DOI: 10.1111/echo.13395

ORIGINAL INVESTIGATION

WILEY Echocardiography

True morphology of mitral regurgitant flow assessed by three-dimensional transesophageal echocardiography

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Introduction: Quantification of mitral regurgitation (MR) by two-dimensional (2D) transthoracic echocardiography (TTE) is based on the analysis of the proximal flow convergence (PFC) and the "vena contracta" (VC). This method assumes geometries and can be misleading. In contrast, three-dimensional (3D) echocardiography directly measures flow volumes and does not assume geometries, which allows for more accurate MR evaluation.

Aims: To report the 3D transesophageal echocardiography (3DTEE) feasibility for MR quantification and evaluate its concordance with 2D echo.

Methods: Twenty-seven consecutive patients undergoing 2D and 3DTEE for presurgical MR evaluation were studied prospectively. MR quantification was performed by classical 2D methods based on PFC. Diameters of the VC in orthogonal planes by 3DTEE were estimated, establishing the VC sphericity index as well as VC area (VCA) by direct planimetry. In case of multiple jets, we calculated the sum of the VCA.

Results: MR assessment by 3DTEE was feasible. An adequate concordance between VC measurements by 2D methods (TTE and TEE) was observed; however, there was a poor correlation when compared with 3DTEE. The sphericity index of the VC was: 2.08 (±0. 72), reflecting a noncircular VC.

Conclusions: 3DTEE is a feasible method for the assessment of the MR true morphology, allowing a better quantification of MR without assuming any geometry. This method revealed the presence of multiple jets, potentially improving MR evaluation and leading to changes in medical decision when compared to 2D echo assessment.

KEYWORDS
mitral regurgitation, proximal flow convergence, three-dimensional echocardiography, vena contracta

1 | INTRODUCTION

Mitral regurgitation (MR) is usually quantified by two-dimensional (2D) transthoracic and transesophageal echocardiography (TTE and TEE, respectively). Assessment of the proximal flow convergence zone (PFC) by echocardiography allows a reliable determination of the effective regurgitant orifice area (ERO) as well as the vena contracta (VC). The PFC is based on a hydrodynamic principle that establishes that flow converges and accelerates and as it approaches a circular regurgitant orifice, dispersing in a large concentric hemisphere with similar velocity.

Based on the continuity equation, the PFC radius is used to derive the ERO. This classical echocardiographic method is called PISA (proximal isovelocity surface area).[1]

The neck adjacent to the PFC constitutes the VC. The diameter of the VC is also used during routine MR quantification. International echocardiographic guidelines recommend measuring this diameter on the anteroposterior axis of the mitral valve from either the long parasternal axis (LAP) or the three-chamber apical view.[1,2]

For the VC to accurately reflect the regurgitant orifice, the latter has to be circular. Nonetheless, this is rarely the case, while the PFC may not be hemispherical. Therefore, the use of PISA to determine the ERO can be misleading, particularly in the presence of eccentric and/or multiple jets.

The introduction of 3D echocardiography (especially TEE) enabled a more comprehensive evaluation of the mitral valve. A "full volume color" allows assessment of the ERO and the area of the VC (VCA).[3–6]

The VCA adopts the actual morphology of the anatomical regurgitant orifice, potentially capturing the true geometry and size of this orifice.

The aims of this study were to report the feasibility of mitral valve 3DTEE assessment and compare it with 2D echo modes.

2 | MATERIAL AND METHODS

We included all consecutive patients undergoing echocardiographic evaluation prior to mitral valve surgery. All patients underwent 2DTEE and 3DTEE evaluation.

2.1 | Echocardiographic examination

2DTTE and TEE as well as 3DTEE examinations were performed with a Philips iE33 ultrasound system (Philips Medical System, Andover, MA, USA). 2D, real time ("live") 3D, and "triggered full volume" digital images were recorded and acquired in digital cine loop.

2DTTE was performed according to standard techniques, estimating the left ventricle (LV) diameters along with the left atrial area and volume. Biplane 2D Simpson and 3DTTE were used for the assessment of LV ejection fraction and volumes.

At that point, TEE was performed with a 5.5-MHz new matrix-array X7-2t transducer under sedation. Full volumes were acquired at 0, 45, 90, 120 and 180 degrees and analyzed in a workstation using a Philips QLAB software version 9.0 (Philips Medical System). Best capture (without stitching artifacts) was chosen for the analysis of the mitral apparatus. 3D mitral annular area and diameters were determined by Philips QLAB software.

