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ORIGINAL PAPER

New echocardiographic method for chronic aortic regurgitation: diastolic retrograde ratio in the descending aorta by vector flow mapping

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Abstract

The aim of this study was to evaluate the diagnostic performance of the diastolic retrograde ratio in the descending aorta in patients with aortic regurgitation (AR) by vector flow mapping (VFM). Conventional Doppler echocardiography and VFM were performed in 73 patients with various degrees of AR and 40 controls. AR severity was assessed by an expert using the currently recommended integrative approach, including vena contracta width (VCW), jet width to left ventricular outflow tract (jet width/LVOT) ratio, and effective regurgitant orifice area (EROA). The retrograde ratio, derived as the quotient of backward flow volume (VF_b) and forward flow volume (VF_f) in the descending aorta, was measured using VFM. The diastolic retrograde ratio was found to increase across groups of subjects with absent (6.1 ± 4.0%), mild (21.3 ± 8.2%), moderate (43.6 ± 9.4%), and severe (70.5 ± 10.5%) AR. Furthermore, in a linear correction model, the retrograde ratio correlated strongly with the VCW ($r = 0.930$, $P < 0.001$), jet width/LVOT ratio ($r = 0.884$, $P < 0.001$), and EROA ($r = 0.927$, $P < 0.001$). In the receiver operating characteristic curve, the retrograde ratio had an area under the curve of 0.958 for a diagnosis of severe AR (SEM: 0.0205, $P < 0.0001$). A retrograde ratio > 56% indicated severe AR with a sensitivity of 93% and a specificity of 89%, whereas a value > 59% indicated severe AR with a sensitivity of 96% and a specificity of 82%. The retrograde ratio in the descending aorta is useful in identifying AR severity. This accurate and simple quantitative parameter should be incorporated in the comprehensive evaluation of AR.

Keywords Aortic regurgitation · Vector flow mapping · Retrograde ratio · Descending aorta

Introduction

As a common valvular disease, aortic regurgitation (AR) occurs when there is a leakage of the valve backward into the left ventricle (LV) during diastole [1]. The management of AR depends on the accurate assessment of severity [2]. However, quantifying AR is much more challenging in routine practice. Doppler echocardiography is the primary imaging method employed, and a multiparametric evaluation is recommended for the diagnosis of AR severity [3]. AR, determined clinically by the volume of regurgitation and the impact on left ventricular size and function, is also associated with aortic blood flow patterns. The guideline for patients with valvular heart disease suggests that the observation of holodiastolic retrograde flow in the descending aorta can help identify patients with severe AR [2]. During the past decades, there has been an increasing interest in the relationship between Doppler parameters in the descending aorta and AR severity [4–6], and a strong association was found between the end-diastolic velocity of reverse flow in the descending aorta and AR severity. However, the hemodynamic characteristics of blood flow in the aorta consist of not only the magnitude but the direction of velocity, which the conventional Doppler ultrasound cannot present completely when the velocity components were not parallel to the ultrasound beam. On the other hand, the blood flow patterns in the aorta is more complex, including not only laminar flow but also turbulence flow and vortex

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flow, which likewise could not be measured by conventional Doppler echocardiography [7, 8].

Recently, a novel echocardiography technology called vector flow mapping (VFM) has been developed to visualize and quantify the flow field both in the ventricles and blood vessels [9, 10]. Conventional Doppler echocardiography cannot measure velocity in the direction perpendicular to the beam, but VFM, based on the continuity equation and speckle tracking [11], provides the possibility of computing velocities perpendicular to the direction of the beam. In VFM, detailed hemodynamic information, including velocity, direction, and flow volume, can be calculated accurately and directly regardless of whether the blood flow pattern is laminar or vortex. VFM allows the measurement of complicated retrograde flow in the descending aorta, and its accuracy in assessing flow dynamics in a left ventricular phantom was validated using stereo particle image velocimetry [12, 13].

