coefficients were used to explore relations between variables. The levels of correlation found between M-mode systolic AVPD and both pulsed TD systolic VTI and colour TD systolic AVPD were compared to those observed with the corresponding peak systolic annular velocities using the Fisher’s Z-transformation of Pearson’s coefficients. The Bland and Altman analysis was used to assess the concordance between M-mode and TD techniques. Data analysis was performed using the SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) software Release 11.5. All statistical tests were two-tailed. The significance level was set at 0.05.

Results
Main characteristics of the study population are presented in Table 1. A close correlation between M-mode systolic AVPD and pulsed TD VTI of systolic annular motion was found (Figure 3, top left panel). M-mode systolic AVPD also correlated with $S_{p2}$ ($R = 0.76$, $P < 0.0001$), but the strength of the relationship was lower than that observed with pulsed TD VTI ($P < 0.0001$ by comparison of correlation coefficients). Bland and Altman analysis evidenced that M-mode systolic AVPD underestimated pulsed TD VTI (mean error $-5.1 ± 1.7$ mm), with a trend towards increased underestimation errors for increasing values of average excursion (Figure 3, bottom left panel). A similarly high correlation was found between systolic AVPD and pulsed TD adjusted VTI (Figure 3, top right panel). Of note, the regression line was very

before data acquisition. A high frame rate (>120 Hz) was used, yielding a temporal resolution of 7 ms. During off-line signal processing, sample position for the duration of the cardiac cycle was adjusted by manually tracking annular motion. From colour TD velocity data, a waveform describing annular displacement was generated using the tissue tracking imaging modality. The profile of tissue tracking curves recorded at the level of mitral annulus in normal individuals substantially resembles that of M-mode annular motion, with an isovolumic contraction component and an ejection component that are generally detectable along the systolic portion of curves in the majority of subjects. Colour TD systolic AVPD was calculated as the difference between peak displacement and the value of displacement recorded at the end of the isovolumic contraction phase (Figure 1, bottom panel). As for M-mode analysis, any component due to post-systolic shortening was excluded from the measurement. Peak annular systolic velocity was also measured in all subjects from colour TD velocity waveforms.
near to the identity line. Bland and Altman plot revealed high concordance between the two variables (mean error $0.1 \pm 1.1$ mm), evidencing a random dispersion of errors for increasing values of average excursion (Figure 3, bottom right panel).

A good correlation between M-mode systolic AVPD and colour TD systolic AVPD was observed (Figure 4, top panel). M-mode systolic AVPD also showed a significant but weaker correlation with colour TD peak systolic annular velocity ($R = 0.68$, $P < 0.0001$; $P < 0.0001$ by comparison of correlation coefficients). Bland and Altman analysis revealed that M-mode systolic AVPD systematically overestimated colour TD systolic AVPD (mean error $3.4 \pm 1.3$ mm), with a trend towards increased overestimation errors for increasing values of average excursion (Figure 4, bottom panel).

### Table 1 Clinical and echocardiographic features of the study population

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value (mean ± SD)</th>
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<tbody>
<tr>
<td>Age (year)</td>
<td>60.5 ± 18.6</td>
</tr>
<tr>
<td>Female gender (n)</td>
<td>40 (43.5%)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>74.0 ± 11.7</td>
</tr>
<tr>
<td>Height (m)</td>
<td>166.5 ± 10.2</td>
</tr>
<tr>
<td>Body surface area (m$^2$)</td>
<td>1.82 ± 0.17</td>
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<tr>
<td>Body mass index (Kg/m$^2$)</td>
<td>26.8 ± 4.9</td>
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<tr>
<td>Heart rate (bpm)</td>
<td>74.5 ± 9.1</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>126.4 ± 10.3</td>
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<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>81.0 ± 6.9</td>
</tr>
<tr>
<td>M-mode systolic AVPD (mm)</td>
<td>13.8 ± 2.6</td>
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<tr>
<td>$S_m$ (cm/s)</td>
<td>10.8 ± 2.4</td>
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<tr>
<td>Pulsed TD systolic VTI (mm)</td>
<td>18.9 ± 3.5</td>
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<tr>
<td>Colour TD peak systolic velocity (cm/s)</td>
<td>7.6 ± 2.2</td>
</tr>
<tr>
<td>Colour TD systolic AVPD (mm)</td>
<td>10.3 ± 2.0</td>
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</tbody>
</table>

AVPD, systolic left atrioventricular plane displacement; $S_m$, systolic peak annular velocity; TD, Tissue Doppler; VTI, velocity-time integral.

