Review Article

3D *Vena Contracta* Area to Quantify Severity of Mitral Regurgitation: A Practical New Tool?

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Mitral regurgitation (MR) is a common form of valvular disease[1] and its severity is associated with excess morbidity and mortality from left ventricular (LV) remodeling, left atrial remodeling, pulmonary pressure elevation, and progression to left and right heart failure.[2-6] Current American Society of Echocardiography (ASE) Guidelines[7] propose *vena contracta* (VC) width as a simple semi-quantitative marker of MR severity. The VC width is defined as the minimal color Doppler diameter at the junction of the flow convergence acceleration zone and the turbulent regurgitant jet just distal to the regurgitant orifice (Figure 1). One limitation of this simple measure is that the VC width is only a single tomographic slice of a three-dimensional flow event. Three-dimensional *vena contracta* area (3D-VC area) is a novel measurement made possible by 3D color Doppler imaging. Here we review the methodology and clinical validation of this new measurement tool for the quantification of MR severity.

Limitations of VC width

VC is an old hemodynamic concept.[8] As a regurgitant jet pass through an orifice area, flow stream lines contract[9] and the VC defines the point at which the jet has its minimal area[8] (Figure 1). Color Doppler VC width has been demonstrated to correlate well with the effective regurgitant orifice size.[9-12]

The relationship between the real hemodynamic VC and the color Doppler VC width was evaluated in one study and it was shown that overestimation can occur as a result of flow dependency and flow entrainment in an *in vitro* model.[13] In clinical studies, overestimation is more prominent in central jets due to flow entrainment,[14] while underestimation is more common in eccentric jets.[15,16] In concept, the size of the VC region is independent of flow rate for any fixed-sized flow orifice;[11] however, during the systolic ejection period the size of the VC region may vary minimally as the dynamic regurgitant orifice varies in size.[17-20] Since the VC width is a single frame measurement, this minor systolic phase variability may lead to over- or underestimation of MR severity, especially under clinical conditions that exhibit the most marked dynamic changes of the regurgitant orifice (such as mitral valve leaflet prolapse).[15,21]

Another limitation of the 2D method is due to the narrow range of values among different grades of MR, in which minor errors in diameter assessment can result in a significant misclassification of MR severity.[21] Also, instrument settings from different vendors can vary the axial and lateral resolution.[9,11,14,22] An additional issue, recently described by Biner et al,[23] is the suboptimal interobserver agreement for differentiating severe from non-severe MR. This was a multicenter study where 18 echocardiography specialists at 11 different institutions manually measured VC width and graded MR as severe if VC was ≥7 mm and as non-severe if VC was ≤6.9 mm. Interobserver agreement was only fair (75 ± 15%) for VC measurements, while the kappa coefficient was 0.28 (95% CI: 0.11 to 0.45).

Although validated for single jets, VC width assessment has not been found to be reliable in cases with multiple regurgitant jets.[24] Currently, 3D echocardiography studies have shown that effective regurgitant orifice area (EROA) is typically asymmetric and the VC width as a surrogate for an irregular regurgitant orifice area is not as accurate, especially in cases of functional MR.[24-30]

3D-VC area validation studies

Most studies comparing VC area to different reference standards have demonstrated a good correlation, and the method appears to be accurate even in cases with the most asymmetric regurgitant jets. 3D-VC area and the 3D-VC area-derived regurgitant volume accuracy has been validated against LV ventriculography, 2D color Doppler methods, 2D volumetric Doppler methods, cardiac MRI, and the integrated approach recommended by ASE guidelines.[7]

Studies using ventriculography as a reference standard

In an early study including 44 patients with at least mild MR by color Doppler, Khanna et al,[31] using transthoracic echocardiography (TTE), measured VC width and calculated VC area from the 2D measurement of VC width, assuming a circular VC area. They also measured 3D-VC area by planimetry, using systematic cropping of the 3D data set. They compared the MR assessment by echocardiography with MR grading by ventriculography. VC area from live 3D was closely correlated with the angiographic grading ($r=0.88$) and had higher agreement than the calculated 2D-VC area.

