Original Article

Intraoperative Comparison of 2D versus 3D Transesophageal Echocardiography for Quantitative Assessment of Mitral Regurgitation

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ABSTRACT

Background: Effective regurgitant orifice area (EROA) can be represented by 3D echocardiographic vena contracta cross-sectional area (3D-VCA) as a reference method for the quantification of mitral regurgitation (MR) without making any geometrical assumptions. EROA can also be derived from 3D PISA technique with a hemispherical (HS) or hemielliptical (HE) assumption of the proximal flow convergence. However, it is not clear whether HS-PISA and HE-PISA has better agreement with 3D-VCA.

Aims: This study was conducted to compare the EROA and Rvol obtained from 3D-VCA with those obtained from 2D-VC, 2D-HS-PISA, 3D-HS-PISA, and 3D-HE-PISA.

Setting: Tertiary care hospital.

Design: Prospective observational study.

Materials and Methods: After anesthesia induction, 43 consecutive patients were evaluated with RT-3D-TEE after acquiring images from midesophegeal views and performing the offline analysis of volume dataset. 3D-VCA was measured using multiplanar reconstruction mode and EROA and regurgitant volume were estimated using HS-PISA and HE-PISA methods. The HE-PISA was calculated by using the Knud Thomsen formula.

Statistical Analysis: Agreement between methods to estimate EROA and regurgitant volumes were tested using Bland–Altman analysis. The interobserver variability and intraobserver variability were assessed using an intraclass correlation coefficient.

Results: The EROA estimated by 3D-VCA was larger than EROA obtained by 2D-HS-PISA and 3D-HS-PISA, which were significantly greater than 3D-HE-PISA. 3D-HS-PISA-EROA showed the best agreement with 3D-VCA (bias: 0.21; limits of agreement: 0.01 to 0.41; SD: 0.1). Correlation between various methods as compared to 3D-VCA was better in the organic MR group than functional MR group.

Conclusion: 3D-HS-PISA showed the best agreement with 3D-VCA compared to other PISA methods. Better correlation between PISA-EROA and 3D-VCA was observed in patients with organic MR than functional MR.

Keywords: 3D echocardiography, mitral regurgitation, proximal isovelocity surface area, transesophageal echocardiography

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INTRODUCTION

The flow convergence or proximal isovelocity surface area (PISA) method has been recommended for grading the severity of mitral regurgitation (MR).[1,2] Vena contracta width (VCW), which is the narrowest portion of the regurgitant color Doppler jet is considered as one of the quantitative parameters for the assessment of severity of MR.[3,4] However, the assumption of circular geometry of the regurgitant orifice is required for the 2D-VCW measurement. The EROA can be represented by the 3D echocardiographic vena contracta cross-sectional area (3D-VCA) without making any geometrical assumptions. The utility of VCA and MR regurgitant volume (Rvol) derived from 3DE in predicting the severity of MR has been validated against left ventricular angiography,[5] 2D volumetric Doppler methods,[6] and cardiac MRI.[7] The American society of Echocardiography (ASE) recommends integration of qualitative, semi-quantitative, and quantitative methods for the estimation of MR severity.[8] Although no parameter has been accredited as the true gold standard for the quantification of MR, some authors have recommended 3D-VCA as the reference parameter for the same purpose.[5] It is presumed that the hemispherical (HS) contour of the proximal flow convergence gives the best estimate of the EROA. However, Yosefy *et al*.[9] using real-time 3D echocardiography (RT-3DE) showed that a significant number of patients with MR predominantly have a hemielliptical (HE) contour of proximal flow convergence rather than the HS contour and suggested that the HE-PISA assumption is more appropriate for the quantification of MR. Therefore, we conducted this study to compare the EROA and Rvol obtained from 3D-VCA with those obtained from 2D-VC, 2D-HS-PISA, 3D-HS-PISA, and 3D-HE-PISA.

MATERIALS AND METHODS

This prospective, observational study was conducted in a tertiary referral center and a university-level hospital annually performing more than 1500 adult cardiac surgeries from January to October 2017. After obtaining the approval from the Institutional Ethics Committee and informed consent from patients, a total of 43 consecutive patients meeting the inclusion criteria were recruited as study subjects. We hypothesized that the EROA obtained from transesophageal (TEE) RT-3D color Doppler methods would be more accurate than the 2D-TEE color Doppler methods. The primary study objectives were to compare the EROA and Rvol obtained by 3D-VC with those obtained by 2D-VCW, 2D-HS-PISA, 3D-HS-PISA, and 3D-HE-PISA methods. The secondary objectives were to assess the shape of the regurgitant orifice in different pathologies associated with MR and to evaluate the intraobserver and interobserver variability in MR quantification. To achieve 80% study power, to detect a small difference with an effect size of 0.5 and alpha error of 0.025, the minimum sample size estimated was 38 patients. A total of 61 consecutive adult patients who underwent cardiac surgery and had at least mild MR and underlying sinus rhythm were recruited for the study. Exclusion criteria were those with eccentric MR, multiple jets, previous mitral valve surgery, cleft mitral valve, infective endocarditis, significant mitral stenosis (area <1.5 cm^2), more than mild aortic valve stenosis or regurgitation, arrhythmias, and myocardial infarction 6 weeks prior to the surgery. Emergency or redo surgeries, esophagogastric pathologies, poor quality 2DE, or 3DE images and surgeries wherein TEE probe placement was contraindicated were also treated as exclusion criteria. A total of 43 patients were finally included as study subjects after the exclusion of 18 patients due to various reasons.

