Quantification of chronic aortic regurgitation by vector flow mapping: a novel echocardiographic method

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Aims
Quantification of aortic regurgitation (AR) using echocardiography is challenging. A newly established echocardiographic method, vector flow mapping (VFM), can directly measure blood flow volume (FV) regardless of rheological characteristics. We intended to assess the accuracy of VFM in the quantification of chronic AR.

Methods and results
Twenty-one patients with chronic AR, along with 21 healthy volunteers selected as controls, underwent conventional echocardiography and estimation of aortic blood flow using quantitative Doppler and VFM. The regurgitation ratio (RegR), derived as the quotient of backward and forward aortic FV in the ascending aorta measured by VFM, increased with AR severity: 1.1 ± 1.5% (normal), 11.4 ± 3.8% (mild AR), 31.2 ± 8.0% (moderate AR), and 59.3 ± 4.7% (severe AR). In a linear regression model, RegR closely correlated with the VC width (r = 0.932) and regurgitation fraction and effective regurgitant orifice measured by the quantitative Doppler method (r = 0.929 and 0.891, respectively). The intra- and interobserver variability of RegR was 4.2 and 6.7%, respectively. There was no difference between RegR measured in the apical five-chamber view and in that in apical three-chamber view using the paired t-test (P = 0.751).

Conclusion
RegR measured by VFM, a new Doppler method allowing quantitative analysis of FV in spite of the presence of turbulent flow, is a highly reproducible parameter with good accuracy for AR quantification.

Keywords
Aortic regurgitation • Echocardiography • Quantitative Doppler • Vena contracta • Vector flow mapping

Introduction
The overall prevalence of chronic aortic regurgitation (AR) is ~13% in men and 8.5% in women. In general, the chronic AR is well tolerated and usually asymptomatic until severe decompensation occurs, but evaluation of its severity is routinely required to provide precise information for further management and prognosis. The most important diagnostic test for non-invasive evaluation of AR is echocardiography.

Various quantitative or semi-quantitative echocardiographic methods have been successfully applied in estimating mitral regurgitation (MR), but AR quantification is much more challenging. The narrow space of the left ventricular outflow tract (LVOT) constrains the regurgitant jet. The ‘free’ jet hypothesis, which was the premise of most assessment techniques for regurgitation, was not fully realized in the AR patients. Approximately 50% of patients with severe AR were shown to have an eccentric AR jet. The complicated hydrodynamic characteristics of the AR jet posed a huge obstacle for measurement using conventional methods.

Because the direct measurement of the AR jet is difficult, reverse flow in the descending aorta has been used as a quantitative parameter for the AR estimation. Reverse flow at the root of the ascending aorta (AAo) is more closely related to the regurgitation jet, but it consists of a complicated vortex flow and so could not be measured by conventional echocardiographic methods that can measure only the laminar flow.

The problem of vortex flow measurement was resolved recently by a newly established echocardiographic method called vector flow mapping (VFM). In the conventional Doppler method, only
velocity components in the beam direction can be measured, whereas information regarding velocity perpendicular to the beam direction is lacking. VFM method is based on a hypothesis that the component of velocity perpendicular to the beam direction can be inferred from distribution of the velocity in the beam direction. In VFM, velocity and direction of real blood flow can be derived from colour Doppler imaging (CDI) using complicated hydrodynamic calculation. Detailed rheological information, including velocity, flow rate (FR), and flow volume (FV), can be calculated directly with high accuracy as to whether the blood flow pattern is laminar or irregular vortex.

Application of VFM provided us with the possibility of measuring complicated reverse flow in the AAo. We therefore proposed a new parameter derived as the quotient of forward flow and reverse flow to quantify AR. This parameter was supposed to be less affected by orifice shape and direction of the regurgitation jet, and was therefore considered to be accurate even in AR patients with an eccentric jet.

Reverse flow at the root of the AAo was assessed using VFM in patients with chronic AR as well as in healthy volunteers to evaluate the accuracy and reliability of VFM in quantifying AR severity.

**Methods**

The study was approved by the Local Ethics Committee of our institution. All subjects gave written informed consent. The registration number was ChiCTR-DT-00000308 (www.chictr.org).