Studies using 2D methods as a reference standard

Iwakura et al[32] compared 3D-VC area with the EROA derived from the quantitative Doppler and proximal isovelocity surface area (PISA) methods in 106 patients with pure isolated MR of at least moderate degree. They concluded that there was a strong correlation between the 3D-VC area and the regurgitant orifice calculated either by quantitative Doppler ($r=0.91$) or by the PISA method ($r=0.93$). However, the PISA method underestimated the area compared with either 3D-VC area or quantitative Doppler EROA, especially in cases of with elliptic orifice shapes.

In 57 patients with mild to severe MR of different etiologies, Kahlert et al[25] found that 2D-VC width and area do not correlate well with 3D-VC area. The best correlation was found for the mean VC width ($r=0.90$). They explained the poor agreement as being due to the asymmetry of the VC area. They demonstrated a good correlation of 3D-VC area with the hemielliptic or hemispheric PISA method. However, hemispheric PISA underestimated the regurgitant orifice in mitral valve prolapse and functional MR and had a worse correlation than hemielliptic PISA. The investigators suggested that direct planimetry of the 3D-VC area is a simple, accurate method for estimating the regurgitant orifice. Using 3D transthoracic echo, our group[26] compared 3D-VC area and Doppler-derived EROA in patients with at least mild MR. We demonstrated a better correlation for 3D-VC area ($r=0.85$, $p<0.001$) than for VC width ($r=0.65$, $p<0.001$), particularly in patients with significant MR. We also demonstrated a strong correlation ($r=0.92$, $p<0.001$) for the 3D-VC area *in vitro* when compared with orifices of known size and varied shapes.

Using real-time 3D echocardiography, Yosefy et al[27] found that VC area correlates strongly with volumetric effective regurgitant area (EROA) in both central and eccentric jets ($r^2=0.86$). In the same study, 2D-VC width was overestimated in cases with eccentric jets, leading to a 45% misclassification rate. Finally, Altioc et al[33] demonstrated a very strong correlation between 3D anatomic regurgitant orifice area (AROA) measured by direct planimetry and 2D PISA EROA ($r=0.96$) and 2D-derived VC area ($r=0.89$). The correlation, however, was not as strong in patients with EROA <0.2 cm^2.

Studies comparing 3D echo to cardiac MRI

In a study of patients with functional MR, Marsan et al[28] compared the 3D-VC area-derived regurgitant volume (multiplying the 3D EROA by the MR time velocity integral [TVI]) with the regurgitant volume (Rvol) measured by cardiac MRI. They showed a strong correlation between the two values ($r=0.94$).

They also demonstrated that the 2D methods (EROA derived from an apical 4-chamber view, or EROA derived from an elliptical shape assumption) underestimated the EROA and regurgitant volume when compared with 3D EROA and cardiac MRI, respectively. In another recent study, Shanks et al[29] found that regurgitant volume derived from 3D transesophageal echocardiography (TEE) VC area was underestimated by only 1.2% compared to cardiac MRI. They also showed that both 2D PISA-derived EROA and Rvol were both underestimated by 0.13 cm^2 and 21.6%, respectively, when compared to 3D EROA and 3D-derived regurgitant volume. A more recent study by Marsan et al[34] also demonstrated that mitral regurgitant volume measured by real-time 3D echocardiography revealed a strong correlation (r=0.93) with regurgitant volume measured by cardiac MRI.

Studies using the ASE guidelines integrated method as a reference standard

The approach recommended by the ASE guidelines[7] for mitral regurgitation grading is the one most commonly employed and uses color Doppler criteria combined with supportive data. Zeng et al[30] reported that 3D-VC area correlated strongly with this ASE-recommended 2D integrative method. They also demonstrated that the 2D PISA method underestimates the EROA, especially in cases with functional MR. This is the first study that provided a cutoff value by direct planimetry of VC area. A cutoff point of 0.41 cm^2 can differentiate moderate from severe MR with a sensitivity of 97% and a specificity of 82%. Moreover, 31.3% of patients would have been upgraded to a more severe grade if the 3D-VC area was used compared with the measured 2D ROA. The latter was more obvious in patients with functional MR.