After anesthesia induction and establishment of standard monitoring, the trachea was intubated and artificial ventilation was instituted. An adult-size RT-3D-TEE probe was inserted and heart was examined using an ultrasound system (iE 33, Philips Ultrasound, Bothell, USA). All echocardiographic examinations were performed before establishment of cardiopulmonary bypass (CPB). The hemodynamic parameters were maintained close to the preoperative levels at the time of acquisition of images. The images necessary for assessment of MR were acquired from midesophegeal views and 3DE analysis was performed later using offline Qlab 3DQ software.

All echocardiographic examinations and data acquisition were performed by echocardiographers trained in RT-3D-TEE. The 2D and 3D vena contracta were acquired from a zoom mode in the midesophageal long axis (MELAX) view with the central beam passing through the leaflet tips at a Nyquist limit of 50 to 60 cm/sec. The color flow sector was made as small as possible to maximize lateral and temporal resolution. The VCW was defined as the narrowest width of the proximal jet measured at or in the immediate vicinity of the MR orifice at the leaflet tips. The severity of MR using VCW was graded as mild (<0.3 cm), moderate (0.3 to 0.69 cm), or severe (>0.7 cm). The EROA was calculated by the formula $2\pi r^2$ and the mitral regurgitant volume (MR-Rvol) by multiplying EROA with MR-VTI. Using MR-Rvol, the severity of MR was graded as mild (<30 ml), mild-to-moderate (30 to 44 ml), moderate-to-severe (45 to 59 ml), and severe (≥60 ml). The proximal flow convergence was acquired in the zoom mode at MELAX view with the baseline shift of the Nyquist limit (30–

40 cm/s) in the direction of MR. The sector width and depth were initially reduced to increase the resolution. Also the color Doppler box size was reduced that would include all the three components of the regurgitant jet [Figure 1a].

The EROA was calculated using the formula EROA = $2\pi \times r^2 \times$ Va/Vmax, where r represents the maximal PISA radius; Va, the aliasing velocity of the proximal flow convergence (same as Nyquist limit) and Vmax, the maximal velocity of continuous wave Doppler MR signal. The maximum radius was measured from the tip of the leaflets to the point of first color aliasing. MR-Rvol was calculated as (EROA × MR-VTI). A 3D color full-volume of MR jet was obtained from the MELAX view over 7 beats using ECG-gating by adjusting the Nyquist limit at 50 to 60 cm/s. Two orthogonal image planes parallel to the regurgitant jet direction were manually aligned across the regurgitant jet; a third cropping plane was placed perpendicular to the jet direction and then moved along the jet direction until the cross-sectional area at the level of the vena contracta was visualized. The frame with the largest VCA in systole was magnified and VCA was measured by direct planimetry of the color Doppler flow signal [Figure 1b]. The shape of EROA was also observed and labelled as circular, elliptical, or crescentic. In the full-volume 3D color dataset, the proximal flow convergence was acquired with the baseline shift of the Nyquist limit (30–40 cm/s) to optimize the visualization of flow convergence. The 3D volume data was presented in 4 quadrants using MPR mode, which included three 2DE orthogonal anatomic planes. The imaging planes were adjusted to get the best possible PISA shell. The 3D-HS-PISA was acquired from the displayed view by measuring the radius of the first aliasing velocity with the Nyquist limit adjusted off-line to 30 to 40 cm/s and using the formula: PISA = $2\pi r^2$. For HE-3D-PISA radius, r was measured as in the method of HS PISA. The blue cropping plane was now aligned perpendicular to regurgitant jet and advanced towards the mitral valve till it cut the PISA shell at its maximum diameter in a plane perpendicular to radius. The two diameters D1 (PISA width) in MELAX plane and D2 (PISA diameter) in the corresponding orthogonal mid commissural view were measured [Figure 1c]. The 3D-HE-PISA was then calculated from these three orthogonal parameters according to Knud Thomsen's formula.[10,11]

HE PISA = 2π ([rp (d1/2)p + rp (d2/2)p + (d1/2) p (d2/2) p]/3)1/p

Where p = 1.6075. The formula was incorporated in Microsoft excel sheet for calculations and values for r, D1 and D2 were entered manually.

During statistical analysis, categorical data was expressed as percentage (number of observations). The statistical mean and standard deviation were calculated for quantitative data and expressed as mean ± SD. Differences between the groups were analysed with the paired *t*-test. Pearson's correlation coefficient was used for all correlation evaluations. The r value of 0 to 0.35, 0.36 to 0.55, and more than 0.55 were considered as poor/weak correlation, good correlation, and significant correlation, respectively. A positive r-value denoted direct correlation whereas a negative value signified inverse correlation. The agreement between the methods to calculate EROA and MR Rvol were tested using Bland–Altman analysis and plotted with lines representing mean ± 1.96SD. The interobserver variability and intraobserver variability was performed using intraclass correlation coefficient (ICC) and expressed as ICC value, 95% limits of agreement. The percentage of underestimation of EROA by different methods compared to 3D-VC-EROA was calculated by ratio of difference between the two methods divided by 3D-VC-EROA ×100.

