Aortic valve closure: relation to tissue velocities by Doppler and speckle tracking in normal subjects

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Aims The aim of this study is to resolve what event in velocity/time curves represents aortic valve closure (AVC) by comparing the timing of AVC visually seen in high frame rate B-mode images with simultaneously recorded apical tissue Doppler imaging (TDI) and speckle-tracking-based velocity/time curves from normal subjects.

Methods and results A total of 73 recordings from 11 normal subjects were analysed. The acquisition frame rate was equal for both TDI and B-mode (mean 147.5 FPS). The study shows conclusively that the initial negative velocity spike at end-systole occurs before AVC, 26.7 ± 6.2 ms before reference (P < 0.001). The event closest to the reference was the time point of zero velocity after the negative spike, 2.6 ± 8.2 ms before reference. These events are related to the reference in the same way for velocity/time curves by speckle tracking, colour M-mode, and pulsed wave tissue Doppler.

Conclusions AVC in velocity/time curves should be positioned at the end of the negative spike after ejection. Establishing AVC from the correct event in velocity/time curves will ensure more consistent displacement, velocity, strain, and strain rate parameters.

KEYWORDS Heart; Echocardiography; End systole; Systolic time interval

Introduction Timing of aortic valve closure (AVC) is important when analysing cardiac data. AVC marks the transition from end ejection to start of diastole. Common echocardiographic approaches for timing AVC are spectral Doppler of the blood flow through the aortic valve and parasternal M-mode of the aortic valve. Other methods include T wave in ECG, phonocardiography of the second heart sound and empirical regression relations. Analysis of left ventricular function can be done with displacement, velocity, strain, and strain rate parameters, typically using either tissue Doppler images (TDI) or B-mode images with speckle tracking. AVC is needed to identify end-ejection for timing of events such as iso-volumetric parameters and postsystolic shortening. Use of TDI or speckle tracking for AVC timing has several advantages: AVC timing can be done without acquiring a separate recording. Timing can be found in the cardiac cycle where it is used for analysis, thus eliminating heart rate variability. Velocity/time curves are well suited for automatic analysis. Several studies have reported usage of tissue velocities for timing AVC, but the studies report different temporal events. Four candidate events are shown in Figure 1. Candidate A is the first time point of negative velocities at end systole. This event has been used both based on pulsed wave (PW) tissue Doppler (first vertical line in Figure 2) and TDI velocity/time curves and TDI colour M-mode (middle panel of Figure 3). Candidate B is the time point of peak negative velocity after A. Candidate C is the time point of peak positive acceleration after A. Locations close to this event has been used with TDI velocity/time curves, even automatically. Candidate D is the time point close to C where the curve crosses zero. Thus, there is no consensus concerning the exact event that marks AVC in velocity/time curves. In this study we identify which event corresponds best to AVC in normal subjects. The reference is valve closure as visible in high frame rate B-mode.

Methods A Vivid 7 (GE Vingmed Ultrasound AS, Horten, Norway) ultrasound scanner with a M3S probe was used to examine 11 healthy male subjects. The study was approved by the regional ethical committee. Informed consent from the test subjects was obtained. To achieve high frame rate, scanning was limited to a narrow sector covering the septum and the aortic valve. Six to nine recordings were acquired for each subject using narrow APLAX and 5CH views to reduce random variations, giving totally 76 recordings. The
The number of recordings acquired on each subject depended on the image quality achieved. More recordings were made on subjects with poorer image quality.

The scanner software was modified to record alternate frames of TDI and B-mode. Both datasets thus had the same frame rate. Mean frame rate was 147.5 frames/s. This B-mode frame rate is in the order of two to three times higher than normal B-mode frame rate for full sector scanning. Each frame had a distinct time stamp set by an internal clock in the scanner. All analysis was performed using the GcMat (GE Vingmed Ultrasound AS, Horten, Norway) ultrasound analysis software.

AVC by B-mode images was used as reference. This time point was found by visually identifying the first frame where the aortic valve was closed, no longer moving independently of the aortic root. Practically, finding this frame was done in the analysis software by stepping forward and backward frame by frame. The time stamp of the chosen frame with respect to the ECG trigger point was then stored. The method is illustrated in Figure 4. The variability of the reference method was investigated by letting a second observer repeat the measurements. The mean value of the two observers was used as the reference timing of AVC in each recording. The B-mode reference frame in each recording was decided before TDI candidates were detected.

