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Assessment of MR Severity by PISA using 3D TEE

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Abstract

Background: 2D PISA method has some technical limitations, mainly the geometric assumptions of PISA shape required to calculate effective regurgitant orifice area (EROA). Real-time three-dimensional (3D) color Doppler imaging allows measurement of PISA without geometric assumptions. The aim of this study was to validate this method in patients with chronic mitral regurgitation (MR).

Methods: 25 patients were included, ten (40%) with rheumatic MR, ten (40%) with functional MR, three (12%) with flail MV, one (4%) with MV prolapse and one (4%) with degenerative MR. EROA, regurgitant volume and regurgitant fraction were assessed using transthoracic 2D and 3D PISA methods. The quantitative Doppler EROA method and trans-thoracic VCW were used as reference methods.

Results: Both EROA and regurgitant volume assessed using the 3D PISA method had better correlations with the reference methods than conventional 2D PISA. A consistent significant underestimation of EROA and regurgitant volume using 2D PISA was observed. On the basis of the quantitative Doppler EROA method 14 patients had severe MR (EROA ≥ 0.4 cm2). Of these 14 patients, 78.5% (11 of 14) were underestimated as having non severe MR (EROA <0.4 cm2) by the 2D PISA method. In contrast, the 3D PISA method had 92.9% (13 of 14) agreement with The quantitative Doppler EROA method 14 patients had severe MR in classifying severe MR. Good intra-observer and interobserver agreement for 3D PISA measurements was observed, with intraclass correlation coefficients of 0.96 and 0.92, respectively.

Conclusion: Measurement of PISA without geometric assumptions using single-beat, real-time 3D color Doppler echocardiography is feasible in the clinical setting. MR quantification using this methodology is more accurate than the conventional 2D PISA method.

Keywords: PISA; 3D Echo; MR; EROA

Introduction

Valvular insufficiencies are among the most frequent heart diseases and mitral regurgitation (MR) is considered the most common valve disease of significant regurgitation (moderate to severe and severe) in the general population [1]. As a result of increased prevalence of rheumatic heart disease in developing countries, and consequently MR, accurate assessment of the severity of regurgitation was demonstrated to be of significant importance for patient management and prognosis and consequently has been widely recognized in guidelines [2].In view of advances in mitral valve repair techniques and their early use to preserve ventricular function, timely diagnosis and accurate assessment of severity of MR are of significant importance for appropriate decision making and patient outcome [3,4].

Two-dimensional (2D) echocardiography with color Doppler is the standard method for noninvasive assessment of severity and etiology of MR [5]. However, accurate quantitative evaluation of MR severity remains challenging because limited scan plane orientation of 2D echocardiography does not provide direct measurement of the regurgitant lesion [3].

Three-dimensional echocardiography which has grown up to a clinically accepted technique has been demonstrated to provide important information for flow quantification and, thus, is promising to overcome the major limitations of 2D-based methods [6]. Effective regurgitant orifice area (EROA) calculation using the proximal iso-velocity surface area (PISA) method has been well validated with in vitro and in vivo models [7]. Despite its usefulness, pitfalls and limitations of this technique are well recognized, the conventional two-dimensional (2D) PISA method is based on the assumption of hemispheric symmetry of PISA and when the EROA is nearly circular. However, PISA can be variable depending on the instrument settings and the shape of the regurgitant orifice, which is reported in several recent studies to be non-circular in most patients [8]. Leading to a

discrepancy between EROA calculated with hemispheric assumption and the actual area.

Three-dimensional (3D) echocardiography can provide the actual geometry of the flow convergence [9], so measurement of PISA with 3D color Doppler echocardiography does not require the use of geometric assumptions and should reduce the errors in calculating EROA present with the 2D method. To overcome the limitations of 2D analysis of PISA shape and size, several research groups either validated in vitro or in vivo estimates of the 3D PISA shape by manual measurements of either three perpendicular PISA diameters [8,10,11] or more diameters [12] or PISA surface [13,14] and found significantly improved accuracy of 3D PISA estimates of EROA and regurgitant flow.