We therefore proposed a new parameter derived from the quotient of backward flow volume (VF_b) and forward flow volume (VF_f) in the descending aorta to identify AR degree. This parameter, termed retrograde ratio, was thought to be less affected by the regurgitation jet and the orifice shape. In addition, the retrograde ratio by VFM would not be restricted to the angle dependency or complex flow patterns. When AR occurs, there is a leakage of the valve backward into the LV during diastole, which results in increasing reversal flow within the descending aorta. Therefore, the objective of this study was to evaluate the feasibility and accuracy of this new parameter by VFM for quantifying AR.

Methods

Study population

The study was approved and conducted in accordance with the Local Ethics Committee of our institution, and all enrolled subjects provided informed consent.

A total of 73 patients (41 men, aged 53.1 ± 15.2 years) with chronic AR (more than 3 months) of various etiologies were consecutively enrolled. Patients with arrhythmia, poor echogenicity, or who are unwilling to participate were excluded from the study. For comparison, 40 healthy subjects (20 men, aged 54.7 ± 10.2 years) without any cardiac disease were included as controls.

Comprehensive Doppler echocardiography

According to the American Society of Echocardiography, the degree of AR was determined using a multiparametric approach and graded as mild, moderate, and severe. Conventional Doppler echocardiography was carried out by an experienced sonographer using ProSound a10 system (Hitachi Aloka Medical Ltd, Tokyo, Japan), with a 5 MHz probe (UST-52105). Left ventricular ejection fraction was calculated using Simpson's biplane method. The color Doppler images of the vena contracta width (VCW) were obtained from parasternal long-axis view and a color sector scan coupled with the zoom mode. VCW was measured as the narrowest flow diameter of the regurgitant jet just below the flow convergence region. The Nyquist limit for color Doppler imaging was set at 50–60 cm/s to improve the accuracy of measurement. The ratio of the jet width to the left ventricular outflow tract (jet width/LVOT) ratio was also measured in parasternal long-axis view. The effective regurgitant orifice area (EROA) was calculated using the proximal isovelocity surface area (PISA) method. The Nyquist limit was shift adjusted to obtain a clearly visible, round, and measurable PISA radius. Furthermore, the PISA radius was measured either in apical view (central jets) or parasternal long-axis view (eccentric jets).

Retrograde ratio by VFM

VFM quantifies velocity vectors of forward and reversal blood flow in the descending aorta on the basis of the continuity equation, taking into account velocity components parallel and perpendicular to the ultrasound beam, the principles of which have been reported previously. The Nyquist limit for two-dimensional color Doppler imaging was set at 60–80 cm/s to mitigate the aliasing phenomenon. The Doppler filter was decreased to its lowest setting, allowing for the detection of low velocities (< 10 cm/s), and the frame rate was in the range of 18–30 frames per second. The color flow sector was focused on the proximal descending aorta, obtained from the aortic arch long-axis view. Images were saved and transferred to an offline workstation (DAS-RS1) in DICOM format for analysis. In the offline analysis, the retrograde time-flow curve was generated by placing a measuring line in the proximal descending aorta just beneath the aortic isthmus and the origin of the left subclavian artery [14], where the blood flow is less influenced by neither the regurgitation jet nor the shape of orifice area. In the time-flow curve, the horizontal axis represents the time of cardiac cycle, whereas the vertical axis represents flow rates through the measuring line (Fig. 1). Forward and backward flow rates and volumes were calculated during systole and diastole, respectively. The retrograde ratio was calculated as $FV_b/FV_f \times 100\%$. All mean values were taken from three measurements in adjacent cardiac cycles.