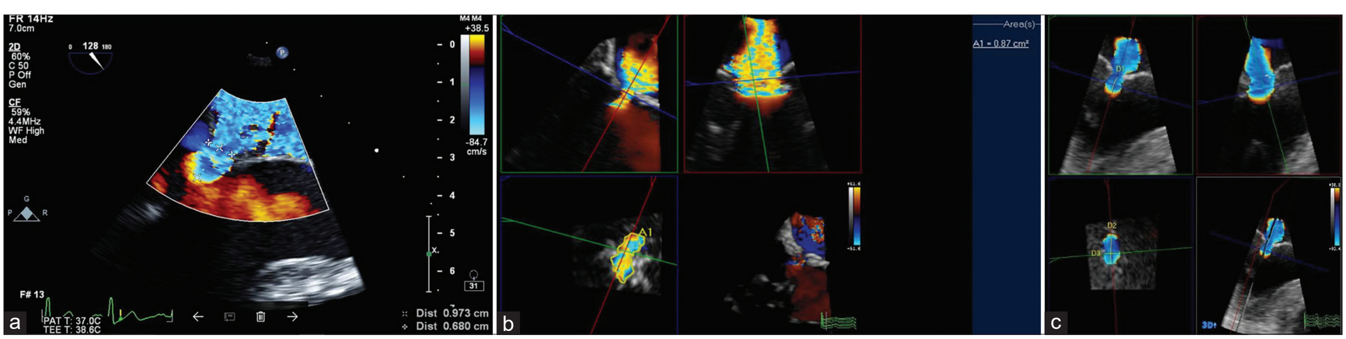

Figure 1: Four methods of measurement of EROA are shown in the figure. (a) Shows 2D-HS-PISA radius measured in midesophageal long axis view using zoom mode (b) Method to measure 3D-VCA from 3D color full volume dataset. The blue window displays enface view of vena contracta which is directly traced to measure its area. (c) Methods of 3D-HS-PISA and 3D-HE-PISA measurements: The diameters D2 and D3 of the PISA shell were measured in the blue window. Abbreviations: - PISA: Proximal isovelocity surface area. MR: Mitral regurgitation; 3D-VCA: 3D vena contracta area; HS: Hemispherical; HE: Hemielliptical

The *P* value of ≤0.05 was considered to be significant for all analyses. Receiver operating curve was used to analyze the value of echocardiographic parameters for grading severe MR. The value having optimal sensitivity and specificity was taken as the cut-off value. Statistical analysis was performed using the SPSS software version 22 and Graph pad prism 5.2.

RESULTS

Sixty one consecutive patients posted for elective cardiac surgery having at least mild MR were enrolled in the study. During the intraoperative period, patients with eccentric MR jets (n = 11), atrial fibrillation (n = 3), infective endocarditis (n = 2), and poor quality echocardiographic images (n = 2) were excluded from the study as per the protocol. About 43 patients satisfied the inclusion criteria. The mean age of the study population was 55.27 ± 15.08 years. More number of patients had functional MR (n = 34) compared to organic etiology (n = 9) as only those with central regurgitant jet were considered. The majority of the patients had elliptical geometry of regurgitant orifice, whereas a crescentic shape was more common in the functional group than the organic group. The demographic features, echocardiographic parameters, and shape of the 3D-VCA in all patients are summarized in Table 1.

Table 1: Demographic profiles and preoperative echocardiographic parameters of patients. Majority of patients had functional MR

Total number of patients		*n*=43
Age (years)		55.27±15.08
Sex		
Male		36 (83.72%)
Female		7 (16.27%)
Height (cm)		161.48±7.63
Weight (kg)		61.11±11.20
BSA (m²)		1.65±0.18
Diagnosis		
CAD		34 (79.06%)
Rh. MV		7 (16.27%)
Prolapse MV		2 (4.65%)
	Shape of VCA by 3DE	
Circular *n* (%)	Elliptical *n* (%)	Crescentic *n* (%)
1 (2.94)	27 (79.41)	6 (17.64)
1 (11.11)	7 (77.77)	1 (11.11)
2 (4.65)	34 (79.06)	7 (16.27)
Etiology of MR		
Functional		34 (79.06%)
Organic		9 (20.93%)
Total		43
Echocardiographic parameters		
LVIDD (mm)		52.51±10.69
LVIDS (mm)		37.13±10.37
LVEF (%)		53.81±12.23
LA diameter (mm)		41.39±8.15

The incidence of MR in operated patients was more among men. CAD: Coronary artery disease; Rh. MV: Rheumatic mitral valve; VCA: Vena contracta area; 3DE: 3D echocardiography; LVIDD: Left ventricular internal diameter during diastole; LVIDS: Left ventricular internal diameter during systole; LVEF: Left ventricular ejection fraction; LA: Left atrium

The mean 2D-VCW of the MR jet was 0.335 cm ± 0.0416 cm. A comparison of 2D-VCW and 3D-VCA showed a significant correlation (r = 0.69, P < 0.0001). In the subgroup analysis, the correlation value was better in organic etiology (r = 0.81) compared to functional etiology (r = 0.66). The EROA was calculated by three methods of PISA, namely 2D-HS-PISA, 3D-HS-PISA, and 3D-HE-PISA. The 3D-HS-PISA was larger than 2D-HS-PISA, but the difference was not significant. Both 2D-HS-PISA and 3D-HS-PISA were significantly larger than 3D-HE-PISA (mean ± SD: 1.88 ± 1.1 cm² vs 1.32±0.79 cm² and 1.97 ± 1.23 cm² vs 1.32 ± 0.79 cm²; both P < 0.001), respectively. All the three PISA methods showed significant positive correlation with each other. In the subgroup analysis, although 2D-HS-PISA correlated well with 3D-HE-PISA in both groups, the correlation in organic MR group (r = 0.97) was better than in functional MR group (r = 0.80).

