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ORIGINAL RESEARCH

Direct Measurement of Multiple Vena Contracta Areas for Assessing the Severity of Mitral Regurgitation Using 3D TEE

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OBJECTIVES The aim of this study was to determine whether direct measurement of multiple-jet vena contracta (VC) areas by real-time 3-dimensional (3D) transesophageal echocardiography is an accurate method for measuring the severity of mitral regurgitation (MR) in patients with multiple MR jets.

BACKGROUND Because of the conflicting requirements of Doppler and imaging physics, measuring VC using 2-dimensional (2D) echocardiography is a difficult procedure for assessing MR severity. A real-time 3D echocardiographic measurement of the VC area has been validated in a single jet of MR, but the applicability of this method for multiple jets is unknown.

METHODS Two-dimensional and 3D transesophageal echocardiography was performed in 60 patients with multiple functional MR jets. MR severity was assessed quantitatively using the effective regurgitant orifice area derived from 3D left ventricular volume and thermodilution data (EROAstd). Manual tracings of multiple 3D VC areas in a cross-sectional plane through the VC were obtained, and the sum of the areas was compared using EROAstd. Similarly, 2D measurement of VC diameter was obtained from a 2D transesophageal echocardiographic view to optimize the largest legion size in each jet. All VC diameters were summed and compared with EROAstd.

RESULTS The correlation of the sum of the multiple 3D VC areas with EROAstd (r = 0.90, p < 0.01) was higher than that of the sum of the multiple 2D VC diameters (r = 0.56, p < 0.01), particularly with MR degrees greater than mild (r = 0.80, p < 0.01 vs. r = 0.05, p = 0.81) and in cases of 3 or more regurgitant jets (r = 0.91, p < 0.01 vs. r = 0.46, p = 0.05).

CONCLUSIONS Direct measurement of multiple VC areas using 3D transesophageal echocardiography allows for assessing MR severity in patients with multiple jets, particularly for MR degrees greater than mild and in cases of more than 2 jets, for which geometric assumptions may be challenging. (J Am Coll Cardiol Img 2012;5:669–76) © 2012 by the American College of Cardiology Foundation

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unctional mitral regurgitation (MR) may cause serious complications such as systolic left ventricular (LV) dysfunction and dilation, and these complications can result in

excess morbidity and mortality (1-3). Thus, an accurate quantification of functional MR severity is essential for effective clinical management and timing for surgical intervention (1,4). Various qualitative and quantitative 2-dimensional (2D) color Doppler techniques for effective regurgitant orifice area (EROA) assessments have been proposed for

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quantifying MR severity (5,6). However, determining EROA using the quantitative Doppler or the proximal isovelocity surface area method is time

ABBREVIATIONS AND ACRONYMS

EROA = effective regurgitant orifice area

EROAstd = effective regurgitant orifice area derived from 3-dimensional left ventricular volume and thermodilution data

LV = left ventricular

MR = mitral regurgitation

TEE = transesophageal echocardiography

3DVCarea = sum of the multiple 3-dimensional vena contracta areas

2DVCdiam = sum of the multiple 2-dimensional vena contracta diameters

VC = vena contracta

consuming and involves imprecise hemodynamic assumptions. EROA hydrodynamically corresponds to the crosssectional area of the vena contracta (VC) (7,8). The VC is located at the smallest region between the proximal laminar flow acceleration zone and the distal turbulent regurgitant jet spray (9). The VC method is simple and less technically demanding than other methods and may be less dependent on loading conditions (10). With a single MR jet, real-time 3-dimensional (3D) transthoracic echocardiography for VC was shown to be better than 2D echocardiography for MR quantification, because it can provide a reliable assessment of regurgitant volume on the basis of an accurate representation of the orifice shape (11-13). The recent introduction of

a 3D matrix-array transesophageal echocardiographic transducer provides 3D images with spatial resolution higher than that provided by transthoracic images, which enables better definition of the MR jet profile. To date, the diagnosis of MR severity has been challenging in patients with multiple jets; thus, we aimed to determine the feasibility and accuracy of 2D and 3D VC methods in diagnosing MR volume in patients with multiple jets using a 3D matrix-array transesophageal echocardiographic transducer.