**Study population**

Patients with chronic AR were included irrespective of cause. Patients with severe dysrhythmia, acute heart failure, or an unstable hemodynamic state who could not tolerate conventional echocardiography were excluded. All subjects underwent conventional echocardiography and assessment by VFM sequentially in the same examination.

**Echocardiography**

Conventional echocardiography was carried out by an experienced echocardiographer using the Prosound a10 diagnostic ultrasound system (Aloka Company, Tokyo, Japan). Aortic flow was observed in the apical five-chamber view (AP5c) and apical three-chamber view (AP3c) for at least five consecutive cardiac cycles.

To achieve a desirable frame rate, expanded tissue harmonics were shut down and the colour flow sector was reduced. Two-dimensional (2D) gain was set to around 50 and flow gain to around 60. The Nyquist limit was 60–80 cm/s to strike a balance between clear display of low-velocity backward flow in the AAo in diastole and the aliasing.

**Echocardiographic grading of aortic regurgitation**

Regurgitation severity (RegS) was evaluated by visual impression of the jet in CDI. Severe, moderate, and mild AR was graded as III, II, and I, respectively, according to guidelines for evaluation of valvular regurgitation. Each subject was assessed by two experienced echocardiographers independently who did not subsequently participate in the offline analysis of VFM. The opinion of a third echocardiographer was requested if there was disagreement. The final results of the RegS assessment were not revealed until the offline analysis of VFM had been completed.

**Vector flow mapping and aortic regurgitation evaluation**

CDI, which represented distribution of normal velocity (velocity component in the beam direction), was transported to an offline work station in DICOM format and analysed using SOP-RS1-6 VFM data analysis software (Aloka). Actual velocity and direction of flow was calculated based on CDI, and then displayed as vectors. A measuring line was placed 5 mm above the annulus to measure the blood flow in the AAo, where the blood flow is less influenced by the shape of the regurgitation orifice and regurgitation jet. The velocity and direction of blood flow along the line was calculated. FR was therefore estimated by integrating the vertical velocity along the measuring line. Forward and backward FR was calculated, and FV estimated as the area under the time–flow curve. AR severity was represented by the regurgitation ratio (RegR), the quotient of backward flow volume (FVb) and forward flow volume (FVf), that is:

\[
\text{RegR} = \frac{FV_b}{FV_f}
\]

RegR was measured in AP3c (RegR-AP3c) and AP5c (RegR-AP5c) view. Subsequent RegR values were the mean of RegR-AP3c and RegR-AP5c (Figure 1).

**Reference method**

The quantitative Doppler method (QDop), a well validated method for eccentric AR quantification, was chosen as the reference method because patients with eccentric AR were included. The regurgitant fraction (RF) and effective regurgitant orifice (ERO) measured by QDop was derived as follows:

\[
\text{Stroke volume (SV)} = \text{cross-sectional area} \times \text{velocity time integral (VTI)}
\]

\[
\text{Regurgitation volume (RVol)} = \text{aortic SV} - \text{mitral SV}
\]

\[
\text{RF} = \frac{\text{RVol}}{\text{aortic SV}} \quad \text{and} \quad \text{ERO} = \frac{\text{RVol}}{\text{Regurgitation VTI}}
\]

VTI was measured at the annulus level by pulse-wave Doppler. The mitral annulus diameter was measured along multiple axes to account for a possible non-circular shape. Pulmonary SV was measured instead of mitral SV for patients with concomitant MR.

Vena contracta (VC) was also adopted as reference method. The width of VC was measured in the parasternal long-axis views in the early diastole.

**Reproducibility**

Intraobserver variability of the VFM method was estimated by the mean coefficient of variance (CV) of RegR value of five consecutive cardiac cycles. Besides, AR jets were sometimes asymmetric, leading to different severity grading in different 2D section views (particularly for eccentric AR). To validate the angle-dependent reproducibility of the VFM estimation for asymmetric AR jets, RegR was measured in both the AP3c and AP5c views to represent the sagittal and coronary sections of the AR jet, respectively. The angle-dependent variability was expressed as the difference between them.