The EROA estimated by 3D-VCA (0.40 ± 0.13 cm²) was larger than the EROA obtained by 2D-VC (0.09 ± 0.02 cm²), 2D-HS-PISA (0.18 ± 0.10 cm²), 3D-HS-PISA (0.19 ± 0.12 cm²), and 3D-HE-PISA (0.12 ± 0.07 cm²). The paired difference between 3D-VC-EROA and EROA obtained by all other methods was statistically significant [Table 2]. The paired differences among the 3D-VC and 2D-VC, 2D-HS-PISA, 3D-HS-PISA, and 3D-HE-PISA were 0.31 ± 0.12, 0.22 ± 0.10, 0.21 ± 0.10, and 0.27 ± 0.09, respectively. There was a significant positive correlation among the paired comparison of different methods. The EROA obtained by 3D-VC method was compared with all other methods and the limits of agreement were plotted. Considering the 3D-VCA as the reference method, all other methods underestimated EROA; however, 3D-HS-PISA-EROA showed the best agreement (bias: 0.21; limits of agreement: −0.01 to 0.41; SD: 0.1). In the subgroup analysis, the correlation between various methods as compared to 3D-VCA was better in the organic MR group than functional MR. Maximum Rvol was seen with 3D-VC-Rvol (mean ± SD 55.86 ± 20.80) and paired difference with all other methods was statistically significant (P < 0.001). All methods showed good correlation with 3D-VC-Rvol [Table 2]. The grade of MR differed when estimated using EROA and Rvol by 3D-VC, 2D-HS-PISA, and 3D-HS-PISA methods. The severity of MR was high when estimated with 3D-VC-EROA and 3D-VC-Rvol parameters. The other methods underestimated the severity grading of MR in comparison with the 3D-VC-EROA and 3D-VC-Rvol [Table 3]. The EROA and Rvol derived from 2D-VC and 3D-HE-PISA showed maximum underestimation of severity grading compared to that from the 3D-VC.

The Bland–Altman plot analysis was performed for the EROA and Rvol obtained by 3D-VC and other methods. All methods underestimated EROA compared to 3D-VC EROA and 3D-HS-PISA EROA which showed the best agreement among the methods used (bias: 0.21; limits of agreement: −0.01 to 0.41; SD: 0.1). Similarly, all methods underestimated Rvol compared to 3D-VC Rvol. The 3D-HS-Rvol showed the best agreement with the 3D-VC-Rvol among the methods used (bias: 29.36; limits of agreement: 0.70 to 58.30) [Figure 2]. As the 2D-VC and 2D-HS-PISA severely underestimated MR, the ROC analysis was performed to find the best cut-off value for severe MR by these methods, which were obtained after selecting the optimal values for sensitivity and specificity. At a sensitivity of 87% and specificity of 59.3%, a value of 2D-VCW of >0.325 cm predicts severe MR. A 2D-HS-PISA-EROA value of >0.149 cm^2 is associated with a sensitivity of 75.0% and specificity of 74.1% that predicts severe MR. A 2D-HS-PISA Rvol value of >21.32 ml predicts severe MR when the sensitivity and specificity are 66.7% and 64.0%, respectively [Figure 3].

The intraobserver and interobserver variability values for different methods used to calculate EROA are mentioned in Table 4. Excellent reliability was found for all methods between two analyses of a single-observer and also between the observers.

DISCUSSION

Quantitative parameters are considered as important criteria to determine the severity of regurgitant lesions. Although, the published literature is inadequate to validate any parameter as a gold-standard for the echocardiographic estimation of EROA, the 3D-VCA may be considered a reference method for the same purpose.[12] Khanna *et al.*[5] showed that 3D-VCA correlates well with ventricular angiographic grading (coefficient $r = 0.88$) and is a feasible method for MR assessment. Excellent correlation between

Table 2: Paired comparison of EROA and Rvol obtained by four methods with that of 3D-VCA: The paired difference between 3D-VC-EROA and EROA obtained by other methods and 3D-VCA-Rvol and Rvol obtained by other methods is significant

Paired comparison	Parameter	Paired difference		*P*	Correlation	
		Mean	STDEV		*r*	*P*
3D-VCA & 2D-VC	EROA (cm^2)	0.31	± 0.12	<0.001	0.713	<0.001
	Rvol (ml)	43.22	± 17.91	<0.001	0.767	<0.001
3D-VCA & 2D-HS-PISA	EROA (cm^2)	0.22	± 0.10	<0.001	0. 676	<0.001
	Rvol (ml)	30.67	± 14.75	<0.001	0.706	<0.001
3D-VCA & 3D-HS-PISA	EROA (cm^2)	0.21	± 0.10	<0.001	0.687	<0.001
	Rvol (ml)	29.36	± 14.62	<0.001	0.720	<0.001
3D-VCA & 3D-HE-PISA	EROA (cm^2)	0.27	± 0.09	<0.001	0.772	<0.001
	Rvol (ml)	38.73	± 14.00	<0.001	0.796	<0.001

There is a significant positive correlation among paired comparison of different methods of EROA and methods of Rvol. STDEV: Standard deviation; 3D: Three dimensional; VCA: Vena contracta area; 2D: Two dimensional; HS: Hemispherical; PISA: Proximal isovelocity surface area; HE: Hemielliptical; EROA: Effective regurgitant orifice area; Rvol: Regurgitant volume