METHODS

Study population. A total of 64 consecutive patients who were scheduled for valve surgery for aortic valve stenosis (n = 49) and mitral valve regurgita-

tion (n = 15) and had at least mild functional MR with multiple regurgitant jets were selected as the study population. Functional MR was defined as leaflet tethering and incomplete leaflet coaptation in the presence of normal mitral valve anatomy and regional or global LV remodeling (14). All patients underwent 2D and 3D transesophageal echocardiography (TEE) under conscious sedation and thermodilution measurements before surgery. Patients with inadequate images by TEE and those with more than mild aortic insufficiency, with nonsinus rhythm, or with left bundle branch block were excluded from the study. Written consent was obtained from all subjects. The study was approved by the Columbia University institutional review board.

TEE and thermodilution method. Images were acquired using an iE33 ultrasound system (Philips Medical Systems, Andover, Massachusetts) equipped with a 2D and fully sampled 3D matrix-array transducer for TEE. In color Doppler mode, 2D VC images were obtained from mid-esophageal views to optimize imaging of each multiple regurgitant jet (Fig. 1A). The beam angle was rotated to 180° to obtain maximize visualization of the VC in each jet. Each of the 2D color jet images was obtained to maintain an angle $<60^{\circ}$ between flow and Doppler beam with the largest legion size. The number of 2D MR jets was then identified by the operator. Color gain was maintained at the maximal percent value to eliminate random noise, and Nyquist limits were set between 40 and 60 cm/s to avoid overestimation or underestimation of 2D VC diameters. For standard measurement of MR severity, effective regurgitant orifice area derived from 3-dimensional left ventricular volume and thermodilution data (EROAstd) was quantified using the following equation:

 $EROAstd = \left[\left(end-diastolic LVV_{3DTEE} - end-systolic LVV_{3DTEE} \right) - SV_{thermodilution} \right] / TVI_{MRjet}$

where LVV_{3DTEE} is LV volume derived by 3D TEE, SV_{thermodilution} is stroke volume derived using the thermodilution method, and TVI_{MRjet} is the velocity-time integral of MR jets. MR severity was also graded on the basis of EROAstd and was classified as mild (<0.20 cm²), moderate (0.2 to 0.39 cm²), or severe (\geq 0.4 cm²) according to the guidelines of the American Society of Echocardiography (15). Two-dimensional TEE was performed first. Each VC diameter of the 2D jets was assessed at the systolic frame showing the largest



QLAB version 7.1 (Philips Medical Systems). lesion size, and the sum of the multiple 2D VC

diameters (2DVCdiam) was compared with EROAstd. In addition, LV ejection fraction was calculated using the modified biplane Simpson method as recommended by the American Society of Echocardiography (16).

3D TEE was then performed in all patients after obtaining 2D images. Datasets of 3D color Doppler for MR were obtained from mid-esophageal views by acquiring 7 electrocardiographically triggered sequential scan volumes composing a full volume of approximately $60^{\circ} \times 60^{\circ}$. Color Doppler Nyquist levels were set as analogous to 2D color Doppler data acquisition. Additionally, full-volume acquisition was performed from the apex to analyze the entire LV volume. To avoid respiratory artifacts, 3D data acquisition was performed under a breath hold. 2D VC diameter was acquired at a median frame rate of 17 Hz (range 14 to 22 Hz), and the median frame rate for 3D VC area was 18 Hz (range 14 to 21 Hz).