As for interobserver variability, the measurements of the VC width, RegR in the VFM method, RF and ERO in the QDop method were repeated independently by second sonographers in all 21 patients.
Statistical analysis
Statistical analysis was carried out using SPSS software (Version 15.0; SPSS Inc., Chicago, IL, USA). Continuous variables were represented as mean ± SD. Means between groups were compared by one-way ANOVA. The RegR was related to RF with linear regression and to categorical variables by non-parametric regression. \( P < 0.05 \) was considered significant.

Results
Baseline and echocardiographic characteristics
Twenty-one patients were in the AR group and 21 healthy volunteers were in the control group. Of the 21 AR patients, 8 (38.1%) had severe AR, 6 (28.6%) had moderate AR, and 7 (33.3%) had mild AR. Four patients with severe AR and two patients with moderate AR were observed to have an eccentric jet (28.6%). Four patients with AR had concomitant aortic stenosis (AS) and five had MR that was more than mild. Baseline characteristics in the AR and control groups are listed in Table 1. Patients in the AR group had significantly higher systolic blood pressure, lower diastolic blood pressure, a larger left ventricle, a lower ejection fraction and a higher prevalence of concomitant AS and MR than the control group.

Correlations between the impressive grading, the quantitative Doppler method and the vector flow mapping method
Forty-two subjects were divided into four groups according to AR severity (no AR, mild AR, moderate AR, severe AR). The mean values of RegR increased accordingly with the visual grading of AR (1.1 ± 1.5% for normal, 11.4 ± 3.8% for mild AR, 31.2 ± 8.0% for moderate AR and 59.3 ± 4.7% for severe AR). A significant difference between severity groups was found in the RegR measured by VFM \( (P < 0.001 \) by ANOVA test; Figures 2 and 3).

RegR measured by VFM were closely correlated with RF \( (r = 0.929, r^2 = 0.862, P < 0.001) \) and ERO \( (r = 0.893, r^2 = 0.798, P < 0.001) \) measured by the QDop and VC width \( (r = 0.932, r^2 = 0.868, P < 0.001) \) (Table 2, Figure 4).

Reproducibility
The intraobserver variability of RegR was 4.2%. As for angle-dependent variability, no significant difference was found between RegR-AP3c and RegR-AP5c by paired \( t \)-test in 21 patients with AR (35.2 ± 21.3% vs. 35.4 ± 21.8%, \( P = 0.751 \)), indicating RegR measured by VFM was less angle-dependent for AR quantification (Figure 5).

The interobserver variability of RegR was 6.7%. In comparison, an interobserver variability of 9.8% for RF and 12.1% for ERO were observed in QDop method. As for VC method, the interobserver variability of VC width was 11.9%.

Discussion
In routine echocardiographic examination, regurgitation can be rapidly graded as mild to severe according to visual impression, but visual grading of severity can be greatly affected by the experience of observers.8–10 Recent studies have shown that even identical images may be graded differently at different times by experienced sonographers.11 Accumulating evidence suggests...
that visual grading of regurgitant severity as a semi-quantitative method is inherently flawed; quantitative evaluation of regurgitation severity is needed. Current quantitative measurements for AR includes jet length/area (jet L/A), VC, proximal isovelocity surface area (PISA), and QDop methods.

Jet L/A methods are simple and convenient for quick assessment in the clinical situation. The jet displayed by CDI represents velocity distribution rather than real blood flow. Jet size can be influenced by many technical factors, impairing reproducibility of the jet L/A method. The regurgitation jet usually expands unpredictably below the orifice, particularly for non-circular orifices and eccentric jets, limiting its clinical application.

The VC method is also simple and sensitive. The VC area measured in three-dimensional (3D) echocardiography has been found to be more accurate than 2D measurement of the VC width/area, rendering the possibility of large errors in percentage caused by small errors in the absolute value. In our study, an interobserver variability of 11.9% was observed while the mean absolute difference between two measurements was only 0.38 mm. Besides, multiple AR jets cannot be measured even in the 3D echocardiography.