Either method, TTE or TEE, may be used to quantify MR severity, however TEE may provide additional information via better imaging from the esophageal window, the excellent quality of the images obtained of the valve apparatus and color flow jets with TEE provide much more accurate information that obtained from the other methods [15].

Methods

Study population

From December 2016 to November 2017 (25) patients with MR were included, ten (40%) with rheumatic MR, ten (40%) with functional MR, three (12%) with flail MV, one (4%) with MV prolapse and one (4%) with degenerative MR. all cases recruited from inpatient and outpatient facilities of Cardiology department in Al-Hussein University Hospital-Alazhar university-Cairo-Egypt. Which met the following criteria: (1) Patients with at least moderate MR in the standard color Doppler evaluation (2) Patients with MR of the etiologies described above. (3) The absence of concomitant lesions (more than mild aortic stenosis, aortic insufficiency, or mitral stenosis). (4) Previous MV operations. and (5) More than one flow convergence regions. During recruitment, many patients were excluded because of the absence of the previous criteria or the presence of rhythm disturbances (as atrial fibrillation (AFib)). All patients underwent echocardiography because of clinical indications and gave written informed consent before undergoing echocardiography in accordance with a protocol approved by the institutional review board.

2D Echocardiography

All patients were examined in the left lateral decubitus position with a commercially available ultrasound system (iE33x Matrix, Philips Medical Systems, Andover, Massachusetts, USA) equipped with X5-1 matrix array transducer. The following measures were taken: (1) LV end-diastolic and end-systolic volumes (LVEDV and LVESV) by the 2D modified biplane Simpson method. (2) EF and fraction shortening calculated automatically by machine software. (3) Vena contracta width (VCW). The vena contracta was imaged and measured as following: (1) From para-sternal long axis (PT-LAX) view. (2) Optimization of color gain/scale.(3) Identify the three components of the regurgitant jet (VC, PISA, jet into LA).(4) Reduce the color sector size and imaging depth to maximize frame rate.(5) Expand the selected zone (Zoom).(6) Use the cine-loop to find the best frame for measurement.(7) Measure the smallest VC (immediately distal to the regurgitant orifice, perpendicular to the direction of the jet).

PISA Method and MR volume

Proximal flow convergence was calculated as following: (1) From Apical four-chamber view, optimize colour flow imaging of MR. (2) Zoom the image of the regurgitant mitral valve.(3) Decrease the Nyquist limit (30-40 cm/s) to optimize visualization of flow convergence. (4) With the cine-mode select the best PISA. (5) Display the color off and on to visualize the MR orifice (color suppress mode). (6) Measure the PISA radius at mid-systole using the first aliasing and along the direction of the ultrasound beam. (7) Take continuous wave Doppler at mitral valve and Measure MR peak velocity and time velocity integral (TVI). (8) Calculate flow rate, EROA, R Volume (Rvol).

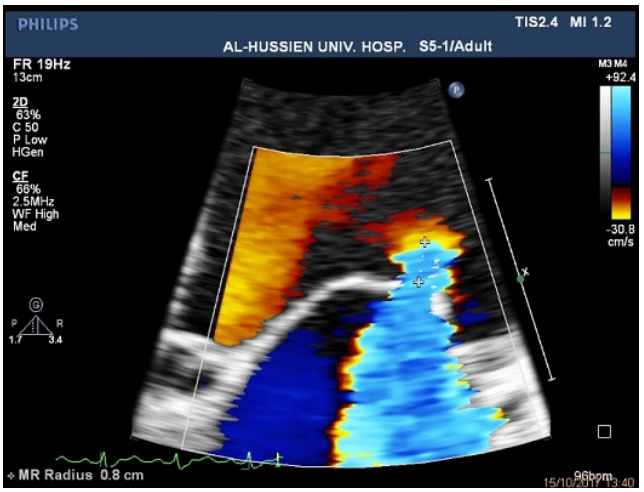

Figure 1. PISA r measurement.