Cardiac output determination using the thermodilution method was performed as previously described (17). All patients had a balloon-tipped, flow-directed thermodilution catheter (Edwards Lifesciences, Irvine, California) inserted through the right jugular vein into the pulmonary artery. Cardiac output was automatically computed after manual injection of 10 ml of 0.9% saline into the right atrium. Injection was repeated 5 times, and the 3 most concordant cardiac output values were averaged and divided by heart rate to calculate stroke volume. The thermodilution measurement was performed consecutively with the acquisition of transesophageal echocardiographic images. 3D data analysis. Analysis of 3D images was performed offline (QLAB version 7.1; Philips Medical Systems). To analyze 3D color Doppler images, the 3D dataset was manually cropped using an image plane perpendicularly oriented to the jet direction at the narrowest cross-sectional area of the jet (13). The asymmetry index of the 3D VC area was calculated using the ratio of the major axis to the minor axis in each MR jet. Three-dimensional VC area was measured by manual planimetry of the color Doppler signal, which involved tilting the image to an "en face" view and selecting the systolic frame with the largest lesion size for each jet (Fig. 1B). 3D VC areas obtained in a crosssectional plane through the VC were added, and the sum of the multiple 3D VC areas (3DVCarea) was compared with EROAstd. Consecutively, endsystolic and end-diastolic LV volumes were measured using a semiautomated method in QLAB version 7.1 (Philips Medical Systems) (Fig. 1C). All measurements, including measurements of 2D VC diameters and 3D VC areas, were averaged over 3 cardiac cycles. Measurements were performed by an experienced operator blinded to the clinical data.

Interobserver and intraobserver variability in 2DVCdiam and 3DVCarea measurements was determined for 10 randomly selected patients. Interobserver variability was calculated as the standard deviation of the differences between measurements made by 2 independent observers who were unaware of the patient data. Intraobserver variability was calculated as the standard deviation of the differences between the first and second measurements (2-week interval) from a single observer.

Statistical analysis. Continuous variables are expressed as mean \pm SD. Categorical data are presented as absolute numbers or percents. Pearson correlation coefficient was used to assess the relationship among 2DVCdiam, 3DVCarea, and EROAstd. The difference between correlation coefficients was tested using the conventional and dependent samples test. Bland-Altman analysis was performed to evaluate the differences between 2DVCdiam and EROAstd or 3DVCarea and EROAstd. Differences were considered significant when p values were <0.05.

RESULTS

Patient population. Our study included 60 patients (30 men, 30 women; mean age 73 ± 7 years) (Table 1). Patient characteristics, including hemodynamic data and echocardiographic measure-

Table 1. Hemodynamic and Echocardiographic Data (n = 60)	
Age (yrs)	73 ± 7
Body surface area (m ²)	1.8 ± 0.3
Hemodynamics	
Systolic blood pressure (mm Hg)	119 ± 19
Diastolic blood pressure (mm Hg)	72 ± 9
Heart rate (beats/min)	70 ± 10
TEE	
2D	
LV end-diastolic volume (ml)	131 ± 39
LV end-systolic volume (ml)	66 ± 30
LV ejection fraction (%)	51 ± 9
MR volume (ml)	26 ± 16
MR EROA (cm ²)	$\textbf{0.17} \pm \textbf{0.10}$
2DVCdiam (cm)	$\textbf{0.41} \pm \textbf{0.14}$
3D	
Mean MR jet number/patient	$\textbf{2.3}\pm\textbf{0.4}$
Asymmetry index in each MR jet	3.1 ± 1.1
3DVCarea (cm ²)	$\textbf{0.23}\pm\textbf{0.13}$
Values are mean \pm SD. EROA = effective regurgitant orifice area; LV = left ventricular; MR = mitral regurgitation; TEE = transesophageal echocardiography; 3D = 3-dimensional; 3DVCarea = sum of the multiple 3-dimensional vena contracta areas; 2DVCdiam = sum of the multiple 2-dimensional vena contracta diameters.	

ments, are shown in Table 1. Of the 64 patients selected for participation in this study, 4 were excluded from analysis because of technically inadequate 3D echocardiographic images.