PISA is an accurate quantitative method that can evaluate ERO area (EROA) and RVol. The EROA estimated by PISA is the maximal EROA. PISA is less accurate in certain clinical conditions, such as aortic valve calcifications, multiple/eccentric jet and aortic aneurysms. The QDop method is not dependent on the jet shape and so is valid for multiple and eccentric jets. Although it has some predominant advantages and has been chosen as the reference method in this study, some inherent limitation must be indicated. The QDop parameters are calculated based on the precise calculation of valvular area, which is very difficult and highly experience-dependent. In this study, a relatively high interobserver variability was observed for QDop parameters.

In contrast to conventional echocardiographic methods with respect to the AR jet, the VFM method enabled direct measurement of reverse flow in the aorta. This is less influenced by orifice shape and LVOT structure and so is valid for multiple and eccentric jets. In the present study, good agreement between RegR measured by VFM and RF, ERO measured by QDop was observed. In addition, excellent reproducibility of the VFM method was observed, suggesting VFM might be more reliable than present methods. For most quantitative assessment techniques, reliability can be affected by different instrument settings, hemodynamic or physiologic status but, in VFM, forward and backward flow is measured at
exactly the same time and shares the same influence of interfering factors. The RegR, as the quotient of the $F_{V_b}$ and $F_{V_e}$ is therefore less influenced by technical factors and has greater reproducibility. Complicated and unpredictable jet shape of eccentric AR is another major obstacle for AR quantification. However, blood flow in the AAo is relatively stable in shape (shape of AAo) and less influenced by the shape of the orifice and jet. As a result, eccentric or multiple jets can be accurately measured by VFM, in

**Figure 3** Time–flow curve and RegR in different AR severity groups. Time–flow curves of four patients from four severity groups. The RegR increased according to AR severity.

**Table 2** Regurgitation ratio, regurgitation fraction, and effective regurgitant orifice in different severity groups

<table>
<thead>
<tr>
<th>Grade of AR</th>
<th>n</th>
<th>RegR (%) by VFM</th>
<th>RF (%) by QDop</th>
<th>ERO (mm²) by QDop</th>
<th>VC width (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>21</td>
<td>1.1 ± 1.5</td>
<td>−12 ± 6.7</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>I (mild)</td>
<td>7</td>
<td>11.4 ± 3.8</td>
<td>160 ± 5.5</td>
<td>9.6 ± 3.9</td>
<td>3.0 ± 0.9</td>
</tr>
<tr>
<td>II (moderate)</td>
<td>6</td>
<td>31.2 ± 8.0</td>
<td>26.2 ± 7.5</td>
<td>16.0 ± 5.5</td>
<td>5.4 ± 1.1</td>
</tr>
<tr>
<td>III (severe)</td>
<td>8</td>
<td>59.3 ± 4.7</td>
<td>59.2 ± 9.8</td>
<td>38.4 ± 12.9</td>
<td>8.5 ± 1.8</td>
</tr>
</tbody>
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**Figure 4** Correlations between RegR and RF (left), ERO (mid) and VC width (right) calculated by QDop method. Continuous lines are regression lines.
which the relatively stable reverse flow in the AAo was measured instead of the complicated regurgitant jet.

The VFM method also has some inherent limitations. Firstly, VFM can be applied only in the offline analysis so far which is time consuming. Secondly, low-velocity backward flow in the AAo cannot be readily observed occasionally (particular in patients with mild AR), which can subsequently impair the sensitivity of VFM in the AR estimation. However, it is not too problematic because quantification of mild AR is of less significance. Thirdly, the current VFM method only measures the FV in the 2D scanning plane. Further studies should be done to establish the relationship between the 2D-FV determined by VFM and spatial-FV in 3D.

Limitations of this study

One main limitation is the relatively small sample size. Subgroup study on patients with eccentric or multiple jets was not possible. Further studies with a larger sample size (particularly concerning eccentric and multiple AR jets) should be done to validate VFM. In addition, this study focused on patients with chronic AR with stable hemodynamic status and sinus rhythm. The value of VFM in patients with acute AR or dysrhythmia is unknown.

Conclusions

This prospective study demonstrated that VFM is an accurate and highly reproducible method for AR quantification, even for eccentric AR, which is difficult to measure by conventional methods.

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