TDI velocity/time curves from basal septum were extracted for each recording. Radial averaging of 0.5 cm was used for calculating velocities. The four AVC candidates in Figure 1 were then identified in the curves and the timing of each candidate relative to the ECG trigger point was stored. Velocity/time curves by speckle tracking were also produced. A sum of absolute differences algorithm implemented at our department was employed and, tracking was done both forwards and backwards and the results were averaged. This algorithm has previously been validated. The tracking was initiated by selecting a 5 × 6 mm² region-of-interest (ROI) in basal septum 300 ms after the ECG trigger point. Eight 5 × 6 mm² ROIs were then placed around the selected point with a maximum distance of 3 mm. All nine ROIs were then tracked through the cardiac cycle and the velocity data averaged to get a single averaged velocity/time curve. The

Figure 1  Aortic valve closure candidates in velocity/time curves: A, the first time point of negative velocities at end-systole; B, the time point of peak negative velocity after A; C the time point of peak positive acceleration after A; D, the time point close to C where the curve crosses zero.

Figure 2  The relation between a tissue Doppler velocity/time curve by autocorrelation and a pulsed wave (PW) tissue Doppler spectrum. The first vertical line corresponds to the temporal position commonly used to represent aortic valve closure in PW tissue Doppler spectrums in literature. A special acquisition resulting in one cardiac cycle of data usable for both tissue Doppler velocity/time curves and PW tissue Doppler spectrums was used. Due to the low pulse repetition frequency in this acquisition mode, the spectrum is aliased. As aliasing is in both positive and negative directions, unwrapping by baseline shift is not possible and, two spectrums have been stacked on top of each other to visualize a continuous curve shape.
mean time interval between the two observers of the reference method by one-way ANOVA analysis with Scheffe’s correction for pairwise comparisons. The mean interval between observers may be taken as the mean uncertainty of the reference method and thus the highest accuracy obtainable.

### Results

The B-mode reference for AVC was found in 73 of 76 (96%) recordings and these recordings only were used in further analysis. The difference between the two observers was at maximum two frames. In 34/73 cases (46.6%), the observers agreed on the same frame for AVC. In 28/73 cases (38.4%), the difference between observers was one frame, and in 11/73 (15.1%) cases two frames. The mean ± SD difference between the two observers was 3.3 ± 2.6 ms.

The results of comparing the various candidates with the B-mode reference are summarized in Table 1. All AVC candidates were found in all subjects, but not in all recordings from each subject. Candidate D was only detected in 61/73 (83.6%) of the total number of curves based on TDI and 56/73 (76.7%) based on speckle tracking. Candidates A, B, and C were found in all curves. The median, 50% percentiles and 95% percentiles of the differences are plotted in Figure 5. An example with the B-mode reference, a speckle-tracking-based velocity/time curve and a TDI-based velocity/time curve is shown in Figure 4. By ANOVA analysis candidates A and B were both significantly further from the reference ($P < 0.001$ and $P < 0.02$, with TDI and $P < 0.001$ and $P = 0.03$ with speckle tracking, respectively) than the mean difference between observers. Neither candidate C nor D was significantly different from mean difference between observers by either method.

At least one visible mitral leaflet was found in 17 recordings originating from 7 of the 11 subjects. The suggested colour M-mode AVC candidate was found in all such recordings. Mean ± SD of the difference between mitral colour M-mode AVC and B-mode AVC reference was $-25.2 ± 10.2$ ms ($P = 0.001$ vs. difference between observers). Mean difference ± SD between mitral colour M-mode AVC and candidate A from TDI was $3.8 ± 6.7$ ms. An example comparing the colour M-mode AVC method with a TDI velocity/time curve from septum and a colour M-mode of septum is shown in Figure 3. An example with TDI velocity/time curve and PW tissue Doppler spectrum both made from one single cardiac cycle dataset is shown in Figure 2.

### Discussion

The B-mode reference for AVC was sufficiently reliable to separate candidates A and B from the reference. This was not the case for candidates C and D. Mean bias between observers was less than one frame. The reason for using B-mode images as reference method was the limitations of other available methods. We only considered methods using data recorded simultaneously with deformation data. Phonocardiography was tried in an earlier study, but has limited precision due to noise and filtering. Using a B-mode beam for traditional M-mode of the aortic valve in apical images would only include one leaflet. An anatomical M-mode would not cope with the cases where the aortic root moves as the valve closes.
The standard deviations were greater for all candidates by speckle tracking than by TDI, except candidate B. Candidate D was also detected in slightly more cases with TDI than with speckle tracking. The quality of the curves made by speckle tracking and thereby the presence of the events used for AVC detection, are also dependent on the actual implementation of the speckle-tracking algorithm. However, the results still indicate that speckle tracking on high frame rate B-mode images can be used for AVC timing. The reason why candidate D was not detected in all curves was that in some curves the velocity trace did not cross zero velocity until after the E-wave, and thus candidate D was not present. Candidate C has previously been detected automatically in all basal segments of apical full sector TDI recordings.1