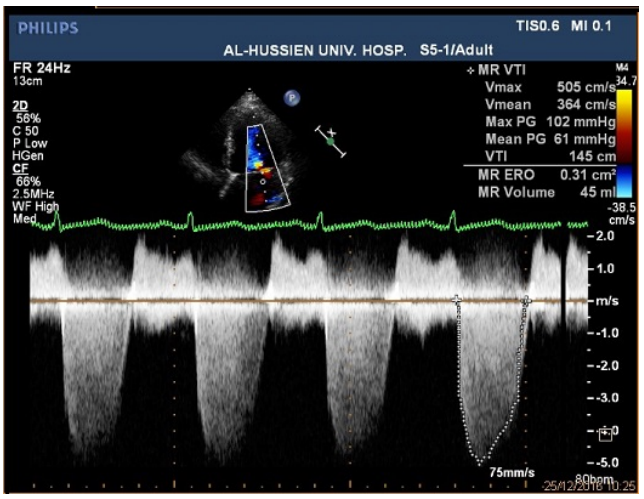

Figure 2. Continuous wave Doppler (CWD) of regurgitant MV.

Flow rate calculated as Flow rate=(2 π x (r)2) VAliasing. The Effective regurgitant orifice area (EROA) calculated using the formula EROA = 2π x (r PISA)2 x VAliasing/Vmax [5], where r PISA is the maximal PISA radius (cm), VAliasing is aliasing velocity of the proximal flow convergence (cm/s), and Vmax is the maximal velocity

of continuous wave Doppler MR signal (cm/s). The severity of MR was graded on the basis of current ASE recommendations as mild (<0.2 cm2), moderate (0.2 to 0.39 cm2), or severe (≥ 0.40 cm2) [16].

MR volume calculated automatically by machine software using these formulae:

Rvol EROA × Regurgitant time-velocity integral (VTI). For MR grading, MR volume <30 ml/beat consider mild MR, 30-44 ml/beat for mild to moderate MR, 45-59 ml/beat for moderate to severe, and >60 ml/beat for severe MR [16].

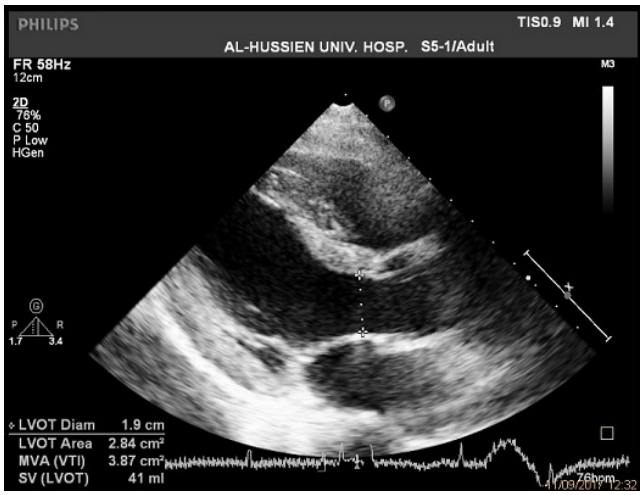

Figure 3. Measurement of LVOT diameter.

Calculation of MVSV and Forward SV (LVOTSV) to calculate Regurgitant fraction:

LVOT diameter (from parasternal long axis view): Diameter is measured from the inner edge to inner edge of the septal endocardium, and the anterior mitral leaflet in mid-systole.

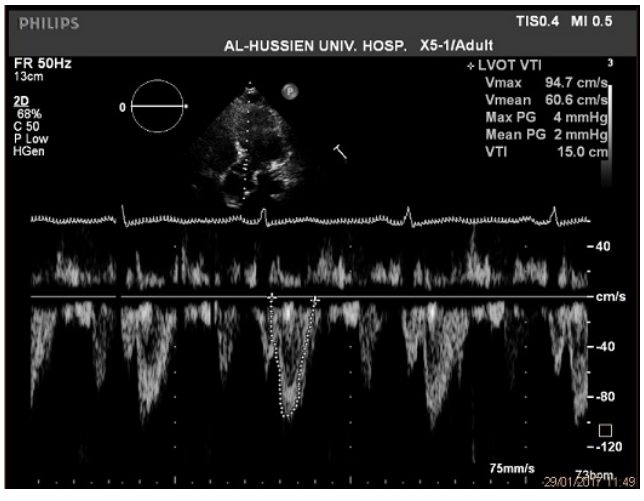

Figure 4. PWD of LVOT.