3 | QUANTIFICATION OF MITRAL REGURGITATION

3.1 | 2D echocardiographic assessment

MR quantification took into account the VC and ERO (PISA method).[1] VC was derived from the diameter adjacent to the PISA region (anteroposterior mitral valve axis or a three-chamber apical view) during systole at the point of best jet visualization. A VC >7 mm was considered severe MR. The ERO (by PISA method) was derived from the following formula:

$$\text{ERO} = \text{Regurgitant flow}/\text{velocity through the orifice}.$$

$$\text{ERO} = (r^2) \times (2\pi) \times \text{aliasing velocity}/\text{Vmax peak MR velocity}.$$

r is the PISA radius and π is equal to 3.14. Vmax is the peak MR velocity measured by continuous-wave Doppler. The ERO was estimated at systolic time and from the view where PISA was clearer and larger displayed. MR was estimated as severe if ERO >0.4 cm^2.

3.2 | 3DTEE assessment

MR quantification was performed using the multiplanar imaging tool (QLAB software), which displays three planes of 2D echo simultaneously.

Two orthogonal image planes parallel to the regurgitant jet direction were manually cropped across the regurgitant jet; a third cropping plane, which was perpendicularly oriented to the jet direction, was 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 VC in systole was magnified, and VCA was measured by direct planimetry of the color Doppler flow signal. To analyze the circularity of the regurgitant orifice, the ratio of the long axis to the short axis of VCA (L/S ratio) was calculated.

A sphericity index was calculated using the ratio of the major axis to the minor axis of the VC. By direct mapping (VCA planimetry), VCA was measured at the transverse plane (Fig. 1, lower right quadrant). The average VCA (VCA av) was derived from two orthogonal VC diameters. As in 2D echo, the 3D VC was measured at an anteroposterior mitral valve axis and compared to the 2D VC values.

The regurgitant jet number per patient was determined in all patients (Fig. 2). In case there were more than one jet, we performed VCA planimetry of each jet and added them together to obtain the total VCA (total VCA planimetry, Fig. 3).

4 | STATISTICS ANALYSIS

A prospective cross-sectional study was conducted.

The quantitative variables were expressed as mean ± standard deviation or medium and interquartile range according to their distribution. Categorical variables were reported as percentages.

Comparisons of categorical variables were made through simple chi-square test. An alpha of <.05 was defined to accept statistical significance.

Agreement was evaluated with Bland and Altman method and Lin coefficient.

5 | RESULTS

Our study included 27 patients (14 men, 13 women; mean age 60.9 ±14. 9 years). Fourteen patients had degenerative mitral valve