Table 3: Regurgitant volume derived by five different methods: On comparing EROA obtained by four methods with 3D-VC, the 2D-VC and 3D-HE-PISA methods show maximum underestimation

EROA & Rvol methods (*n*=43)	Rvol (ml)	Percent underestimation of EROA by other methods compared with EROA from 3D-VC			MR severity grading				
		Mean (%) STDEV		*P*	Parameter	M	M-M	M-S	S
		Organic MR (*n*=9)	Functional MR (*n*=34)						
3D-VC	55.86±20.80				EROA	0	8	19	16
					Rvol	2	9	14	18
2D-VC	12.64±4.02	79.8±5.7	75.5±5.4	0.042	EROA	43	0	0	0
					Rvol	43	0	0	0
2D-HS-PISA	25.19±15.41	38.0±21.5	60.0±13.5	0.004	EROA	30	7	5	1
					Rvol	30	9	2	2
3D-HS-PISA	26.50±17.31	36.7±21.7	57.4±16.5	0.003	EROA	29	7	6	1
					Rvol	29	9	3	2
3D-HE-PISA	17.13±10-45	60.6±10.8	72.2±7.9	0.001	EROA	39	4	0	1
					Rvol	39	4	0	1

The severity grading of MR based on the EROA and Rvol obtained by all the five methods shows that the grade of MR in the other four methods is underestimated compared with 3D-VC-EROA and 3D-VC-Rvol. EROA: Effective regurgitant orifice area; Rvol: Regurgitant volume; MR: Mitral regurgitation; STDEV: Standard deviation; M: mild; M-M: Mild-to-moderate; M-S: Moderate-to-severe; S: Severe

Table 4: Table shows intraobserver and interobserver variability values for different methods used to calculate EROA. Excellent reliability was found for all methods between two analyses of a single-observer and also between the observers

Method	Intraobserver variability		Interobserver variability	
	ICC	95% confidence interval	ICC	95% confidence interval
2D-VCW	0.96	0.93-0.98	0.92	0.88-0.96
2D-HS-PISA-EROA	0.94	0.90-0.96	0.93	0.90-0.96
3D-HS-PISA-EROA	0.96	0.92-0.99	0.95	0.92-0.98
3D-HE-PISA-EROA	0.93	0.91-0.95	0.91	0.86-0.96
3D-VC-EROA	0.94	0.92-0.96	0.92	0.88-0.96

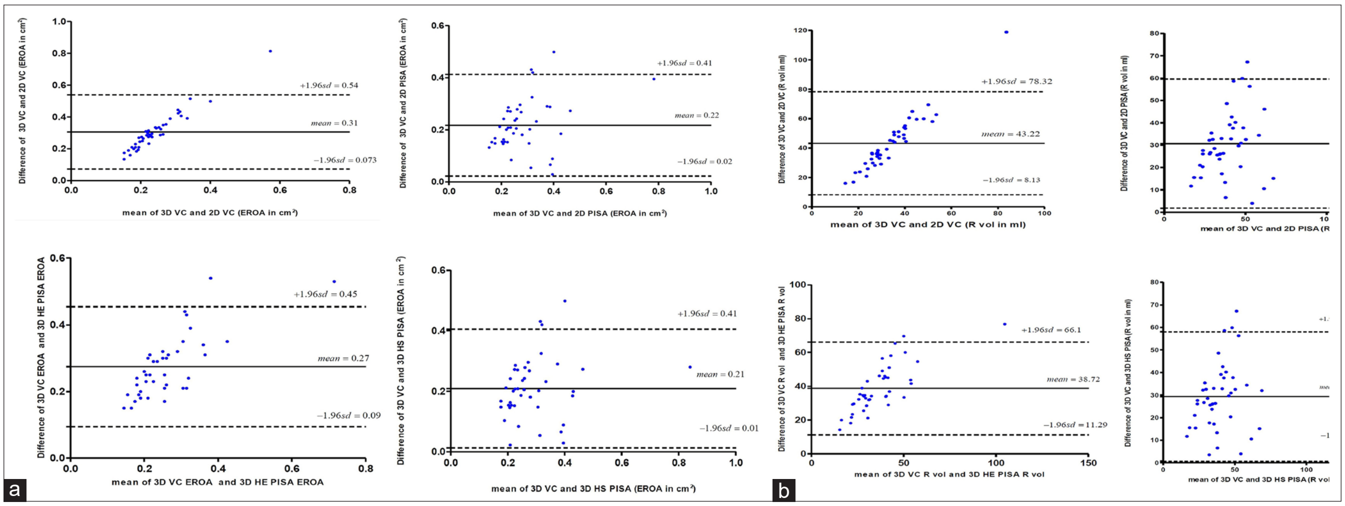

Figure 2: Bland–Altman plot analysis of EROA (a) and Rvol (b) obtained by 3D-VC and other methods: (a) Difference in the paired EROA is plotted on the ordinate against mean EROA on abscissa. (b) Difference in the paired-Rvol is plotted on the ordinate against mean-Rvol on abscissa. The observed mean difference is displayed as a continuous black line and the limits of agreement are displayed as dashed black lines. All methods underestimated EROA and Rvol compared to 3D-VC EROA. 3D-HS EROA showed the best agreement among the methods used