Direct assessment of 2D VC diameter and 3D VC area. 2D TEE images revealed that 11 patients had 3 MR jets and 49 had 2 MR jets. However, 3D TEE images showed 3 MR jets in 18 patients and 2 MR jets in 42 patients. According to 3D TEE, the median number of MR jets per patient was 2.3 (Table 1). As expected, the shape of the 3D VC area in most MR jets (94%) appeared noncircular (asymmetry index 3.1) (Table 1). The median 2DVCdiam and 3DVCarea were 0.41 \pm 0.14 cm and 0.23 ± 0.14 cm², respectively (Table 1). The mean analysis times for 2DVCdiam and 3DVCarea were 3.8 ± 1.1 min and 6.6 ± 2.1 min, respectively. Relation of 2DVC diam and 3DVC area with EROAstd. Amoderate correlation was observed between 2DVCdiam and 3DVCarea (r = 0.63, p < 0.001). Among all patients, a greater correlation was observed between EROAstd and 3DVAarea (r = 0.90, p < 0.001) than between EROAstd and 2DVC diam (r = 0.56, p < 0.001) (p < 0.001) (Fig. 2A). Bland-Altman analysis revealed closer limits of agreement between EROAstd and 3DVCarea than between EROAstd and 2DVCdiam (Fig. 2B). These results indicate that direct measurement of multiple VC areas using 3D imaging is a more accurate method of MR severity assessment than 2D imaging.



Effect of MR severity and MR jet number on the accuracy of VC measurements. Semiquantitative assessment of MR by TEE revealed that 37 patients had mild MR, 12 had moderate MR, and 11 had severe MR. The accuracy of 2D and 3D VC measurements in relation to MR severity is shown in Figures 3A and 3B. In patients with MR greater than the mild level, 3DVCarea was more highly correlated with EROAstd than with 2DVCdiam (r = 0.80 vs. r = 0.05, respectively, p < 0.01). In contrast, in patients with mild MR, 2DVCdiam and 3DVCarea showed similar correlations with EROAstd (r = 0.43 vs. r = 0.41, respectively, p = NS).

To evaluate the effect of MR jet number on the VC method, we examined the applicability of 2D and 3D VC methods in patients with different numbers of MR jets, as assessed using 3D TEE. In this study population, 42 patients had 2 MR jets and 18 patients had 3 MR jets. MR severity was similar between the 2 groups (EROA_{std} 0.17 \pm 0.10 cm² vs. 0.23 \pm 0.14 cm², respectively, p =

0.07). Figures 3C and 3D show the correlations of 2DVCdiam and 3DVCarea with EROAstd on the basis of the number of MR jets. In patients with 2 MR jets, both 2DVCdiam and 3DVCarea correlated well with EROAstd, but the correlation of 3DVCarea was significantly better (r = 0.63, p <0.001 and r = 0.90, p < 0.001, respectively; p for correlation coefficient difference < 0.01). As the number of jets increased, the correlation of 3DV-Carea with EROAstd remained excellent (r = 0.91, p < 0.001), whereas the correlation of 2DVC diam with EROAstd deteriorated (r = 0.46, p = 0.05; for the correlation coefficient difference p < 0.01). Observer variability. Interobserver agreement was good for both 2DVCdiam and 3DVCarea, with the mean absolute differences of 0.06 \pm 0.03 cm (12 \pm 7%) and 0.06 \pm 0.03 cm² (12 \pm 5%), respectively. Similarly, intraobserver agreement for 2DVCdiam and 3DVCarea was good, with the mean absolute differences of 0.05 \pm 0.03 cm (10 \pm 6%) and $0.05 \pm 0.03 \text{ cm}^2$ (10 ± 5%), respectively.