Diameter measurements are most accurate using the zoom mode with careful angulation of the transducer and with gain and processing adjusted to optimize the images. LVOT diameter is measured for subsequent calculation of the LVOT cross-sectional area (CSALVOT) to be used in the continuity equation (Figure 3). LVOT flow was recorded with pulsed wave Doppler at the same point of LVOT diameter measurement (from the apical 5-chamber view) for measuring the velocity-time integral of LV outflow (VTILVOT).

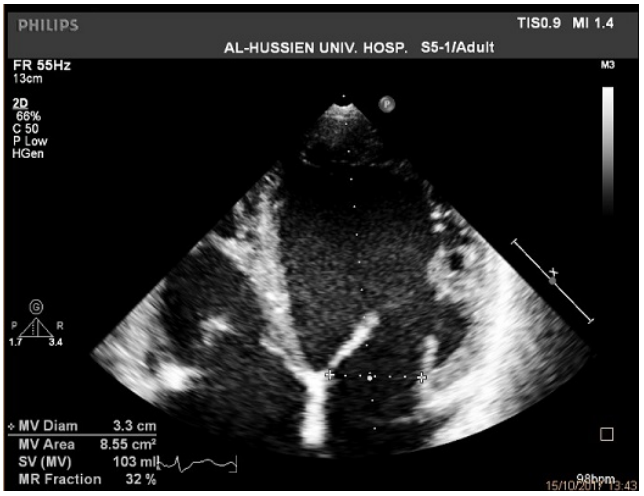

Figure 5. Mitral annulus diameter measurement.

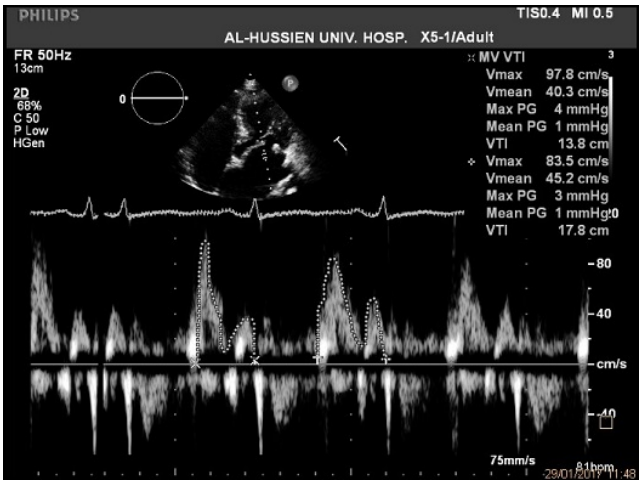

Figure 6. PWD of MV annulus and VTI.

Mitral annulus diameter: (from apical 4 chamber view)

Diameter of mitral annulus measured at mid diastole from the medial to the lateral edges of the MV annulus. Mitral inflow (LV inflow): was recorded with pulsed wave Doppler at the same point of mitral annulus diameter measurement (from the apical 4-chamber view) for measuring the velocity-time integral of LV inflow (VTILV inflow).

Calculation of the stroke volumes

(a)Forward SV: The stroke volume (SV) was derived as the product of CSALVOT and the VTILVOT. (b)MV SV: flow to LV across the incompetent MV was derived as the product of CSAMA and the VTILV Inflow. Calculation of Rvol: as the difference between Forward SV and MV SV.

Rvol=MVSV – ForwardSV. Calculation of Regurgitant fraction (RF %). RF= Rvol/MVSV

Calculation of EROA derived from 2D-Quantitative-Doppler: After calculation of Rvol as the difference between MVsv & forwardSV. EROA obtained as the following:

EROA=Rvol/VTILV Inflow.

