Improved stroke volume assessment in the aortic and mitral valves with a new method in subjects without regurgitation

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Abstract
Background Echocardiography combining Doppler and two-dimensional data is recommended for quantitative assessments of valvular regurgitation. We applied a new method to calculate the mitral annulus (MA) area in combination with multiple sample sites. Individuals without regurgitation in whom the valvular and left ventricular stroke volumes (SV) should be identical were investigated in order to evaluate the feasibility in quantitative assessments of valvular regurgitation.

Methods and results Twenty subjects were included. Flow velocity was registered with pulsed Doppler in different positions in the left ventricular outflow tract (LVOT) and in the MA. The MA area was assumed to be either circular, using the diameter from a four-chamber projection, or elliptic, using the major diameter from a parasternal short axis and a minor diameter from an apical long axis. Left ventricular (LV) SV was measured from LV volumes using the biplane method. The overall difference between LVOT SV and mitral SV using one centrally located measurement and elliptic MA was 3.2 ± 15.6 ml (P = 0.38), 0.9 ± 15.7 ml between LVOT SV and LV SV (P = 0.80) and −2.2 ± 15.2 ml between mitral SV and LV SV (P = 0.54). The corresponding standard deviation of the differences as a percentage of the mean value was 24%, 25% and 23%. A circular shaped MA overestimated the mitral SV compared with LVOT SV (P = 0.009) and LV SV (P = 0.004). Increasing the number of sample sites in the LVOT or MA did not further improve the results.

Conclusion Doppler and two-dimensional echocardiography can be used to quantify regurgitation in groups of patients. In individual patients the wide distribution of differences between valves and LV SV implies that the method should be used in conjunction with other Doppler echocardiographic parameters.

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Introduction

At many echocardiographic laboratories, valvular regurgitation is currently assessed qualitatively with grading from mild to severe using a combination of two-dimensional echocardiography, color Doppler and continuous wave Doppler parameters. The severity of valvular regurgitation increases continuously with an increasing regurgitation fraction and converting a continuous change into categories therefore inherently introduces inaccuracies. In recent decades, the results of valvular surgery on patients with regurgitation have improved and, in order to avoid a suboptimal result due to the development of irreversible left chamber dysfunction, early intervention in asymptomatic or mildly symptomatic patients has been proposed.1,2 A reliable non-invasive method for the accurate quantification of valvular regurgitation is therefore needed in order to detect the progress of severity and to optimize the timing of surgery. Doppler echocardiographic methods have been used to quantify regurgitation,3-6 but their applicability has been questioned7-9 and these methods have not been widely used. According to current recommendations,10,11 these methods can be applied, but the need for individual training and practice in patients without regurgitation is underlined.

Most previous studies assume that the spatial velocity distribution in the left ventricular outflow tract (LVOT) and the mitral annulus (MA) is flat using only one sample site and further that the MA is circular in shape.3-6 These assumptions about velocity distribution and MA shape are known to be simplifications.12-14 In the present study, we therefore applied a new method to calculate the MA area with an elliptic shape and we used multiple sample sites. We investigated individuals without regurgitation, in whom the valvular and left ventricular stroke volumes should be identical, in order to evaluate the feasibility of this method for the quantification of valvular regurgitation.

Methods

Study subjects

Twenty healthy individuals, 13 women (mean age 38 years, range 19–55 years), without regurgitation in the aortic valve and with only trace regurgitation in the mitral valve, were included. All the subjects were in sinus rhythm and they were selected on the basis of good image and Doppler quality. The study was approved by the human ethics committee at Sahlgrenska University Hospital.

Echocardiography

Echocardiography was performed using an Acuson Sequoia, with a 3.5 MHz transducer (Acuson, Mountain View, CA). The patients were examined in the left lateral position. The Doppler recordings were made at a speed rate of 100 mm/s with 5 mm sampling volume size. The two-dimensional and Doppler data were stored digitally and measurements were performed off line. All Doppler and two-dimensional measurements were performed by one experienced investigator.