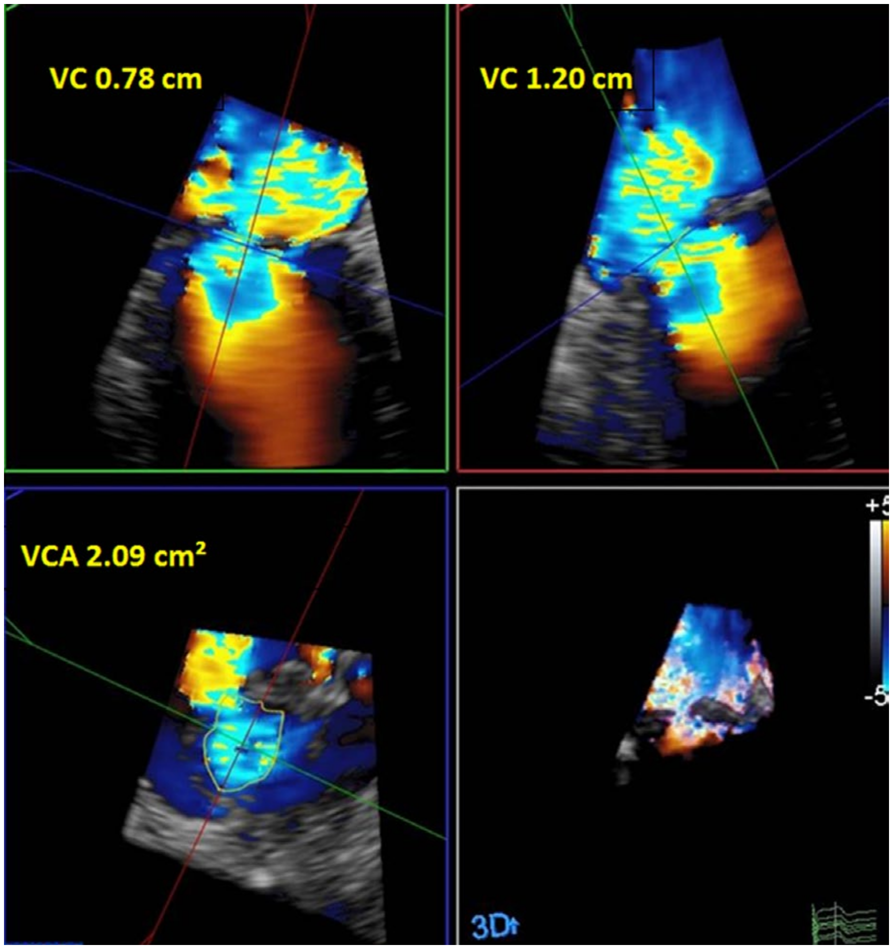

FIGURE 1 Capture color with 3DTEE: measurement of VCA planimetry and major/minor diameters of VC in Barlow's disease. Observe the morphology of the PFC and measurement of diameters of the VC in longitudinal and orthogonal planes. The lower right quadrant (transverse plane) shows the VCA by direct planimetry measurement

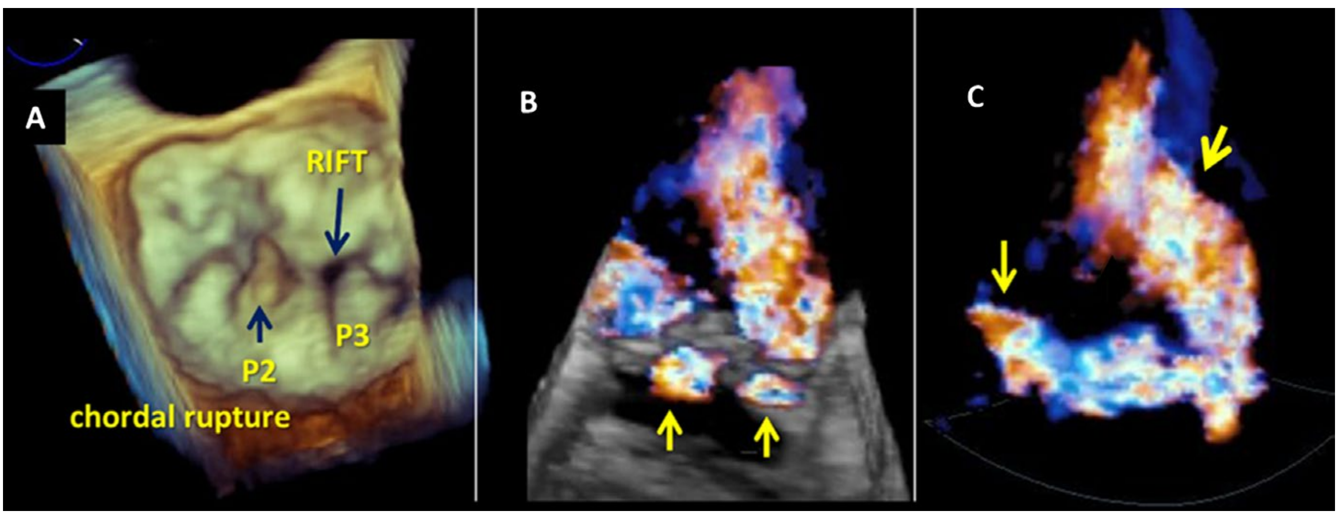

FIGURE 2 3DTEE color Doppler in a patient with two different mechanisms of mitral regurgitation. **A.** 3DTEE live capture. **B.** 3DTEE color capture finds two PFC (arrows) clearly visible and with the possibility of independent analysis in patient with chordal rupture of posterior leaflet (at the level of the P2 segment) and a rift segment P3 (degenerative disease) **C.** Two jets of different origin and direction with 3DTEE color capture

disease, type II Carpentier classification: five patients with chordal rupture, three with Barlow's disease, and two status postsurgical repair, while eight patients had type III Carpentier disease: one status postmyocardial infarction, two with a history of endocarditis, and one with congenital mitral cleft. Twenty-one of 27 (77%) had surgical mitral valve repair/replacement for severe MR.

Patient characteristics, including hemodynamic data and echocardiographic measurements, are shown in Table 1.