Transesophageal 2D/3D echocardiography

TEE imaging was performed immediately after the transthoracic studies using an X7-2t transducer connected to the Philips iE33x Matrix system capable of acquiring fully sampled 3D images. The mitral valve was interrogated by using multiple planes, including, four-chamber and five-chamber views, and slight variations of them. All measurements were acquired from 3D TEE full-volume data sets, which included both gray scale images of the MV apparatus and superimposed simultaneously acquired CFD images of the MR jet set initially at a Nyquist limit of 50 to 60 cm/s. Volume rates in the range of 30 to 40 Hz were enabled to assure optimal temporal resolution, first by adjusting the pyramid-shaped region of interest to the smallest volume that encompassed the entire mitral complex and second by using a routine protocol for obtaining hybrid reconstruction full-volume CFD data sets from six consecutive heartbeat sub-volumes, which were gated to the electrocardiogram while mechanical respiration was temporarily suspended to prevent stitching artifacts. All images were digitally stored for offline analysis (3DQ, QLAB 10.4; Philips Medical Systems). Using multiplanar reconstruction of the 3D TEE volume data set, measurement of PISA radius (r), PISA width (D1) from the 4-chamber view and PISA length (D2) from the chamber view. In some cases, color scale baseline (Aliasing velocity) shifted to be between 30 to 40 cm/s, during acquisition and then for avoidance of time consumption during acquisition had adjusted during offline analysis. Zoomed images used for accurate measurements of (r, D1 &D2).

The obtained measures are used to calculate HE-PISA through application of the following Thomsen formula: HE-PISA=4 [(r × (D1/2))P + (r × (D2/2))P + ((D1/2) × (D2/2))P/3]1/P [17].

Then EROA calculated as the following: EROA=(HE-PISA × Aliasing velocity)/Vmax. To be expressed in cm2. Then Rvol calculated as: Rvol=EROA × VTI of regurgitant jet. To be expressed in ml. Then RF calculated as: RF=(Rvol/MVSV) × 100. To be expressed in %.

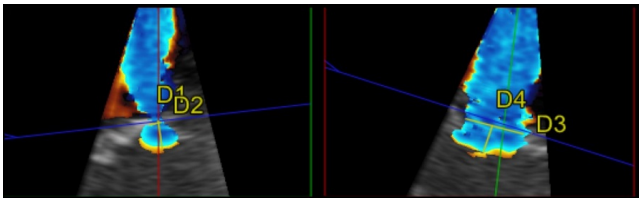

Figure 7. Measurement of PISA r, width, and length.

Statistical Analysis

Continuous variables are expressed as mean 6 SD. Categorical data are presented as absolute numbers or percentages. Correlations between 2D and 3D PISA measurements and those obtained by reference methods were assessed using simple linear regression analysis. Bland-Altman plots were constructed to demonstrate agreement between methods.18 Graphed data indicate mean test value 6 2 SDs and measurement bias. Inter observer and intra-observer reproducibility were evaluated using intraclass correlation coefficients. Differences were considered statistically significant at $p<0.05$ (two sided). Statistical analysis was performed using SPSS version 20.0. (SPSS, Inc., Chicago, IL).

Results

Clinical and echocardiographic characteristics of the 25 patients studied are summarized in Table 1. The mean age was 45.12 ± 13.56 years, and 11 patients (44%) were men. The mean heart rate was 79.92 ± 5.24 beats/min during transthoracic echocardiography and 88.28 ± 7.35 beats/min during TEE imaging. Neither systolic blood pressure (122.88 ± 13.32 vs 124.84 ± 6.85 mm Hg) nor diastolic blood pressure (76.20 ± 10.44 vs 84.52 ± 5.61 mmHg) differed significantly between transthoracic echocardiography and TEE imaging. Ten patients (40%) had rheumatic MR and ten (40%) had functional MR and five patients (20%) had degenerative MR.

Demographic Data	**Total [N=25]**
Sex	
Female	14 (56%)
Male	11 (44%)
Age (years)	23-68 (45.12±13.56)
Clinical characteristics	Total [N=25]
Aetiology	
Rheumatic	10 (40%)
DCM	5 (20%)
ICM	5 (20%)
Degenerative	
Flail	3 (12%)
Sclerotic	1 (4%)
MV prolapse	1 (4%)

Sinus	25 (100%)
Heart Rate	69-88 (79.92±5.24)
Systolic	100-145 (122.88±13.32)
Diastolic	60-100 (76.20±10.44)

Table 1. Demographic data distribution and clinical characteristics distribution of the study group.