Statistical analysis

Continuous variables were expressed as mean ± SD and categorical variables were represented as percentages. For

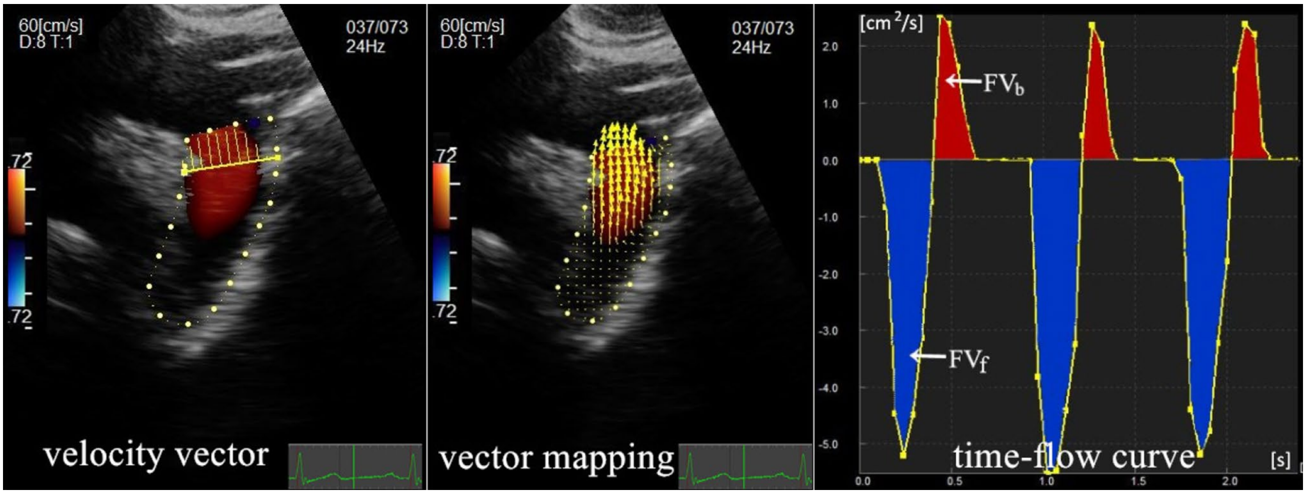

Fig. 1 Velocity vector (left) and vector mapping (middle) of the retrograde during diastole in the descending aorta and time-flow curve through the measuring line (right). In the picture of velocity vector, the long yellow line across the lumen of descending aorta is measuring line and the short yellow lines superimposed on the measuring line represents the distribution of velocity vector. In the picture of vector mapping, yellow line with arrow represents the direction of vector, and the length represents the magnitude of the velocity. FV_b backward flow volume through the measuring line, FV_f forward flow volume through the measuring line

the validation study, relationships between new and conventional parameters were explored using Pearson correlation analysis. The differences among groups were compared by one-way ANOVA. A receiver operating characteristic (ROC) curve was drawn to assess sensitivity and specificity of retrograde ratio for diagnosing severe AR. The Youden index was used to determine the optimal threshold. Inter-observer and intra-observer reproducibility of quantitative measurements were tested using the intra-class correlation coefficient (ICC). $P < 0.05$ was considered statistically significant.

Inter-observer and intra-observer variability in measurements of retrograde ratio by VFM was assessed in 40 randomly selected subjects, 20 AR patients and 20 controls. Inter-observer variability was evaluated independently by performing new measurements by another experienced sonographer. Intra-observer variability was evaluated by the same sonographer on two different occasions.

Results

Patients' characteristics

73 patients were in AR groups and 40 healthy subjects were in control group. All patients were in stable sinus rhythm and no significant mitral regurgitation. Fifty-six patients had pure AR and 17 had associated aortic stenosis. The causes of AR were bicuspid and degenerative aortic valve disease (24.6% and 65.3%, respectively), annular dilation (5.8%) and valve prolapse (4.3%). Demographics of patients were summarized in Table 1. There were no significant differences in age, gender, heart rate, or BSA between the AR groups and control group. Patients with moderate and severe AR had higher systolic blood pressure, lower diastolic blood pressure, a larger left ventricle and a lower ejection fraction.