The left ventricular outflow tract (LVOT) cross-sectional area was assumed to be circular (πD²/4). The LVOT diameter was measured in the parasternal long axis using an early or mid-systolic stop frame with the best image quality, according to the trailing edge to leading edge principle.15 The MA area was estimated assuming a circular or elliptic shape. The circular area was calculated using the early diastolic diameter from an apical four-chamber view. The major (D1) and minor (D2) diameters were obtained from a short-axis view and the apical long axis (Fig. 1) in order to calculate the elliptic area (πD1D2/4). Efforts were made simultaneously to visualize the posteromedial and anterolateral commissure (Fig. 1). The major axis was determined in early diastole by measuring the distance between the commissures. The minor axis was determined from an apical long-axis projection. Measurements were performed from the junction between the posterior leaflet and the left atrium wall and at the left atrium side corresponding to the insertion of the aortic valve at the beginning of diastole.

Velocity recordings from the LVOT were obtained from an apical five-chamber view. The sample volume was placed just proximal to the aortic valve in three different positions: central (LVOT1), septal (LVOT2) and mitral (LVOT3). In the mitral valve, the sample volume was placed at the annulus level in five different positions, three in the apical four-chamber view (central position, MA1, inferoseptal, MA2, lateral, MA3) and two in the apical long-axis view (anteroseptal, MA4, inferolateral, MA5). Fig. 2 shows a short-axis view of the mitral orifice with the different sample sites indicated.

The velocity profiles were traced along the brightest part of the spectral display (modal velocity).

Calculations

Using Doppler and two-dimensional echo data, stroke volumes were calculated in the LVOT and
MA as the cross-sectional area (CSA) times the area under the velocity curve (velocity time integral = VTI):

(1) General formula: \(SV (ml) = CSA (cm^2) \times VTI (cm)\)

Stroke volumes were further calculated in two ways, from the central velocities (central) and using the average of the velocity integrals in the valve plane (flow profile adjusted).

Stroke volumes were calculated from diastolic and systolic volumes using Simpson's rule (LV SV). From two apical orthogonal views, volumes were calculated using planimetry. The image quality was regarded as acceptable for measurement when at least 75% of the endocardial border was visualized.

Statistics

The results are expressed as the mean ± SD. To evaluate interobserver variability, 10 patients Doppler and valve orifice diameter measurements were performed by two investigators. The difference in SV between different valves and the LV SV was tested using a paired \(t\)-test, together with differences in the VTI in different positions in the CSA. A \(P\)-value of <0.05 was considered significant. The relationship between SV in different valves and LV SV was assessed by linear regression and Bland-Altman analyses. The magnitude of the difference between SV and the interobserver variability were described by the coefficient of variation, which was expressed as either the mean value of differences (group) or the standard deviation of the difference (individual) between two measurements, both divided by the mean value of the two measurements.

Results

Stroke volume assessed using a circular or elliptic CSA in the mitral annulus

Stroke volume calculated assuming that the MA had an elliptic shape revealed no differences...
between MA (mitral SV) compared with SV in LVOT (LVOT SV) and the biplane method (LV SV, Fig. 3). The MA diameter was 3.1 ± 0.42 cm in the four-chamber view, 2.8 ± 0.32 cm in the apical long axis and 3.3 ± 0.36 cm in the short axis. The circular CSA was significantly larger than the elliptic CSA, 7.6 ± 2.2 cm² versus 6.4 ± 1.4 cm² (P = 0.009). The mitral SV calculated with the central velocity using a circular shape on the mitral CSA resulted in significantly larger SV compared with LV SV (P = 0.004), LVOT SV (P = 0.009) and the mitral SV assuming an elliptic shape (P = 0.01, Fig. 3).

The velocity profile in different valves

In the MA, we observed a significant skewness in the velocity profile (Fig. 4). The smallest velocity integrals were registered at the periphery of the lateral, inferolateral and anteroseptal part of the MA. In the LVOT, we also observed a significant skewness in the flow profile (Fig. 4). The largest VTI was observed in the septal position, while the lowest VTI was observed in the mitral position.

The stroke volumes calculated with flow profile adjustment did not significantly change the results (Table 1). In the MA, however, the difference did reach borderline significance (P = 0.06).