MR Quantification by the 2D and 3D PISA Methods Compared with Reference Methods:

The quality of the PISA zone images was excellent for both 2D-TTE and 3D TEE echocardiography. The duration of EROA assessment by the 3D PISA method was 4 to 5 min. Three-dimensional PISA measurements were optimal in all patients. PISA geometry was hemielliptic rather than hemispheric in the majority of patients (92%), even in patients with degenerative MR. Patients with functional MR had a more elongated and hemielliptic shape of PISA compared with patients with degenerative MR. EROA, Rvol, and regurgitant fraction determined by the two techniques are reported in Table 2 for comparison.

	2D-PISA-EROA cm2	3D PISA-TEE-EROA cm2	t-test	p value
EROA cm2				
Mean ± SD	0.30 ± 0.13	1.37 ± 4.72		
Range	0.07-0.74	0.18-0.96	7.862	0.007
Rvol ml				
Mean ± SD	43.50 ± 18.28	58.83 ± 17.20		
Range	13-97	31-100	9.327	0.004
RF%				
Mean ± SD	38.56 ± 13.95	50.27 ± 11.75		
Range	14.6-80	29.8-84	10.308	0.002

Table 2. Comparisons between 2D-PISA-EROA cm2 and 3D PISA-TEE-EROA cm2 according to EROA cm2, Rvol and RF%.

Using the 2D PISA method, the derived EROA was significantly smaller than that obtained by the reference method, quantitative Doppler-EROA (Table 3).

2D Trans thorathic	2D Trans thorathic (PISA-EROA cm2)	2D Trans thorathic (Vena contraca width cm)	2D Trans thorathic (Quantitative doppler EROA)	ANOVA	p value
Mean ± SD	0.30 ± 0.13	0.63 ± 0.13	0.50 ± 0.46		
Range	0.07-0.74	0.3-0.85	0.19-2.6		
#		<0.001	0.015		
##			0.094	8.865	<0.001

Note: Post Hoc: Difference between 2D Trans thorathic (PISA-EROA cm2) with 2D Trans thorathic (Vena contraca width cm) and 2D Trans thorathic (Quantitative doppler EROA). Post Hoc: Difference between 2D Trans thorathic (Vena contraca width cm) and 2D Trans thorathic (Quantitative doppler EROA)

Table 3. Comparisons between 2D-Trans Thorathic PISA, vena contraca width cm and quantitative Doppler - EROA cm2.

In contrast, using the 3D PISA method, the resultant EROA was very close, although a little smaller than that obtained by the reference methods (Table 4).

	3D PISA-TEE-EROA cm2	2D Trans thorathic (Vena contraca width cm)	2D Trans thorathic (Quantitative doppler EROA)	ANOVA	p value
Mean ± SD	0.41 ± 0.16	0.63 ± 0.13	0.50 ± 0.46		
Range	0.18-0.96	0.3-0.85	0.19-2.6		
#		0.009	0.316		
##			0.1	3.66	0.031

Note: Post Hoc: Difference between 3D PISA-TEE-EROA cm2 with 2D Trans thorathic (Vena contraca width cm) and 2D Trans thorathic (Quantitative doppler EROA). Post Hoc: Difference between 2D Trans thorathic (Vena contraca width cm) and 2D Trans thorathic (Quantitative doppler EROA)

Table 4. Comparison between 3D PISA-TEE, vena contraca width cm and quantitative Doppler according to EROA cm2.