All these studies of 3D-VC area have demonstrated the utility, accuracy and reproducibility of the novel 3D method; however, one of the most challenging tasks for a clinician is to quantify MR severity when multiple regurgitant jets are present. Hyodo et al[24] demonstrated that summation of 3D-VC areas is an accurate technique for grading MR in patients with multiple regurgitant jets and functional MR. They measured the sum of the 3D-VC areas, the sum of 2D-VC widths, and the EROAstd, which is the EROA assessed by the formula EROAstd = [(3D LV end-diastolic volume - 3D LV end-systolic volume) - stroke $volume_{thermodilution}$] / TVI_{MRjet}, as the reference method. The authors concluded that there is a good correlation (r=0.90) between the summation of 3D-VC areas and the EROAstd. This strong correlation continued to hold even in patients with 3 distinct MR jets (r=0.91). This study was the first of its kind, and adds value to the already existing evidence for the usefulness of 3D-VC area in even the most difficult situations with multiple regurgitant MR jets.

Image acquisition and measurement for VC area

Before starting the TTE or TEE study in our practice, we first obtain an excellent quality electrocardiogram tracing. Usually, parasternal or apical views have been used in most studies with 3D TTE imaging, while either a four-chamber or a long-axis view are used with the 3D TEE approach. The acquisition sector angle, the color sector size and the imaging depth should be adjusted to increase the temporal resolution, including the flow convergence zone, the VC, and at least a proximal part of the regurgitant jet. Of course stitching sub-volumes can maximize the frame rate. Tissue gain settings and color gain are kept in the same ranges as in 2D color imaging. Just before acquisition, an end-expiratory breath hold is requested of the patient to eliminate potential stitching artifacts from chest wall motion. Three dimensional color Doppler acquisitions are performed to optimize the volume imaging rate (temporal resolution); however, single heartbeat or multiple beat protocols are used, depending on heart rhythm regularity.

Once the 3D color Doppler data have been acquired, images can be cropped to depict two long-axis views of the jet (Figure 2). Recently, image acquisition and display using 3D echocardiography[35] recommend one with the narrowest and one with the broadest jet width to identify the true cross-sectional area of the jet. The translation of the plane orthogonal to the regurgitant jet axis will facilitate the visualization of the *en face* view of the VC area. Different systolic frames are examined to find the most suitable frame for measurement (the one with the largest area). Finally, the VC area is manually traced. The procedure to identify and measure the 3D-VC area is simple, relatively quick to perform (3.5 ± 1.5 min),[26] and has been shown to be highly reproducible[24-27,29,30,32-34] when specific protocols and training are provided.

Benefits of the 3D-VC area

The above studies have confirmed that 3D-VC area assessment is not only feasible and fairly rapid, but

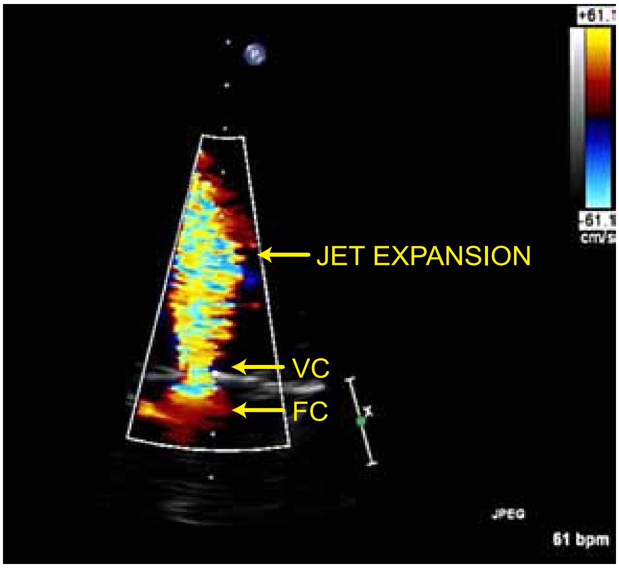

Figure 1. The mitral regurgitation (MR) jet is composed of 1) the flow convergence region (FC) proximal to the anatomic regurgitant orifice, 2) the *vena contracta* (VC) where the jet width is smallest, and 3) the downstream expansion of the MR jet.