	Cut-off	AUC(95% CI))	Sensitivity %	Specificity %	Asymptomatic 95% Confidence interval Lower bound	Upper bound
VCW	≥0.325	0.802 (0.736-0.868)	87	59.3	.673	.932
2D PISA EROA	≥0.149	0.814 (0.744-0.884)	75	74.1	.676	.952
2D PISA Rvol	≥21.32	0.753 (0.676-0.831)	66.7	64	.609	.897

Figure 3: The cut-off values for severe MR using 2D echocardiographic parameters from ROC analysis. Considering 3D VCA as gold standard cut off values for 2D-VCW, 2D-PISA-EROA and 2D-PISA-Rvol were significantly low

the 3D-VCA and quantitative 2D Doppler parameters was demonstrated by others.[6,13] Grading the MR is reliable with 3D-VCA, which distinguishes moderate from severe MR for all etiologies. It remains accurate to represent the EROA in the presence of central as well as eccentric jets and also in the presence of multiple jets,[14,15] and agrees with the parameters obtained by 3D ventricular volumes and thermodilution data. MR volume estimated using 3D-TEE was found to have excellent correlation with CMR volume[7] with a marginal underestimation by 1.2%. In a similar study, Marsan *et al.*[16] reported the correlation between the CMR-MR volume and 3D-VCA-derived MR volume with an insignificant difference of 0.08 ml/beat.

The regurgitant orifice is often inadequately visualized on 2DE and planimetric measurement of orifice area is rarely possible. The 2D-VCW, which is regarded a simple and quick surrogate parameter for the EROA, has precision only for the circular regurgitant orifice. As the vena contracta is always a three dimensional structure having a variable length and width, the MR quantification using VCW is erroneous in the presence of elliptical or crescentic shape of regurgitant orifice. In our study, we found that VCW significantly underestimated the EROA. The circular shape of the regurgitant orifice was observed only in 4.65% of our patients. The elliptical shape of the regurgitant orifice was common in patients with organic etiology, whereas the crescentic shape was seen more commonly in the functional subgroup. In subgroup analysis, the correlation between 3D-VCA and 2D-VCW was found better in the MR of organic etiology compared to the functional etiology which is consistent with other studies.[17] Since our study was confined to the central jets, we observed a strong correlation between the 2D-VCW and 3D-VCA in the organic group.

Grading the severity of MR using PISA method shows excellent correlation with angiographic methods.[18] The concept of flow convergence is based on the assumption that the base of the hemisphere is planar and there is no constraining to the flow. This method may not be accurate for eccentric jets where the flow field is restricted.[19] The EROA and Rvol estimated using PISA technique were shown to have a significant agreement with the data derived from the thermodilution technique only for central jets. Significant overestimation was seen in eccentric jets which were mostly due to flail leaflets.[20] All patients in our study had central jets.

The hemispheric assumption holds true only if the ERO geometry remains circular. However, the ERO is rarely circular and may vary in shape from elliptical (most common) to crescentic or irregular. Therefore, the hemispheric PISA assumption especially in cases of functional MR, where the regurgitant orifice elongates along the mitral valve leaflet coaptation line, may lead to a discrepancy between estimated EROA and the actual area. Previous studies have shown that the EROA estimated by both HS-PISA and HE-PISA methods correlate well with 3D-VCA; however, which method has a better agreement with the 3D-VCA is still not established. The eccentricity of ellipse is an indicator of the deviation of the ellipse from a circle. Gorodisky *et al.,*[21] using CMR found that in all cases of MR, including organic MR, PISA is eccentric in shape. It suggests that the 3D PISA shape resembles a hemiellipse rather than the hemisphere. The correlation between 3D PISA-EROA and 3D-VCA was better in the organic subgroup than functional in our study subjects. Using the Bland–Altman analysis, we found that both 3D-PISA methods underestimated the 3D-VC-EROA. Since in our study, a large number of patients had the elliptical shape of regurgitant orifice, we expected that the 3D-HE-PISA would offer a more accurate value for EROA than the 3D-HS-PISA. However, the 3D-HS-EROA showed the best agreement among the methods used. Contrary to our observation, the hemispherical assumption of PISA was found to underestimate the regurgitant orifice area more than the hemieliptical assumption of PISA in some of the published studies. This underestimation was more evident in the functional subgroup.[10,17] Ashikhmina *et al.*[10] reported larger values for HE-PISA than HS-PISA, although both were less than 3D-VCA in their patients. Contrary to the observation of Ashikhmina *et al.*, we found that the 3D-HE-PISA significantly underestimated the EROA compared to other PISA methods. A majority of our patients had functional MR due to coronary artery disease. The characteristics of regurgitant orifice in functional MR under anesthesia do not remain constant throughout the systole, but vary under the influence of multiple factors such as the fixed versus compliant nature of regurgitant orifice, left ventricular remodelling and dysynchrony, changing loading conditions, and severity of MR. Due to these irregular dynamic conditions, the shape of the regurgitant orifice may vary from circular to elliptical or crescentic at any given point of time, which directly influences the geometry of the PISA as well.

The PISA is a three-dimensional structure which has three radii (r-1, r-2, and r-3). The height-radius r-1 is considered as a radius for both HS- and HE-PISA. The other two base-radii r-2 and r-3 are presumed to be equal to r-1 in hemispherical geometry, whereas in hemielliptical geometry the r-2 and r-3 may be different from r-1. For HE-PISA to be larger than HS-PISA, the sum of the two orthogonal base-radii (r-2 and r-3) must be more than twice the height-radius (r-1) of PISA. We observed that similar to the 3D-VCA, the 3D-PISA shells also elongate along the commissural plane but remain constricted in the anteroposterior plane. In most of the cases, the anteroposterior radius (r-2) was less than the radius (r-1) of PISA. Therefore, for HE-PISA value to become more than HS-PISA, the radius along the commissural plane (r-3) must be significantly large to compensate for the reduction in the r-2 [Figure 4].