Correlation between EROA obtained by the 2D and 3D PISA methods with quantitative Doppler echocardiography are shown in Figures 8 and 9, respectively. Acceptable correlation was observed between 2D PISA–derived EROA and the reference methods (with VCW, r=0.418, p=0.037; with quantitative Doppler echocardiography-EROA, r=388, p=0.046). However, the regression equation indicated a consistent significant under estimation of EROA using the 2D PISA method. A better correlation was observed between 3D PISA–derived EROA and that obtained by the reference methods (with VCW, r=0.590, p=0.002; with quantitative Doppler echocardiography-EROA, r=0.441, p=0.027). Linear regression showed an excellent correlation, with uniform clustering of data around the regression line. Bland-Altman analysis showed better agreement when comparing 3D PISA–determined EROA with the reference methods than when comparing the former with 2D PISA – determined EROA. On the basis of quantitative Doppler–derived EROA, 14 patients had severe MR by American Society of Echocardiography guidelines (EROA ≥ 0.4 cm2) [16], 6 in the group with rheumatic MR and 6 in the group with functional MR and 2 in the group of degenerative MR. Of these 14 patients, 78.5% (11 of 14) were underestimated as having non-severe MR (EROA<0.4 cm2) by the 2D PISA method. Underestimation of severe MR by the 2D PISA method was more trast, the 3D PISA method had 92.9% (13 of 14) agreement with quantitative Doppler–derived EROA, in classifying severe MR. Good intra-observer and interobserver agreement for 3D PISA measures was shown, with intraclass correlation coefficients of 0.96 and 0.92, respectively.

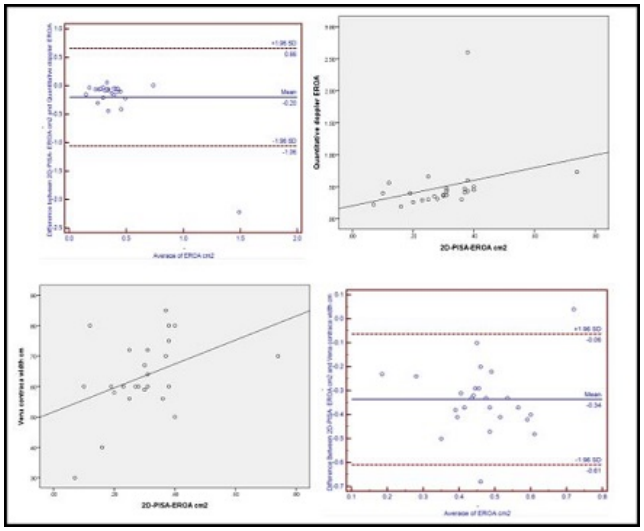

Figure 8. Positive correlation and significant between (2D-PISA and Vena contraca width cm of EROA cm2. Bland-Altman plot showing correlation and agreement between EROA by 2D-PISA and Vena contraca width cm.

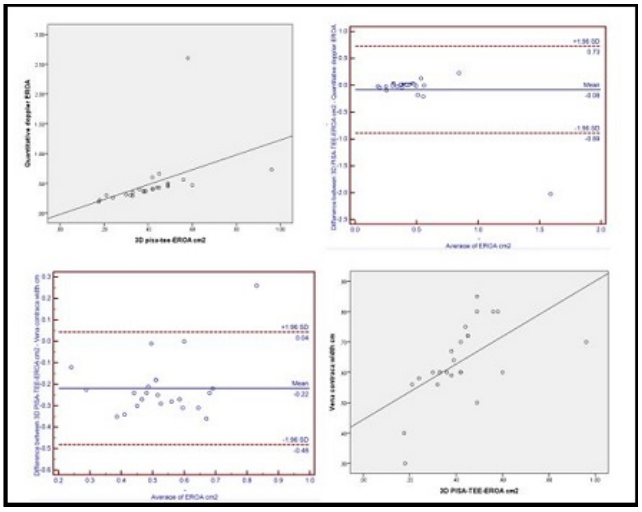

Figure 9. Positive correlation and significant between (3D-PISA-TEE and Vena contraca width cm of EROA cm2. Bland-Altman plot showing correlation and agreement between EROA by 3D-PISA and Vena contraca width cm.