Figure 3. Correlations Between EROAstd and 2DVCdiam or 3DVCarea in Mild MR and in Moderate and Severe MR and Correlations Between EROAstd and 2DVCdiam or 3DVCarea in 2 and 3 MR Jets

(A) Correlations were similar in the sum of the multiple 2-dimensional vena contracta diameters (2DVCdiam) (left) and the sum of the multiple 3-dimensional vena contracta areas (3DVCarea) (**right**) in patients with mild mitral regurgitation (MR) (r = 0.43 vs. r = 0.41, respectively) (n = 37). (B) Correlation was better in 3DVCarea (**right**) than in 2DVCdiam (left) in patients with moderate and severe MR (r = 0.80 vs. r = 0.05, respectively) (n = 23). (C) Correlations were good in both 2DVCdiam (left) and 3DVCarea (**right**) in patients with 2 jets (r = 0.63 vs. r = 0.90, respectively) (n = 42). (D) Correlation was better in 3DVCarea (**right**) than in 2DVCdiam (left) and with 3 MR jets (r = 0.91 vs. r = 0.46, respectively) (n = 18).

DISCUSSION

Although color Doppler imaging has been used for decades to measure MR severity, efforts to better understand and improve the clinical utility of this diagnostic tool are still ongoing. Recent studies have explored the use of 3D color Doppler imaging in VC methods for determining MR severity in patients with single jets (11-13). However, given the complex 3D geometry of the mitral valve coaptation surface, it is common for diseased valves to have multiple regurgitant lesions. Furthermore, mitral repair techniques that alter mitral valve geometry may induce multiple, smaller residual regurgitant jets, particularly in doubleorifice repair, in which the scallop of the anterior and posterior leaflets is approximated (18). In the present study, we aimed to determine whether MR severity in patients with multiple MR jets can be evaluated via direct measurement of multiple-jet VC areas through the summation of these areas. It should be noted that determining MR severity of multiple jets in most patients, including those after double-orifice mitral repair, is an important clinical issue.

We demonstrated that direct measurement in multiple VC methods using 3D TEE provides an accurate assessment of MR severity in patients with multiple jets. Notably, the sum of multiple VC parameters led to a representation of EROA. Furthermore, 3DV-Carea was highly correlated with EROAstd, and the correlation was better than that of the classic 2DVCdiam in patients with multiple MR jets. Such correlation was particularly good in cases in which the degree of MR severity was greater than mild and in cases of multiple regurgitant jets, for which geometric assumptions are necessary for 2DVCdiam. These findings imply that the 3D VC method is an effective tool for the accurate assessment of MR severity, even in patients with multiple jets.

Sum of multiple VC diameters and areas as a parameter of MR severity. Accurate grading of MR severity is an important but controversial issue. Currently, VC diameter measured by 2D echocardiography has been proposed as a direct measurement method for EROA (7,8,15), with the assumption that EROA shape is either circular or elliptical. However, EROA is often irregularly shaped, a common occurrence in patients with heart diseases. Consequently, accurate estimation of EROA using 1 or 2 diameter measurements becomes difficult in patients with functional MR, particularly in those with regurgitant mitral orifices that are elongated along the semi-lunar-shaped leaflet coaptation line. By applying 3D echocardiography, we can overcome this limitation of 2D echocardiography and accurately depict the orifice shape and therefore quantify the regurgitant volume. Previous studies have shown that 3D echocardiographic measurement of VC area is well correlated with MR severity in patients with single MR jets (11-13). In accordance with these observations, we also found that 3D echocardiographic measurement of VC area can provide accurate MR severity in patients with multiple MR jets. Lin et al. (19) reported that although regurgitant volumes are the same between single and multiple jets, color Doppler jet area is larger in multiple jets. Potential overestimation of regurgitant volume using color Doppler flow jets area can occur; thus, this method is not recommended for assessing MR severity in patients with multiple MR jets. In contrast, we showed that by quantifying the regurgitant volume of all jets by calculating the sum of each VC area in 3D VC method, we not only eliminated the possibility of overestimation but also accurately presented the EROA representing the severity of multiple jets.