Doppler echocardiographic indices and retrograde ratio by VFM in AR patients

The mean values of VCW, jet width/LVOT ratio, and EROA by conventional Doppler echocardiography and the retrograde ratio by VFM according to the AR grading are summarized in Table 2. The mean values of the retrograde ratio increased accordingly with the AR grading for controls (6.1 ± 4.0%) and for those with mild AR (21.3 ± 8.2%), moderate AR (43.6 ± 9.4%), and severe AR (70.5 ± 1.5%), respectively (Figs. 2, 3). Close correlations were found between retrograde ratio and VC ($r = 0.930$, $P < 0.001$), jet width/LVOT ratio ($r = 0.884$, $P < 0.001$), and EROA ($r = 0.927$, $P < 0.001$) (Fig. 4). In the ROC analysis, the area under the curve (AUC) for retrograde ratio was 0.958 (SEM: 0.0205, $P < 0.0001$). Using ROC curves, a sensitivity of 93% and a specificity of 89% were obtained when the cutoff value for retrograde ratio was set at 56% (the Youden index was used). When the cutoff value was set at 59%, the sensitivity was 96%, but the specificity dropped to 82% (Fig. 5).

The control group: A1, A2, A3; the mild AR group: B1, B2, B3; The moderate AR group: C1, C2, C3; the severe AR group: D1, D2, D3.

Table 1 Baseline and echocardiographic characteristics

	Mild AR (n = 30)	Moderate AR (n = 15)	Severe AR (n = 28)	Controls (n = 40)
Age (year)	54.5 ± 13.0	55.2 ± 15.6	52.3 ± 14.4	54.7 ± 10.2
Male sex (%)	16 (53)	9 (60)	16 (57)	20 (50)
Heart rate	69 ± 7.8	70 ± 9.0	68 ± 7.7	70 ± 8.3
BSA (m^2)	1.67 ± 0.11	1.60 ± 0.10	1.65 ± 0.09	1.69 ± 0.11
SBP (mmHg)	120.2 ± 11.1	130.3 ± 10.2	129.3 ± 15.1	119.3 ± 15.2†
DBP (mmHg)	79.8 ± 12.9	63.1 ± 22.3	58.7 ± 20.2	78.2 ± 14.1†
EDD (mm)	45.9 ± 3.0	57.8 ± 6.5	69.8 ± 12.7*	45.1 ± 3.3†
ESD (mm)	28.2 ± 2.5	37.4 ± 5.9	46.7 ± 11.9*	28.2 ± 2.7†
EDV (ml)	96.6 ± 17.4	167.7 ± 45.6	267.9 ± 122*	96.4 ± 17.8†
ESV (ml)	30.7 ± 8.9	68.2 ± 22.6	119.5 ± 86.1*	30.6 ± 6.9†
EF (%)	67.4 ± 4.9	60.2 ± 5.2	58.1 ± 9.3	68.8 ± 3.5†

SBP/DBP systolic/diastolic blood pressure, *EDD/EDV* end-diastolic diameter/volume, *ESD/ESV* end-systolic diameter/volume, *EF* ejection fraction

†P < 0.001 vs. moderate AR and severe AR

*P < 0.05 vs. moderate AR

Table 2 Doppler echocardiographic indices and retrograde ratio by VFM in AR patients

Parameters	Mild AR (n = 30)	Moderate AR (n = 15)	Severe AR (n = 28)	Overall P value
VCW (mm)	2.6 ± 0.4	5.0 ± 0.7	9.3 ± 1.6	< 0.001
Jet width/LVOT ratio (%)	19.3 ± 6.1	51.2 ± 8.8	68.9 ± 6.5	< 0.001
EROA (mm^2)	6.8 ± 1.7	25.0 ± 4.3	34.7 ± 3.1	< 0.001
Retrograde ratio (%)	21.3 ± 8.2	43.6 ± 9.4	70.1 ± 10.6	< 0.001

Reproducibility

As shown in Table 3, intraobserver and interobserver variability for retrograde ratio were low, with highly significant agreement between observers.