Table 1 Aortic valve closure (AVC) candidates compared with B-mode AVC

<table>
<thead>
<tr>
<th>Candidate</th>
<th>TDI-based velocity/time curves</th>
<th>Speckle-tracking-based velocity/time curves</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$-26.7 \pm 6.2$ ms</td>
<td>$-31.3 \pm 6.8$ ms</td>
</tr>
<tr>
<td>B</td>
<td>$-12.3 \pm 4.5$ ms</td>
<td>$-13.6 \pm 3.9$ ms</td>
</tr>
<tr>
<td>C</td>
<td>$-6.8 \pm 4.6$ ms</td>
<td>$-3.9 \pm 8.9$ ms</td>
</tr>
<tr>
<td>D</td>
<td>$-2.6 \pm 8.2$ ms</td>
<td>$-1.6 \pm 9.0$ ms</td>
</tr>
</tbody>
</table>

Mean $\pm$ SD of mean difference between each candidate and the B-mode AVC reference (mean of observer 1 and observer 2) for each subject.

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Figure 4 B-mode reference method for aortic valve closure (AVC). The time interval between each frame in this example is 6.7 ms. AVC is detected in B-mode images as the first frame where the valve is closed (no longer moving). Looking at the coaptation point in the frames, the valve is evidently not fully closed in frame 52, and just as evidently closed in frame 54, with no further change to frame 55. There is a slight difference in the coaptation point itself from frame 53 to 54, which was more evident by frame by frame scrolling. Thus the time point of closure was set to frame 54 in this recording, although there may be a case for frame 53. This illustrates the variability of the reference between observers. The velocity/time curves originate from the position of the circular marker. The lower right plot shows the timing of some of the B-mode frames relative to the velocity/time curves.

Figure 5 Box plots with the median (line inside boxes), 25% and 50% percentiles (box edges) and the 2.5% and 97.5% percentiles (whiskers) for the aortic valve closure candidates and the two observers of the reference method. To produce the plot, first the difference between each candidate and the mean of observers is calculated for each recording. Then the mean differences for each subject are calculated and used to define the box plot.
The B-mode frame rate used for speckle tracking in this study is at present not realistic for clinical studies with full sector recordings. Having high frame rate is a clear advantage for speckle tracking as there is less movement from frame to frame and, thereby, less displacement. The speckle tracking approach in this study is also different from the commercial speckle tracking methods due to the absence of overall smoothing. While the speckle tracking frame rate used in this study is clinically unrealistic, the TDI frame rate used is typical for clinical TDI.

The colour M-mode-based approach was in mean only 3.8 ms later than candidate A by TDI velocity/time curves. This was expected as the start of the thin blue line corresponds to the first negative velocities of the base after systole. The slight delay might be due to propagation time of the mechanical wave from the septum to the part of the mitral leaflet where the colour M-mode was drawn. In some texts, AVC is placed at a different temporal position in velocity/time curves than in PW tissue Doppler spectrums. From the example (Figure 2) and the algorithms used to calculate the two kinds of velocity information it is not reasonable that AVC measured by one method should appear at a different temporal location than measured by the other method. This observation is supported by Pai and Gill, who using PW Doppler flow and PW tissue Doppler found that the blood flow of ejection ended 19 ± 23 (mean ± SD) ms after candidate A.

This study only included normal subjects at resting heart rates. But in literature, there is not even consensus of the placement of AVC in velocity data from normal ventricles, and therefore research referring to AVC can be ambiguous and the results incomparable. The results of this study therefore have a bearing on normal physiology as seen by tissue Doppler. AVC in normal physiology must first be clarified before various pathologies can be investigated. Conduction abnormalities as well as disturbed regional contraction will lead to abnormal velocity/time curves. At higher heart rates, the time intervals shorten, also leading to changed curves. However, the experience of Voigt et al. seems to indicate that timing by TDI is feasible also in pathological conditions and at high heart rates during stress echo. This will have to be addressed in further studies.

The main limitation of this study is the reference method used for AVC timing. With mean 2D frame rate of 147.5 frames/s, the temporal resolution of the reference method was ~6.8 ms. Aortic valve is a 3D structure, and 2D imaging cannot pinpoint the exact time point of complete coaptation of all three cusps. However, with 3D imaging the frame rate would be too low for adequate temporal analysis.

AVC timing can be done by using either TDI or high frame rate speckle tracking of the base of the septum in apical views of normal subjects. The initial negative velocities after systole of the base of the septum occur significantly before AVC, with differences against reference exceeding 20 ms. The time point closest to AVC is the time point of zero velocity after the initial negative velocities at end-systole, but this event cannot be found in all velocity/time curves. Both this event and peak positive acceleration after systole will detect AVC with <10 ms difference from the reference. Peak positive acceleration can be detected in all recordings. An automatic method for detecting this event has previously been published.

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Conflict of interest: Potential conflicts of interest are: A.S. has received fees from GE Vingmed Ultrasound AS for lectures. H.T. is used as a consultant to GE Vingmed Ultrasound AS. S.A.A. was employed by GE Vingmed Ultrasound AS for a period when he was granted six months leave of absence from his Ph.D. work.

References