### Discussion

### Main findings

This study performed a direct comparison between standard M-mode and TD for the assessment of mitral annulus systolic excursion in a population of healthy subjects. Our results show that: (i) after exclusion of the isovolumetric components of annular excursion, a close correlation exists between systolic annular displacement directly measured by standard M-mode and that indirectly estimated by temporal integration of velocities measured by either pulsed TD or colour TD; (ii) despite the high levels of correlation, M-mode systolic AVPD significantly underestimates pulsed TD VTI and overestimates colour TD systolic AVPD; (iii) taking into account the confounding effect of pulsed TD envelope thickness, the discrepancies between M-mode and pulsed TD were considerably reduced, suggesting an important role of velocity dispersion in determining the discrepancies between the two techniques.
greater absolute errors for increasing values of excursion. Worthy of note, these data may be in accordance with the recent finding that annular velocities taken at the outer edge of pulsed TD envelope tend to overestimate the corresponding digitized M-mode velocities. Our results also agree with a recent study conducted on 15 patients with end-stage renal disease and 10 controls, which showed that total annular displacement assessed by tissue tracking was significantly lower than that estimated by standard and anatomical M-mode. The different physiological aspects of mitral annulus motion explored by pulsed TD and colour TD—in particular the spectral overlap of annular velocities for the latter—are likely to have played a major role in determining such discrepancies. In this view, it could be hypothesized that the effective annular excursion amplitude during the ejection phase of LV systole may be affected by both maximal and mean annular velocities in a hardly predictable fashion, thus reflecting the high complexity of annular systolic dynamics. In addition, other aspects including changes in alignment of the Doppler beam occurring during systolic displacement, potential beat-to-beat variability in annular excursion, and the confounding effects of LV twisting and end-diastolic longitudinal contraction of left atrial myocardial fibers may have contributed to the observed discrepancies.

Interestingly, the concordance between M-mode and pulsed TD in our population was improved when VTI was calculated by considering the midpoints of pulsed TD envelope thickness. Accordingly, compared with standard measurements at the outer points of the pulsed TDI envelope, peak annular velocities taken at the midpoints of the envelope have been recently reported to show better concordance with peak velocities obtained from digitized M-mode imaging of annulus motion. However, it should also be pointed out that estimation of envelope midpoints by manual tracing of outer and inner contours of pulsed TD signals represents a very rough adjustment for the spectral dispersion of annular velocities. Moreover, in some patients the outer and particularly inner contours of pulsed TD envelope tend to be smoothed and may be difficult to be identified. In this view, further studies are needed to test the validity of this approach for pulsed TD velocity measurements. Nonetheless, these evidences may suggest that inhomogeneity of annular velocities recorded within the sample volume could have an important role in determining the discrepancies between pulsed TD and M-mode.

Clinical implications and study limitations

Regardless the pathophysiological mechanisms underlying the observed discrepancies, the good correlations found in this study suggest that assessment of systolic AVPD by standard M-mode imaging of the mitral annulus may be considered a simple, fast, and reliable tool for the analysis of mitral annulus systolic motion in clinical practice. This could be particularly useful when examinations are performed using machines without TD capabilities. However, when using systolic AVPD as an index of LV systolic function, it should be carefully taken into account that the effective concordance between M-mode and more sophisticated techniques in the evaluation of annular systolic excursion is sub-optimal.

Correlation between M-mode and TD

The strict correlation of M-mode systolic AVPD with systolic VTI determined by either pulsed or colour TD reflects an expected agreement between mathematically equivalent variables—i.e. a direct measure of annular excursion, and derived measures of annular excursion obtained by integrating velocity over time. Notably, in this study annular excursion was measured by different techniques during the ejection phase of LV systole. This allowed to overcome the confounding effect of longitudinal isovolumic components of displacement, which have been recently shown to account for as much as 14% of the total longitudinal myocardial shortening in healthy subjects. These findings extend our previous observation of moderate correlation between total AVPD and Sm in normal individuals, as they point out that the concordance between M-mode and TD tends to increase when the comparison is performed by analyzing variables with homogeneous dimensional value and similar pathophysiological meaning.

Discrepancies between M-mode and TD

Despite the high levels of correlations found in this study, discrepancies between M-mode and TD techniques were clear in our population. Systolic annular excursion measured by M-mode systematically underestimated that obtained by tracing of pulsed TD systolic VTI and overestimated that measured by tissue tracking, with a tendency towards
Some limitations should be considered in this study. Systolic annular motion in normal left ventricles is not uniform along the whole annulus circumference, so that the findings of this study cannot be generalized to annular sites other than the lateral one. Moreover, the choice of other LV walls (e.g. the inferior) for the analysis of LV long-axis function could have reduced the confounding effect of angle-dependency. The study population was assumed to be healthy based on history, clinical examination, electrocardiography, and echocardiography, but the presence of sub-clinical coronary artery disease cannot be ruled out. This study focused on the ejection phase of LV systole, but it should be taken into account that small discrepancies in systolic time intervals may exist between M-mode, TD techniques, and conventional Doppler analysis. Measurements in this study were not performed simultaneously. Off-line assessment of annular motion by anatomical M-mode, pulsed TD, and colour TD in the same cardiac cycle would have probably increased agreement among techniques. Lastly, because by design this study only included healthy subjects, the range of systolic indices observed in our population was relatively narrow. Thus, the concordance between M-mode and TD in the assessment of mitral annulus excursion over a larger range of systolic indices remains to be established. It should also be considered that identification of the isovolumic phases in the annular motion profiles recorded by M-mode and tissue tracking may be somewhat difficult in patients with LV systolic dysfunction, due to the flattening of the curves. Considering the important role of LV long-axis systolic indices as early markers of contractile impairment, further studies shall be performed to analyze the concordance between systolic annular excursion values measured by M-mode, pulsed TD, and colour TD in pathological conditions, and to assess their feasibility and possible different prognostic significance.

Conflict of interest: none declared.

References