Discussion

This study represents the first attempt to investigate AR through the retrograde flow of the descending aorta using the new VFM technique. In AR patients, we have demonstrated the accuracy of the retrograde ratio in the quantification of AR in comparison with recognized conventional Doppler echocardiographic methods. Furthermore, this new index was found to have high sensitivity and specificity in distinguishing severe AR from less severe AR.

Severe AR progressively results in LV dysfunction and heart failure due to volume load. Therefore, quantifying AR is crucial for decision making and especially for surgery timing. Several Doppler echocardiographic indices have been validated, including PISA and VCW. The VC method correlates best with objective measures of AR [15, 16]. However, the main disadvantage of the VC method is the small values of VCW, which may cause large errors in the percentage due to small errors in the absolute value. Moreover, patients with multiple jets cannot be evaluated using this method. PISA is a highly recommended and accurate method that can quantify EROA and regurgitation volume [17, 18]. This method, however, also has limitations in some conditions with nonplanar or confined flow convergence zones, such as aortic valve calcifications and aneurysmal dilation of the ascending aorta. Each parameter has an inherent limitation due to issues regarding feasibility and diagnostic accuracy. In addition, the measurements mentioned previously can be greatly influenced by the experience level of sonographers and may be graded differently at different times even by experienced doctors. In a previous multicenter study, the researchers noted a significant inter-observer variability in the characterization of the indices of regurgitation [19]. In the present study, a strong association was observed between the retrograde ratio by VFM and VCW, jet width/LVOT ratio, and EROA by conventional Doppler echocardiography. However, the VFM method depends on neither the shape of jet nor the structure of LVOT, and so is valid for multiple and eccentric jets. Furthermore, a relatively high interobserver variability was observed for this new parameter.

We have further demonstrated that the retrograde ratio is a readily obtainable echocardiographic parameter that could distinguish severe AR from less severe AR. Discrimination of severe AR from mild or moderate AR plays a crucial role in surgical treatment selection and prognosis evaluation. In