The relationship between stroke volume in different valves

The correlation between LVOT SV and mitral SV (Fig. 5) using one central velocity recording was moderate (R² = 0.44). The flow profile adjusted method strengthened the linear relationship only slightly (R² = 0.50). The Bland-Altman plot in Fig. 5 shows that, with both the central velocity and the flow profile adjustment, the difference between LVOT SV and mitral SV increased significantly with increasing SV. Table 2 shows that, using the central velocity method, the mitral CSA, LVOT CSA and mitral VTI contributed significantly to the observed difference between mitral SV and LVOT SV. However, using the flow profile adjustment method, only the mitral CSA was important (R² = 0.36, P = 0.009).

The mean difference between LVOT SV and mitral SV as a percentage of the mean value was
small (Table 3). In a group of patients, the SV using the central velocity did not differ by more than 5%, while the difference was only 1% using flow profile adjustment. However, the SD of these differences reveals a wide distribution. In an individual patient, the standard deviation of difference using the central velocity was 15.6 ml between LVOT and MA, which represents 24% of the mean value. The corresponding figures with flow profile adjustment were 15.7 ml in LVOT, which represents 25% of the mean value, and 15.2 ml in the MA, which represents 24% of the mean value.

**Interobserver variability**

For an individual patient, the measurements made by two observers could differ 18–20% for the Doppler VTI, 10% for the LVOT diameter and 18–22% for the major and minor axis of the MA (95% confidence limits of difference). The corresponding variability comparing groups were 4–10% for the Doppler VTI, 4% for the LVOT diameter and 20–24% for the major and minor axis of the MA.

**Discussion**

In the present study, we have shown that it is possible, in a group of individuals without valvular regurgitation, to calculate the SV in the LVOT, MA, using Doppler echocardiography, and the LV SV, using two-dimensional echocardiography, that are

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\begin{table}
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\caption{Stroke volume in different locations calculated with the central velocity or adjusted to flow profile}
\begin{tabular}{|c|c|c|}
\hline
 & LVOT & Mitral annulus \\
\hline
Central (ml) & 63.5±11.9 & 67.3±20.7 \\
Flow profile & 63.1±12.6 & 64.1±18.9 \\
adjusted (ml) & & \\
\hline
P-value & 0.86 & 0.06 \\
\hline
\end{tabular}
\end{table}
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The mean difference between LVOT SV, mitral SV and LV SV as a percentage of the mean value was small (Fig. 6, Table 3). In a group of patients, the SV using the central velocity did not differ by more than 1.4% in LVOT and 3.2% in the MA. The corresponding figures with flow profile adjustment were only 0.8% in LVOT and 1.5% in the MA. However, the SD of these differences reveals a wide distribution. In an individual patient, the standard deviation of difference using the central velocity was 15.7 ml in LVOT and 15.2 ml in the MA, which represents 25% and 23% of the mean value. The corresponding figures with flow profile adjustment were 15.7 ml in LVOT, which represents 25% of the mean value, and 15.2 ml in the MA, which represents 24% of the mean value.
similar in overall terms. However, in individual subjects, we found a wide distribution of differences between the sites and between the Doppler and two-dimensional methods, which limits the usefulness of Doppler and two-dimensional echocardiography in the quantification of valvular regurgitation.

Sources of variation

The observed differences between LVOT SV and the mitral SV can be explained in principle by errors in the assessment of the VTI and CSA. In the study, both the central velocity and multiple sample sites in LVOT and MA were investigated in order to correct for a possible skewness in the velocity profile. We observed a skewness in velocity distribution in both the LVOT and the MA. Calculating the SV after flow profile adjustment, however, did not influence the results in LVOT and, in the MA, the difference was small in absolute terms and only reached borderline significance ($P=0.06$).

In the MA, we calculated the CSA with a circular shape but also assuming an elliptic shape. The MA is known to be elliptic, but current recommendation\textsuperscript{11} state that the diameter in the four-chamber view should be used when the mitral SV is calculated. In a transesophageal study, Pu et al. used the four-chamber and two-chamber diameters assuming an elliptic shape.\textsuperscript{17} They found a better correlation with thermodilution when the elliptic area was used, compared with a circular CSA. To our knowledge, our study is the first in which the MA has been estimated using the distance between commissures assessed from a parasternal short-axis projection as the major axis and the apical long axis as the minor axis. This approach ought to be better than using a combination of four- and two-chamber diameters, as none of them represents the true anatomic major and minor axis. Interestingly, we found that the recommended method with a circular CSA resulted in a significantly larger SV compared with LVOT, while the elliptic CSA produced a similar mitral SV and LVOT SV. The diameter in the four-chamber view is only slightly shorter than the distance between the commissures. However, the long-axis diameter is markedly shorter than the four-chamber diameter, resulting in a smaller CSA when an elliptic shape is assumed.