Factors affecting the accuracy of VC methods. In patients with mild MR, similar correlations with EROAstd of both 2DVCdiam and 3DVCarea were observed in this study. An overestimation using the VC method for small valvular defects in an in vitro model (20) and in a mild disease in vivo model (21) were in agreement with our findings. This may be partly attributed to clustering of data over a narrow range of severity. In addition, the accuracy of these measurements for mild jets may be affected by mechanical limitations, including image pixilation. The development of an ultrasound machine with a higher frame or volume rate might resolve these problems. Furthermore, the hydrodynamic principle of VC might not be applicable in lower flow mild regurgitant states, in which the MR jet tends not to converge to the small cross-sectional area between the proximal laminar flow acceleration zone and the distal turbulent regurgitant jet spray, thereby leading to low accuracy of 2D and 3D VC methods. However, because mild MR severity is typically diagnosed qualitatively, this limitation is not an issue in clinical practice. However, in patients with clinically significant MR, 3DVCarea is better correlated with EROAstd than with 2DVCdiam. The regurgitant mitral orifice is often irregularly shaped, so defining MR by a 1-diameter measurement using 2D echocardiography would not accurately represent its real shape. In the case of 3D echocardiography, the color Doppler dataset can be analyzed randomly from any plane, thereby projecting the exact shape of the jets, which in turn provide a good correlation with EROAstd, particularly in patients with non-circular-shaped orifices and clinically significant MR.

As the number of MR jets increases, proper evaluation of all existing jets becomes difficult using 2D echocardiography. In cases of 2 MR jets, both 2DVCdiam and 3DVCarea were well correlated with EROAstd. However, in cases of 3 regurgitant jets, only 3DVCarea, not 2DVCdiam, showed a good relationship with EROAstd. In fact, 2D TEE cannot depict all regurgitant jets, because of the limited scan plane orientation, which may conceal other possible jets. Moreover, although total MR severity was similar between patients with 2 jets and 3 jets, each MR jet may be smaller in patients with 3 rather than 2 jets. This may lead to misjudgment of an accurate jet number and volume using 2D TEE in patients with 3 jets (20,21). Nevertheless, with a multiple number of MR jets for which quantification is necessary and assumptions regarding orifice geometry may be challenging, the 3D VC method is the appropriate choice to accurately reflect MR severity in patients with multiple MR jets.

This study provides initial evidence on the objective diagnosis of MR severity in patients with multiple jets using 3DVCarea, but confirmation is needed in patients with different MR etiologies and with different valve anatomy (i.e., after valve repair). In addition, the number of patients with more than mild MR was relatively small. A larger study population would be ideal. Furthermore, the findings in this study were achieved under ideal conditions, in which VC measurements may appear different from those encountered in clinical routine practice. However, by avoiding artifacts and using a higher volume rate of 3D color images, the accuracy of VC measurements is guaranteed. Standard measurement of MR severity was based on 3D LV volume and thermodilution measurement in this study (22). The interobserver and intraobserver agreement of end-diastolic LV volume and endsystolic 3D LV volume measurements were 5.3 \pm 3.1% and 5.8 \pm 3.5%, and injection was repeated 5 times, with the 3 most concordant cardiac output values averaged for the cardiac output measurements, indicating a highly reproducible standard for assessing MR severity. Recently, 3D cardiac magnetic resonance has been proposed as a reference method for measuring MR volume. Further studies comparing the 3D VC method with 3D magnetic resonance imaging may reveal relevant information in assessing MR severity. In addition, for the EROAstd measurement, we measured the velocity-time integral of 1 MR jet and applied it to other jets. The velocity-time integral of every MR jet should be the same value from Pascal's law, and this application of the velocitytime integral might be appropriate.

CONCLUSIONS

Direct measurement of multiple VC areas using 3D TEE, which can accurately depict orifice shape and exact jet number, provides a simple parameter that accurately reflects MR severity. These findings demonstrate that the 3D VC method holds promise as an effective tool for accurately assessing MR severity, even in patients with multiple regurgitant jets.

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