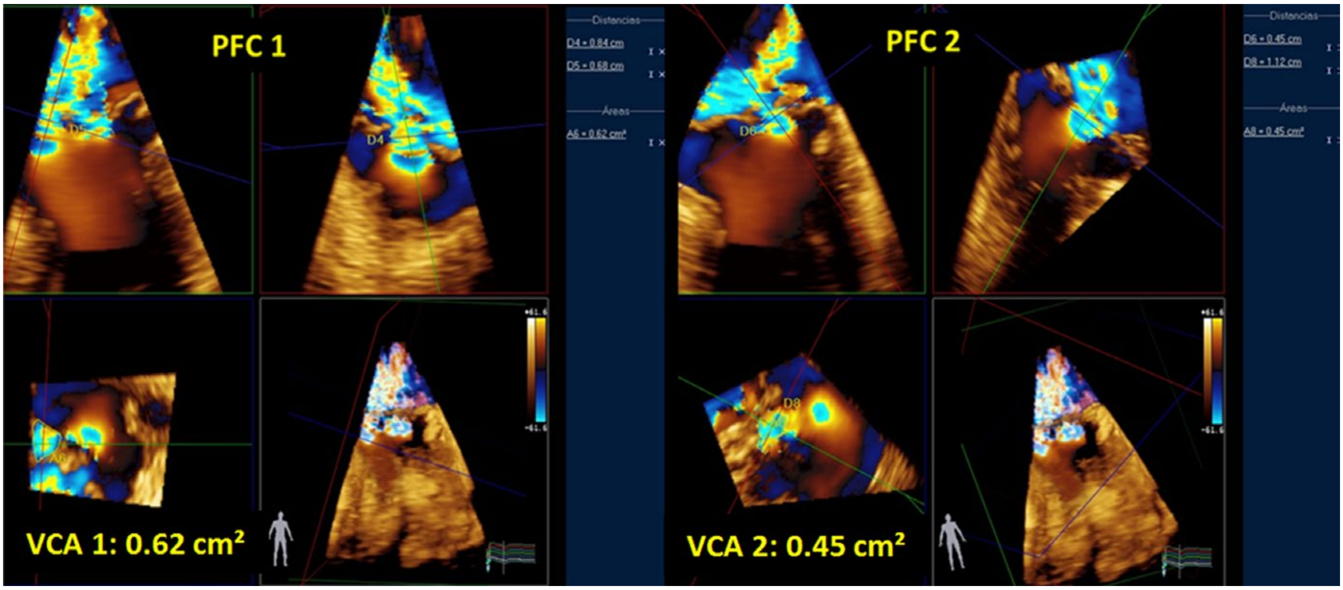

FIGURE 3 3DTEE captures color in a patient with several rupture chordae. Total VCA is the sum of VCA 1 + VCA 2 (1.07 cm^2)

TABLE 1 Clinical features and echocardiographic findings of population

Parameter	N total = 27
Asymptomatic % (n)	37 (10)
Dyspnea % (n)	51.8 (14)
Heart failure % (n)	11 (3)
AF % (n)	40.7 (11)
LVEDD/bs mean±standard deviation	32±5
LVEDD/bs >3.0 [a] 3.6 [b] %	100%
LVSD/bs mean±standard deviation	20±6.8
LVSD/bs >2.1[a]/2.5[b] % (n)	49.9% (11)
Fey <50%	21.4% (3)
VFSLV mean±standard deviation	70.1±50
VFSLV/bs >3.1[a]/2.4[b] % (n)	64.7% (11)
VFDLV mean±standard deviation	149±65
VFDLV/bs >74 [a] / 61 [b] % (n)	70.5 (12)
Vol LA/bs >48 [c] % (n)	82.3 (14)
Mitral annulus (ETE3D QLAB) cm^2 area [d]	12.5 (±3.8)
Anteroposterior mitral ring diameter mm	37.9 (±5.6)
Mitral ring intercommissural diameter mm	40.8 (±7.1)

AF, atrial fibrillation; LVEDD/bs, diastolic left ventricular diameter corrected by body surface; LVSD/bs, systolic left ventricular diameter corrected by body surface; Fey, ejection fraction; VFSLV/bs, volume of end of systole of the left ventricle fixed body surface; VFDLV/bs, volume of end of diastole of the left ventricle fixed body surface; Vol LA/bs, left atrial volume fixed by body surface area.

[a]Upper limit of normal for men.

[b]Upper limit of normal for women.