In most of our patients, the regurgitant orifice was elliptical (79%) and the HE-PISA was smaller than HS-PISA because the summation of r-2 and r-3 was less than twice the r-1. Therefore, the assumption that HE-PISA would be more accurate than HS-PISA for EROA estimations in asymmetric PISA shells may not be true for all the subsets of patients. Similar findings were reported in another study,[16] wherein the authors noted that patients with functional MR had the smallest VCA. The mean EROA calculated by the HS-PISA method had larger values than that of HE PISA. Schmidt *et al.*[22] studied the feasibility and

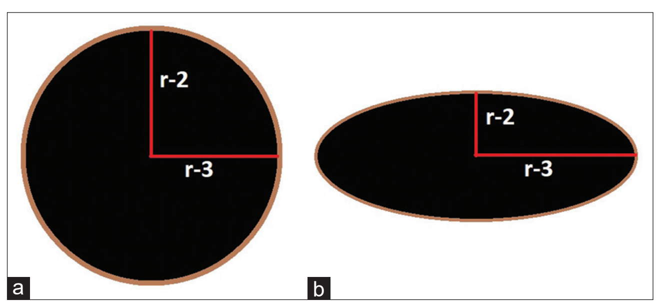

Figure 4: Base of the 3D-HS-PISA (a) and 3D-HE-PISA (b) are shown in the diagrammatic representation. The radius r-1, which represents the height of both HS-PISA and HE-PISA, is same and not shown in the diagram. The r-2 and r-3 represent radius of the minor axis and major axis of base of the PISA, respectively. In HS-PISA, r-1, r-2, and r-3 are equal, whereas in HE-PISA, r-2 is less than r-3. If the value of addition of r-2 and r-3 in HE-PISA is less than the addition of r-2 and r-3 in HS-PISA, the volume of HE-PISA would be less than that of HS-PISA

application of semi-automated PISA detection software. They found a better diagnostic performance in circular rather than elongated PISA shells not only for 2D-PISA but also for 3D-PISA. It suggests that the 3D PISA measurements work better for circular orifices. As with every technique, 3DE also has its limitations. It has poor temporal resolution, which can be overcome by multiple beat full volume acquisitions. But cardiac arrhythmias, respiratory motion or probe motion may lead to stitching artefacts. It also has limited spatial resolution. Currently, VCA measurement requires manual alignment of plane perpendicular to VC. Small mistakes in alignment can lead to under or overestimation of the EROA.

PISA is generally measured at only a single frame in systole, resulting in the overestimation of true flow, since the regurgitant flow varies over time, especially in cases of mid-systolic and late-systolic MR.[21] Automated 3D PISA measurements using dedicated softwares would probably overcome this problem. Recent studies[23] comparing the 3D PISA using automated softwares have shown increased accuracy and less underestimation of EROA with these techniques compared to 2D-PISA or geometrically assumed 3D-PISA. However, the EROA derived by automated 3D-PISA measurement was found to be less than the 3D-VCA.

We do acknowledge the limitations to our study. EROA is a dynamic concept and changes throughout systole. Our reference standard of 3D-VCA derived EROA from a single largest frame may not represent the EROA for the entire systole. Calculating the mean value by averaging EROA from all systolic frames would have better represented the EROA; however, this time-consuming and cumbersome method may not be suitable for the intraoperative period. An automated EROA detection software taking the temporal variation into account would mitigate this problem, although, it is not yet validated. We excluded patients with eccentric jets from our study population. Since eccentric jets are common in patients with organic pathology, we could include a very small number of patients with this pathology in our study. With the current limitations to technology, no geometric assumptions would be ideal for the 3D PISA measurement. The development of automated software for PISA measurements in future may have an edge over the geometric PISA assumptions. The cardiac MRI-based 4D-PISA may be able to assess MR severity quantitatively without any geometric assumptions.[21]