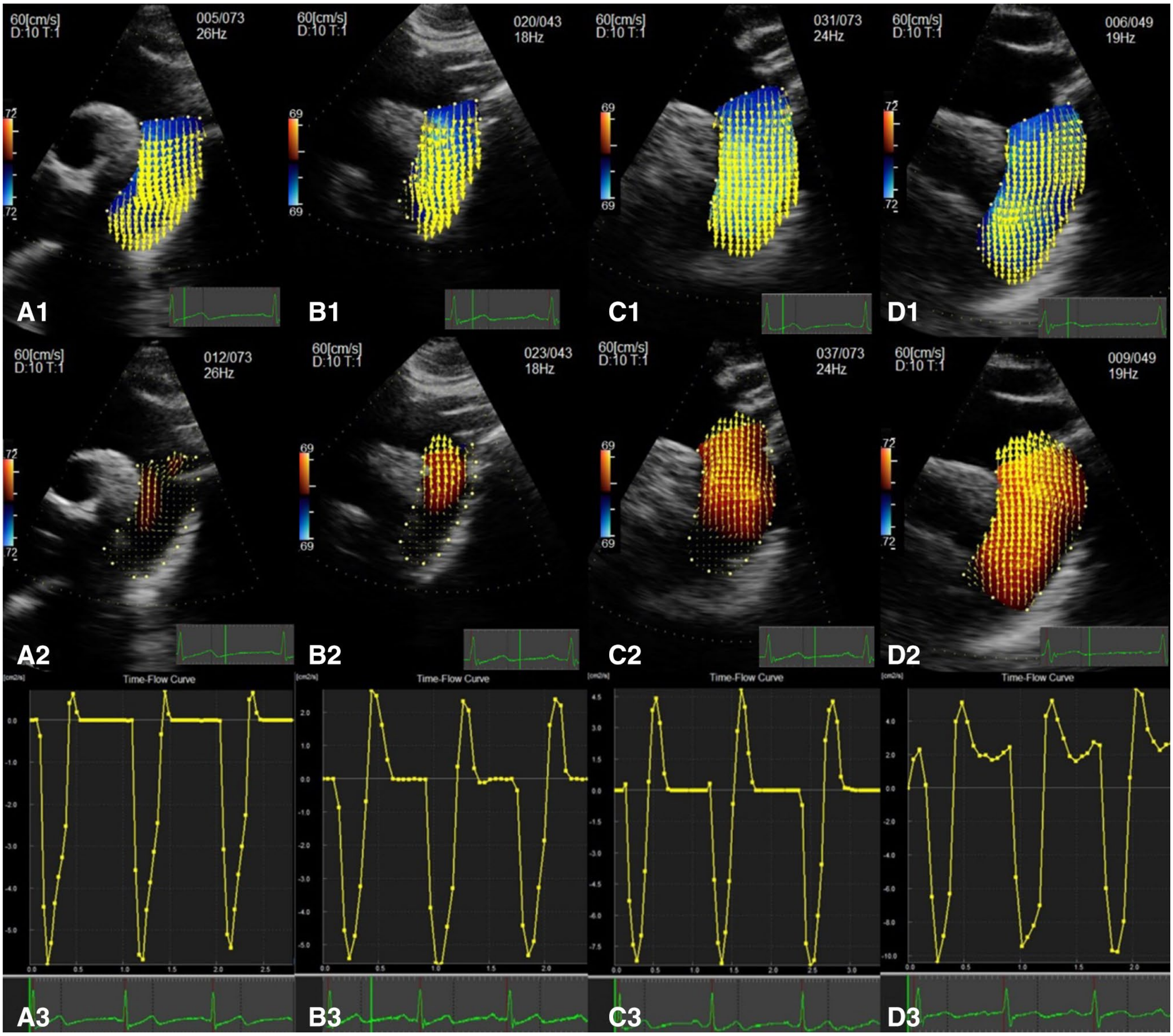

Fig. 2 The vector mapping of retrograde in the descending aorta during systole (A1–D1) and diastole (A2–D2) and the time-flow curve (A3–D3) by VFM in four groups

this study, a cutoff value of 56% has yielded 93% sensitivity and 89% specificity in diagnosing severe AR, revealing that the retrograde ratio is also useful and reliable for clinical decision making.

Under normal conditions, retrograde flow occurs in the ascending aorta during diastole as a support mechanism for the coronary artery blood flow [20]. Our study observed early diastolic retrograde flow along the inner wall of the descending aorta, not only in all AR patients, but also in normal individuals. The occurrence of retrograde flow in the descending aorta in normal individuals in the present study is consistent with prior reports. Patients with a more severe AR may have a greater degree of diastolic retrograde flow in the aorta, reflecting a larger amount of retrograde flow through the incompetent aortic valve [21, 22]. Doppler echocardiography of the descending aorta can be easily performed, and quantifying the ratio of backward to forward flow in the descending aorta by Doppler approach was first attempted in 1975 by Boughner [4]. Since then, a number of studies have reported Doppler methods to quantify blood flow information in AR patients at the level of the descending aorta [5, 6, 14]. Doppler parameters such as the velocity of end-diastolic flow reversal, the time integral of the reversal flow, and the ratio of reversed to forward flow have all been used to grade AR and reported good correlations with AR severity. Tribouilloy et al. [14] found that an end-diastolic flow reversal velocity of > 18 cm/s just beneath the aortic isthmus identified AR patients with a regurgitant