[c]Criteria for severely dilated left atrium (both sexes) according to parameters of quantification recently published[10]

[d]Mitral annular area by normal 3DTEE according to our laboratory <of 7.07 cm^2.[11]

5.1 | 2D assessment

VC diameter by TTE (LAP) was 0.60 ±0.13 mm and by TEE (three-chamber apical view) was 0.64±0.15 mm. The ERO by TTE (PISA) was 0.50 ±0.18 cm^2 and by TEE was 0.52 ±0.20 cm^2.

5.2 | 3DTEE assessment

We were able to measure the VC diameter and perform VCA planimetry (3DTEE) in all cases. Mean minor VC diameter was 0.56±0.20 mm, while average (major and minor axis) VC diameter was 0.85±0. 26 mm. Mean VCA by average of orthogonal planes was 0.62±0.40 cm^2 and VCA direct planimetry was 0.82±0.37 cm^2. Nineteen (70%) patients had more than one PFC while in 11 of 19 (57.9%) patients was able correctly to individualize each PFC and measured VC and VCA (Fig. 4). Total VCA planimetry (Σ of each VCA) was calculated as 0.92±0. 32 cm^2. The sphericity index of the VC was 2.08±0. 72 (Fig. 5).

5.3 | Comparison between 2D and 3D quantification methods

There was good agreement between 2D methods, whereas 2D and 3D methods had poor agreement owing to an underestimation of VC and ERO values by 2D echo (Table 2).

6 | DISCUSSION

2D echocardiographic quantification of MR by PISA method assumes that the ERO is circular. Nevertheless, 3D assessment has demonstrated that true ERO is not circular but linear and amorphous and in many cases divided into multiple orifices.[5–8]

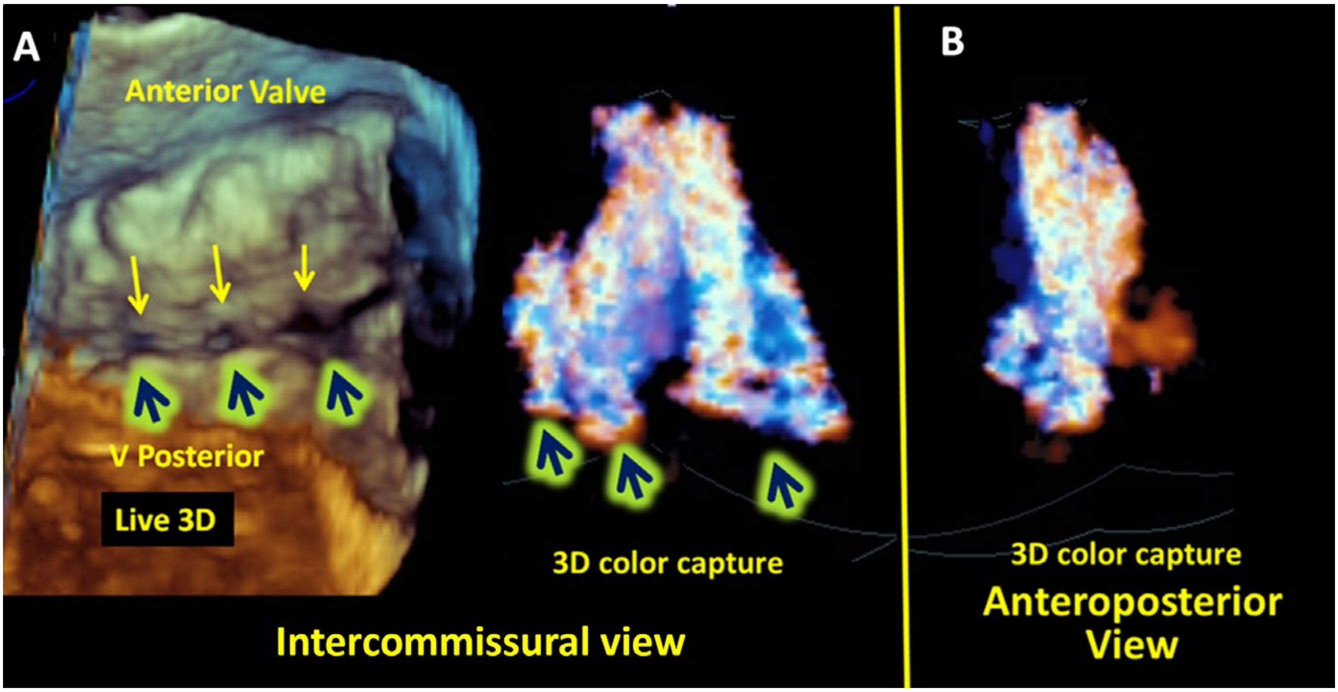

FIGURE 4 Barlow's disease with 3 visible PFC. Observe the (**A**) intercommissural view (arrow) in the 3 PFC capture with 3DTEE color correlated with three regurgitant orifices visible to the naked eye in the 3DTEE image of right (3DTEE Live). On the left in (**B**) anteroposterior view of the 3DTEE color the PFC seems to be less narrow