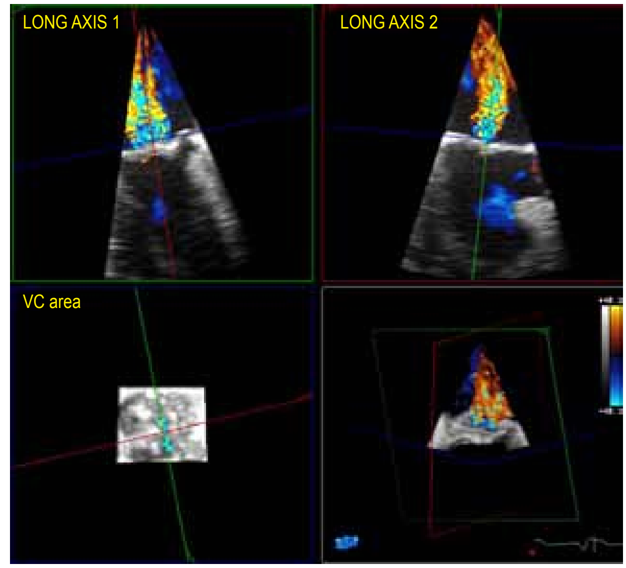

Figure 2. A three-step cropping approach. Step 1: Rotation and cropping of the volumetric color Doppler dataset to bisect the long axis of the regurgitant jet in 2 orthogonal planes (green and red plane). Step 2: Translation of the blue plane orthogonal to the regurgitant jet axis will facilitate the visualization of the *en face* view of the *vena contracta* (VC) area. Step 3: The VC area is traced manually.

also widely accessible. It is an accurate method of estimating the regurgitant EROA and correlates well with cardiac MRI, 2D Doppler methods, and left ventriculography. One of the greatest benefits of the method is that 3D-VC area assessment is not dependent on any flow or geometric assumptions. Direct measurement has revealed asymmetry of VC area, especially in cases with functional MR.[25] It has been shown to be applicable either in cases of eccentric MR jets or in cases with multiple regurgitant orifices.[24,25,27] The measurement techniques are vendor-independent, as the cropped VC cross-sectional area can be formatted and measured using various software workstations developed by manufacturers. From the published literature it is clear that the direct measurement of 3D-VC area is a useful new tool. Importantly, cutoff points to differentiate moderate from severe MR have been determined.[30]

Limitations of 3D-VC area

Although the published experience with 3D-VC area determination is promising, like all single measurement tools it remains imperfect. One of the main limitations of 3D echocardiography is the poor temporal resolution.[35] Manufacturers have tried to solve this limitation by developing multiple beat 3D echocardiography, stitching together multiple acquisitions of narrow volumetric data to reconstruct one volumetric set with improved temporal resolution. However, stitch artifacts can affect image quality, especially in sub-volumes acquired in cases of arrhythmias, patient respiration and motion, or probe motion during the procedure. Adjusting the imaging volume using smaller sector angle images, a shallower depth and a low line density can help to increase the frame rate.

The 3D-VC area technique also has limited spatial resolution.[35] This was more prominent in the assessment of small regurgitant orifices (mild MR).[26,30] Increasing the line density, adjusting the depth and the focal zone, will also improve the lateral resolution. The acquired 3D color Doppler data are usually processed using multiplanar reformatting of the regurgitant jet by software that enables a user to rapidly identify the 3D-VC area. Inappropriate cropping might lead to overestimation of the regurgitant orifice, especially in cases with eccentric jets.[30] After the VC area has been identified, interobserver variability can be noted, depending on which systolic frame was used for 3D color regurgitant orifice assessment, and the true VC might be missed, leading to over- or underestimation of the EROA.

Finally, technical settings have not been standardized between different studies. As in 2D color Dop-

Table 1. Three-dimensional *vena contracta* area studies for mitral valve regurgitation.