The correlation between SV at different sites using Doppler echocardiography was no more than moderate ($R^2$ range 0.44 to 0.50). We also observed that the difference increased with increasing SV and the mitral CSA was the most important

<table>
<thead>
<tr>
<th>Table 2</th>
<th>The importance of cross-sectional area (CSA) and velocity time integral (VTI) in relation to the observed differences between SV in the LVOT and mitral annulus</th>
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<tbody>
<tr>
<td></td>
<td>Cross-sectional area</td>
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<tr>
<td></td>
<td>Mitral CSA</td>
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<tr>
<td>Central velocity</td>
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<tr>
<td>Correlation coefficient – $R^2$</td>
<td>0.26</td>
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<tr>
<td>$P$-value</td>
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<tr>
<td>Flow profile adjusted</td>
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<tr>
<td>Correlation coefficient – $R^2$</td>
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<tr>
<td>$P$-value</td>
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<th>Table 3</th>
<th>Difference between SV in different valves and the LV SV</th>
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<td>Mitral versus LVOT</td>
<td>LVOT versus LV SV</td>
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<tr>
<td>Central</td>
<td>Flow profile adjusted</td>
</tr>
<tr>
<td>Mean difference (ml)</td>
<td>3.2 ± 15.6</td>
</tr>
<tr>
<td>Mean value (ml)</td>
<td>65.8 ± 14.9</td>
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<tr>
<td>Mean difference as % of mean value</td>
<td>4.7</td>
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<td>SD of difference as % of mean value</td>
<td>23.7</td>
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</table>
In the present study, we aimed to estimate the true anatomic area by calculating the elliptic area. The MA is, however, a complicated three-dimensional structure with a saddle form that changes during diastole, and the interobserver variability was more pronounced in the measurement of the MA compared with the LVOT. It is therefore conceivable that the mitral CSA contributes most to the observed difference between SV in the LVOT and the MA.

When Doppler echocardiographic SV was compared with two-dimensional LV SV, we found a moderate correlation ($R^2$ range 0.35 to 0.52). In the LVOT, the difference increased with increasing SV and this could be explained by the assessment of diastolic and systolic volumes. This is an expected finding, as any error in the planimetry
measurement will be more pronounced in a large left ventricle compared with a smaller one.

Previous studies

There are many reports on Doppler echocardiography and the opportunity to estimate SV. Only a few studies present data from individuals without regurgitation which can be compared with our results. Lewis et al. and Rokey et al. used the same method in their estimation of SV, assuming a circular shape for the MA CSA and the modal velocity. Both investigators describe the correlation between LVOT SV and MA SV as good. However, they actually present data that show either marked interobserver variability or state that the false regurgitation fraction can be as much as 20%. This is therefore more a question of differences in the interpretation of data than differences in results. Enriques-Sarano et al. obtained better results in normal subjects without regurgitation with a 5% false regurgitation fraction. However, they used an inconsistent method to calculate SV, applying the modal velocity in the MA and the peak velocity in the LVOT.

Clinical implications

These results and previous reports impose restrictions on the use of Doppler and two-dimensional echocardiography in the quantification of valvular regurgitation. If we study the effect of a medical intervention or the natural history in a group of patients with regurgitation and the parameter of interest is the mean value in the group, it is possible to use the Doppler echocardiographic method. However, in individual patients, the wide distribution of differences between SV in different valves limits the usefulness of Doppler and two-dimensional echocardiography. In a subject without regurgitation, the SV in LVOT and MA can differ by as much as 30 ml (95% confidence interval). It is therefore obvious that, with standard echocardiography, quantification should not be used alone to assess the severity of regurgitation in individual patients. However, quantification can be used applying the proposed method to assess the MA, and in conjunction with other Doppler echocardiographic parameters.

Acknowledgements

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References