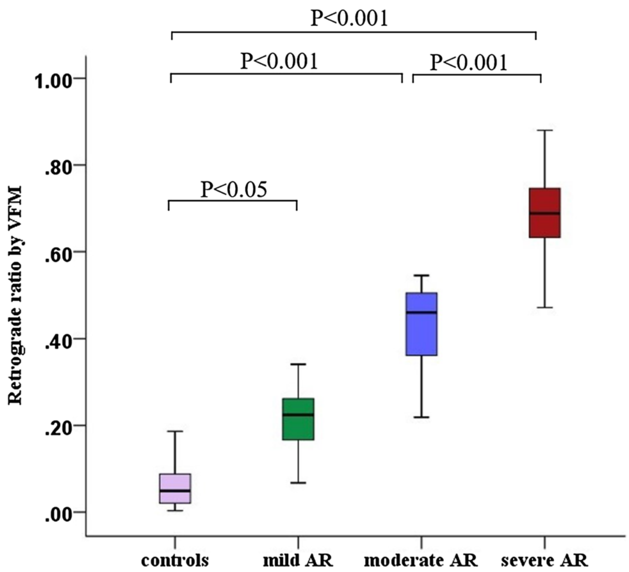

Fig. 3 Significant differences of the retrograde ratio among four groups (controls vs. mild AR vs. moderate AR vs. severe AR)

fraction of 40% with a sensitivity of 88.5% and a specificity of 96%. Touche et al. [15] used pulsed-wave Doppler echocardiography to relate the magnitude of descending aortic flow reversal to AR severity and reported a nearly ideal relationship between the echocardiography-derived regurgitant fraction in the descending aorta and angiographic regurgitant fraction (r = 0.99). However, the value of the previously mentioned methods in quantifying AR may reduce when the direction of velocity is not parallel to the beam and can be affected by the experience level of sonographers. Furthermore, the measurement using the methods mentioned can only represent the sampling point in the descending aorta, but the distribution of the retrograde flow in the elbow may be asymmetrical, the measurement at one point may underestimate the reverse flow. VFM is based on the hypothesis that the velocity profiles perpendicular to the beam direction can be acquired by the principle of the continuity equation and speckle tracking; it is less affected by the angle. Furthermore, in VFM analysis, the forward and backward flow rates and volumes were obtained from the blood flow on a sampling line across the descending aorta. These data were automatically calculated by a software, making the assessment of fluid information more convenient and accurate. In addition, in VFM analysis, the forward and backward flow rates and volumes were obtained by the blood flow information on a sampling line across the descending aorta. These data were automatically calculated by a software, making the assessment of fluid information more convenient and accurate.

Despite being a newly emerging technique, several quantitative parameters in the VFM method, including flow velocity, vortex details, and energy loss of flow, have been studied and proven to be of considerable use in the clinical setting [11, 23, 24]. Fukuda et al. [23] have studied the vortex information obtained using VFM in the left ventricle during isovolumic systole in patients with heart failure. They observed that the duration of vortex in left ventricular outflow tract during isovolumic systole was shorter in the patients with heart failure than in controls, and speculated that this phenomenon may indicate a decrease in cardiac function. Takashi et al. [25] used VFM to assess the energy loss (EL) of the blood flow in post-stenotic dilatation above the pulmonary valve stenosis; they observed a high EL in the main pulmonary artery, even though no pressure drop was detected during catheterization. The EL considerably decreased after pulmonary valve repair. Furthermore, the potential application of VFM in the quantification of valve regurgitation has recently been reported. Li et al. [26] used VFM to determine backward and forward flow volumes in the aortic root, and found significant correlations of the AR ratio with conventional Doppler methods for quantifying AR. However, there have been some concerns on whether the accuracy would be affected by the aliasing phenomenon