Discussion

The present study demonstrates that measurement of MR PISA with full volume, real-time 3D color Doppler echocardiography in clinical setting is feasible without relying on hemispheric assumptions by the transthoracic approach. In our study, both EROA and mitral Rvol calculated by the 3D PISA method showed better correlation and agreement with the previously validated reference methods than those calculated by the 2D PISA method. Our data show that the hemispheric 2D PISA approach results in an important underestimation of MR degree compared with the quantitative Doppler method derived EROA and TTe VCW In contrast, the 3D PISA method was more accurate in MR quantification .A high percentage of patients 78.5% (11 of 14) with severe MR (EROA ≥ 0.4 cm2) by quantitative Doppler–derived EROA, were underestimated as having moderate or less MR by the 2D PISA method. This is a particularly important range in which surgery may be contemplated. In contrast, 3D PISA had high agreement (92.9%) with quantitative Doppler–derived EROA, in classifying severe MR. In addition, the 3D PISA method was easy to perform, and the time consumed was low. Our results suggest that with the severity of MR assessed with quantitative Doppler echocardiography or angiography [18]. This method has been included in guidelines for quantification of MR as a cornerstone technique [16]. However, important problems and pitfalls have been defined in the application of the proximal flow convergence method for the quantitative assessment of valvular regurgitation severity. This method is based on the assumption of hemispheric symmetry of the velocity distribution proximal to the regurgitant lesion, which may not hold for eccentric regurgitant jets, multiple jets, or complex or elliptical regurgitant orifices. A further limitation is related to the need to accurately define the regurgitant orifice level on the 2D color Doppler image. This limitation is important, because this radial measure is squared to derive iso-velocity surface area, and minor inaccuracies result in imprecise determination of EROA. Previous studies have reported that EROA obtained using the PISA method underestimates MR degree in patients with non-hemispheric geometry of PISA [19]. Moreover, it has been demonstrated that EROA calculated using a hemielliptic assumption of PISA is more accurate than that using the hemispheric assumption in the PISA method [20,21]. However, even the hemielliptic assumption may not be accurate enough for determining EROA when the shape of PISA is complex. Three-dimensional color Doppler echocardiography is expected to overcome the limitations of the 2D PISA method. Three-dimensional imaging has the advantage of avoiding any geometric assumptions and determining the actual PISA. Therefore, complete 3D visualization of the convergent flow zone is the ideal solution for the accurate calculation of EROA. Chandra et al. [22] studied the effects of mitral valve orifice geometry on PISA pattern by 3D color Doppler TEE imaging. They found that a central regurgitant orifice is suitable for 2D PISA measurements but complex mitral valve orifice resulting in eccentric jets yielded non axisymmetric iso-velocity contours, for which the assumptions underlying flow convergence are problematic. Recent advances in 3D echocardiography have enabled high–frame rate acquisition of volumetric color Doppler flow images in a single heart cycle. Experimental in vitro studies have demonstrated that the PISA might be measured with 3D color Doppler echocardiography even in complex geometric flow fields [23-26]. On the basis of our data, the measurement of PISA with 3D Doppler echocardiography is a promising method to overcome the limitations of the 2D PISA method, in cases of MR.

Study Limitations

A limitation of all clinical studies of MR is the lack of a gold standard against which to compare the results of different methods. In this study, we used two different reference techniques to reduce as much as possible and complement their respective limitations. The current 3D color Doppler imaging techniques offer images with lower frame rates than conventional 2D echocardiography. In this study, the PISA method was applied using a single systolic frame, specifically, the

one with the largest flow convergence region, assuming that it corresponded to the time of maximum regurgitant flow. This approach can be limited by the lower temporal resolution of 3D color Doppler, so the selected convergence region may not necessarily be the absolute largest. In an effort to minimize the potential effect of low temporal resolution, several cine loops were analyzed in each patient, looking for the largest convergence zone in each cineloop.

Conclusion

Measurement of PISA without geometric assumptions by transesophageal, real-time, 3D color Doppler echocardiography provides more accurate MR assessment than the 2D PISA method. We demonstrated its potential applicability to the clinical setting, showing feasibility in patients with various degrees of MR. This method is relatively easy to perform, less time consuming and worthy of application in routine echocardiographic practice. The 3D PISA method may become the standard approach for determining EROA.

Conflicts of Interest

Authors have no conflict of interest to declare.

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