First Author	Year	Study type	Method compared	Reference Standard	Correlation (r)	Results
Khanna et al.[31]	2004	44 patients with at least mild MR	3D-VC area	Left ventriculography grade I-III	r=0.88	3D-VC area strongly correlated with angiographic grading
Iwakura et al.[32]	2006	106 patients with at least moderate isolated MR	3D-VC area	Orifice area by quantitative Doppler method,	r=0.91	3D-VC area strongly correlated with quantitative Doppler method
				PISA EROA	r=0.93	Strong correlation between PISA EROA and 3DVC area
Kahlert et al.[25]	2008	57 patients with mild to severe MR of different etiologies	3D-VC area	Hemispheric 2D PISA EROA Hemielliptic 2D PISA EROA 2D calculated VC area (4CH, 2CH)	r=0.93 r=0.96 r=0.78	3D-VC area strongly correlated with 2D PISA EROA-HS 3D-VC area strongly correlated with 2D PISA EROA-He Moderate correlation between 3D-VC area and 2D-VC area
Little et al.[26]	2008	61 patients with at least mild MR	3D-VC area	Doppler derived EROA	r=0.85	3D-VC area had a strong correlation with Doppler derived EROA, particularly in patients with moderate to severe MR
		in vitro: 4 different shape orifices	3D-VC area	Geometric orifice area	r=0.92	3D-VC area strongly correlated with known orifice area
Yosefy et al.[27]	2009	45 patients with mild or greater MR	3D-VC area	EROA by 2D volumetric method	r^2=0.86	3D-VC area strongly correlated well with Doppler derived EROA
Marsan et al.[28]	2009	64 patients with mild to severe functional MR	3D-VC area derived Rvol 3D-VC area	Rvol by cardiac MRI 2D EROA 4CH Rvol 2D EROA 4CH, elliptical	r=0.94	Strong correlation between the two techniques, 2D 4CH approach Rvol underestimated Rvol by cardiac MRI Underestimation of EROA by 2D approach
Shanks et al.[29]	2010	30 patients with MR	3D-VC area derived Rvol	Cardiac MRI Rvol		3D TEE underestimated Rvol by 1.2% compared to MRI
			3D-VC area	2D PISA EROA		2D TEE underestimated EROA by 0.13 cm^2
			2D PISA Rvol	VC area derived Rvol		2D TEE underestimated Rvol by 21.6 % compared to 3DTEE
Marsan et al.[34]	2011	52 patients with MR	3D-VC area derived Rvol	Cardiac MRI Rvol	r=0.93	Strong correlation between the two methods
Altioc et al.[33]	2011	72 patients with mild to severe MR	Anatomic ROA	2D PISA EROA 2D-VC area	r=0.96 r=0.89	AROA strongly correlated with 2D PISA EROA AROA strongly correlated with 2D-VC area
Zeng et al.[30]	2011	83 patients with at least mild MR	3D-VC area	2D ROA (integrated approach)	r=0.88	Underestimation of 2D ROA in functional MR patients by 27 % Strong correlation between methods, cut off value of 0.41 cm^2 to differentiate moderate from severe MR
Hyodo et al.[24]	2012	60 patients with multiple functional MR jets	sum of 3D-VC areas	EROA std	r=0.90	Strong correlation between 3D-VC area and EROA std

pler imaging, it is important to recognize that adjustment of color gain settings, wall filter, depth, Doppler frequency, sector size, frame rate, tissue gain, write priority algorithm and different commercial analysis software can lead to errors in accurately defining the 3D-VC area.

Future perspectives

Currently, many laboratories perform focused 3D echocardiography studies in daily practice.[36] Advances in 3D echocardiography color Doppler acquisition are expected to improve the currently limited temporal and spatial resolution. Different imaging ultrasound vendors will develop new commercial software with automated display of cut planes providing rapid and accurate assessments. To date, the studies reported have used different ultrasound machines and various software analysis programs, without standardizing 3D Doppler acquisition. It is now clear that a widely available technical settings algorithm for the measurement of VC area should be proposed to all manufacturers of echocardiography machines.

Conclusions

The 3D-VC area represents the effective regurgitant orifice of an MR lesion and provides a reproducible assessment of MR severity. In addition, the area measurement can be multiplied by the MR TVI to estimate regurgitant flow volume. Although 3D-VC area measurement is feasible, as a multitude of clinical studies over the last several years have validated the accuracy and utility of the method, its use is limited in widespread clinical practice. Continued advances in 2D and 3D ultrasound technology should eliminate many of the current limitations (especially 3D spatial and temporal resolution). Ongoing efforts by imaging researchers and clinicians alike will determine the role of 3D-VC area measurement; however, this novel parameter will almost certainly be included in the next iteration of the echocardiographic guidelines for the quantification of MR severity.

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