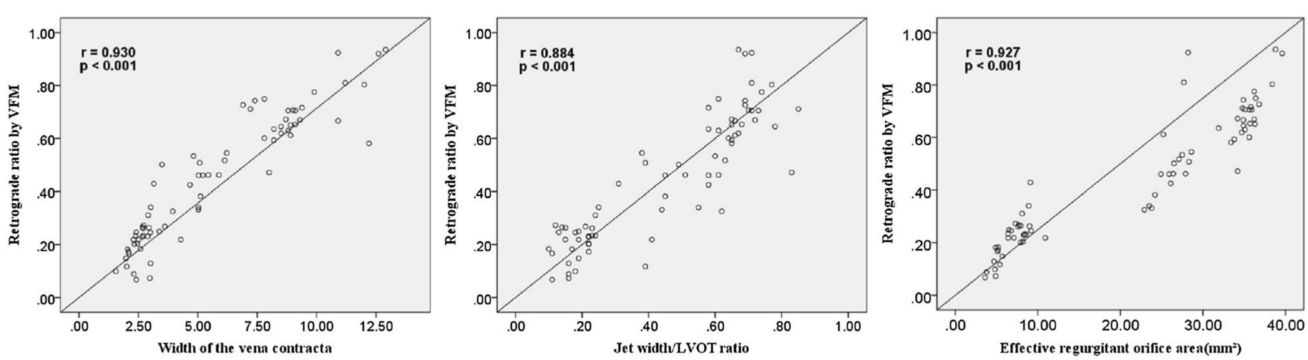

Fig. 4 Scatterplots showing correlation between the retrograde ratio and VCW (left), jet width/LVOT ratio (middle) and EROA (right) by conventional Doppler echocardiography

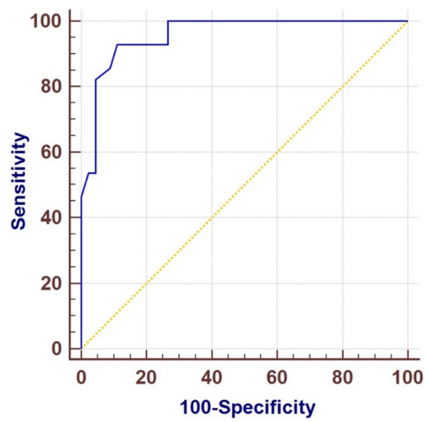

Fig. 5 ROC curve of retrograde ratio for distinguishing between severe AR and less than severe AR. AUC of retrograde ratio was 0.958. Blue line represents the ROC curve for retrograde ratio. Yellow line represents reference

Table 3 Intra-observer and inter-observer reproducibility of measurements

	ICC (P)	95% Confidence interval	
		Lower bound	Upper bound
Intra-observer	0.95 (<0.001)	0.917	0.976
Inter-observer	0.92 (<0.001)	0.849	0.956

ICC intra-class correlation coefficient

due to the reversal velocity in the aortic root beyond the Nyquist limit. In addition, some previous studies of the flow profiles in the aorta showed an irregular flow velocity pattern in the ascending aorta with moderate or severe regurgitation [22]. In contrast to the ascending aorta, the descending aorta produces a much flatter velocity profile and has a better acoustic window in the suprasternal view. Stugaard et al. [27] calculated flow energy loss within the LV secondary to aortic regurgitant turbulent flow by VFM in dogs and human patients, and reported a certain relationship between diastolic energy loss and AR severity. However, some researchers have been concerned with regard to the accuracy of the results due to the high velocity of regurgitant flow in the LV, which exceeded the Nyquist limit. In the present study, the velocity of retrograde flow was not too high, so the Nyquist limit for two-dimensional color Doppler imaging was high enough to mitigate the aliasing phenomenon. Ashley [28] has applied VFM to quantify pulmonary regurgitation in patients with congenital heart conditions after right ventricular outflow obstruction repair. His study has proven the accuracy of VFM-derived pulmonary regurgitant ratio in diagnosing PR severity, suggesting that VFM has significant clinical translational potential for the quantification of flow volume in congenital heart conditions.

Study limitations

There were several limitations to this study. First, the findings of the present study, although statistically significant, were based on a relatively small sample size for each subgroup. Second, further study with a larger sample size is required to validate the accuracy of VFM. Third, the lack of a robust standard reference method for quantifying AR makes it a challenge to determine with certainty which method has the tendency to under- or overestimate. Finally, aortic stiffness, blood pressure, and age were known to be factors influencing aortic retrograde flow, which cannot be eliminated or unified in the study.

Conclusion

The retrograde ratio derived from VFM in the descending aorta is an accurate and a promising parameter in the identification of AR severity. This method should be systematically incorporated in the comprehensive evaluation of AR by echocardiography.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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