In summary, the quantitative assessment of MR can be successfully performed using intraoperative TEE 2D color Doppler and 3D color full volume dataset. All the three methods of PISA and 2D-VCW were found to have significant positive correlations with 3D-VCA. The 3D-HE-PISA, however, significantly underestimated the EROA compared to other PISA methods. The correlation between PISA-EROA and 3D-VCA was better in the organic subgroup than functional. All methods to derive EROA underestimated EROA compared to 3D-VC-EROA. The 3D HS EROA showed the best agreement among the methods used. Similarly, the MR Rvol obtained by 2D-HS-PISA, 3D-HS-PISA, and 3D-HE-PISA techniques had significant positive correlations with the Rvol of 3D-VCA. The 3D-HE-PISA significantly underestimated the Rvol. The elliptical shape of vena contracta was most commonly seen in the MR of both functional and organic etiologies. The crescentic shape was more commonly seen in the functional group than the organic group.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, *et al.* American Society of Echocardiography. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777-802.
2. Lancellotti P, Moura L, Pierard LA, Agricola E, Popescu BA, Tribouilloy C, *et al.* European Association of Echocardiography. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: Mitral and tricuspid regurgitation (native valve disease). Eur J Echocardiogr 2010;11:307-32.
3. Hall SA, Brickner ME, Willett DL, Irani WN, Afridi I, Grayburn PA. Assessment of mitral regurgitation severity by Doppler color flow mapping of the vena contracta. Circulation 1997;95:636-42.
4. Fehske W, Omran H, Manz M, Kohler J, Hagendorff A, Luderitz B. Color-coded Doppler imaging of the vena contracta as a basis for quantification of pure mitral regurgitation. Am J Cardiol 1994;73:268-74.
5. Khanna D, Vengala S, Miller AP, Nanda NC, Lloyd SG, Ahmed S, *et al.* Quantification of mitral regurgitation by live three-dimensional transthoracic echocardiographic measurements of vena contracta area. Echocardiography 2004;21:737-43.
6. Iwakura K, Ito H, Kawano S, Okamura A, Kurotobi T, Date M, *et al.* Comparison of orifice area by transthoracic three-dimensional Doppler echocardiography versus proximal isovelocity surface area (PISA) method for assessment of mitral regurgitation. Am J Cardiol 2006;97:1630-7.
7. Shanks M, Siebelink HM, Delgado V, van de Veire NR, Ng AC, Sieders A, *et al.* Quantitative assessment of mitral regurgitation: Comparison between three dimensional transesophageal echocardiography and magnetic resonance imaging. Circ Cardiovasc Imaging 2010;3:694-700.
8. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, *et al.* Recommendations for noninvasive evaluation of native valvular regurgitation: A report from the American Society of Echocardiography Developed in Collaboration with the Society

for Cardiovascular Magnetic Resonance. J Am Soc Echocardiogr 2017;30:303-71.
9. Yosefy C, Levine RA, Solis J, Vaturi M, Handschumacher MD, Hung J. Proximal flow convergence region as assessed by real time 3-dimensional echocardiography: Challenging the hemispheric assumption. J Am Soc Echocardiogr 2007;20:389-96.
10. Ashikhmina E, Shook D, Cobey F, Bollen B, Fox J, Liu X, *et al*. Three-dimensional versus two-dimensional echocardiographic assessment of functional mitral regurgitation proximal isovelocity surface area. Anesth Analg 2015;120:534-42.
11. Thomsen K. Available from: http://www.numericana.com/answer/ellipsoid.htm. [Last accessed on 2013 Sep 16].
12. Lombardero M, Henquin R, Perea G, Corneli M, Izurieta C. True morphology of mitral regurgitant flow assessed by three-dimensional transesophageal echocardiography. Echocardiography 2017;34:87-93.
13. Yosefy C, Hung J, Chua S, Vaturi M, Ton-Nu TT, Handschumacher MD, *et al*. Direct measurement of vena contracta area by real-time 3-dimensional echocardiography for assessing severity of mitral regurgitation. Am J Cardiol 2009;104:978-83.
14. Zeng X, Levine RA, Hua L, Morris EL, Kang Y, Flaherty M, *et al*. Diagnostic value of vena contracta area in the quantification of mitral regurgitation severity by color Doppler 3D echocardiography. Circ Cardiovasc Imaging 2011;4:506-13.
15. Hyodo E, Iwata S, Tugcu A, Arai K, Shimada K, Muro T, *et al*. Direct measurement of multiple vena contracta areas for assessing the severity of mitral regurgitation using 3D TEE. JACC Cardiovasc Imaging 2012;5:669-76.
16. Marsan NA, Westenberg JJ, Ypenburg C, Delgado V, van Bommel RJ, Roes SD, *et al*. Quantification of functional mitral regurgitation by real-time 3D echocardiography: Comparison with 3D velocity encoded cardiac magnetic resonance. JACC Cardiovasc Imaging 2009;2:1245-52.
17. Kahlert P, Plicht B, Schenk IM, Janosi RA, Erbel R, Buck T. Direct assessment of size and shape of noncircular vena contracta area in functional versus organic mitral regurgitation using realtime three dimensional echocardiography. J Am Soc Echocardiogr 2008;21:912-21.
18. Bargiggia GS, Tronconi L, Sahn DJ, Recusani F, Raisaro A, De Servi S, *et al*. A new method for quantitation of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. Circulation 1991;84:1481-9.
19. Simpson IA, Shiota T, Gharib M, Sahn DJ. Current status of flow convergence for clinical applications: Is it a leaning tower of "PISA"? J Am Coll Cardiol 1996;27:504-9.
20. Pu M, Vandervoort PM, Griffin BP, Leung DY, Stewart WJ, Cosgrove DM 3rd, *et al*. Quantification of mitral regurgitation by the proximal convergence method using transesophageal echocardiography: Clinical validation of a geometric correction for proximal flow constraint. Circulation 1995;92:2169-77.
21. Gorodisky L, Agmon Y, Porat M, Abadi S, Lessick J. Assessment of mitral regurgitation by 3-dimensional proximal flow convergence using magnetic resonance imaging: Comparison with echo-Doppler. Int J Cardiovasc Imaging 2018;34:793-802.
22. Schmidt FP, Gniewosz T, Jabs A, Münzel T, Hink U, Lancellotti P, *et al*. Usefulness of 3D-PISA as compared to guideline endorsed parameters for mitral regurgitation quantification. Int J Cardiovasc Imaging 2014;30:1501-8.
23. Hien MD, Weymann A, Rauch H, Grossgasteiger MC, Motsch J, Rosendal C. Comparison of intraoperative three-dimensional Doppler color flow mapping to assess mitral regurgitation. Echocardiography 2012;29:84957.