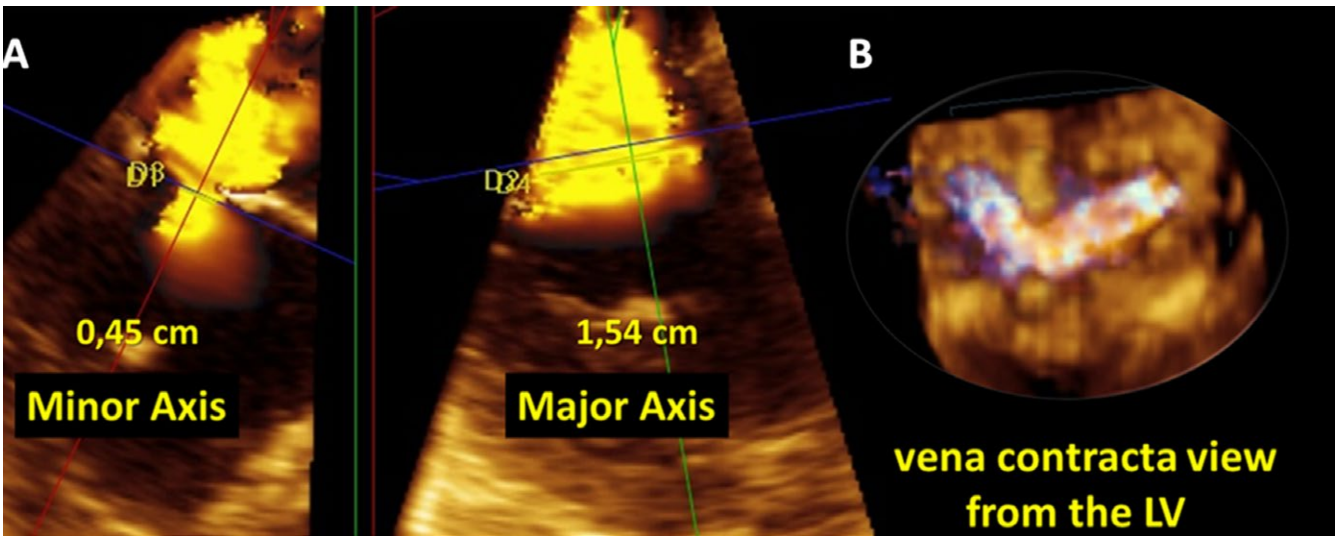

FIGURE 5 **A**. 3DTEE capture color: Observe the marked difference between diameters major and minor of longitudinal and orthogonal planes, in patient with degenerative disease. **B**. Shows not spherical appearance of the FPC and morphology not circular of the vena contracta view from the LV (transverse plane)

In the present study, we obtained VC values (area and orthogonal diameters) by 3DTEE without assuming geometries. This quantification technique was quick and feasible.

VCA size and morphology assessment by 3D color Doppler constitutes an approximation of the ERO. In the present study, sphericity index confirmed that the shape of the VC was not circular (Fig. 5).

The latter finding reflects what is observed in daily practice: the regurgitating orifice has a diverse and tough-to-classify morphology, which explains the lack of agreement between the VCA by 3DTEE and the ERO by 2D. On the other hand, to quantify MR by 2DTTE or TEE, VC was measured only in an anteroposterior diameter, which theoretically corresponds to its narrow profile. In addition, there was no concordance between the VC measured at the anteroposterior view by 2DTTE or 2DTEE when compared to the average VC diameter by 3DTEE. The latter findings may be due to the fact that the MR jet crosses the regurgitant orifice with

TABLE 2 Agreement among 2D ETT, 2D TT3, and 3DTEE

Measurement	CI 95% Bland and Altman Agreement	Lin coefficient
VC 2DTEE (mm) vs VC 2DTTE	−0.25 to 0.17	.67
VC 3DTEE (mm) vs VC 2DTTE	−0.38 to 0.32	.14
VC 3DTEE (mm) vs VC 2DTEE	−0.27 to 0.43	.14
ERO 2DTEE cm^2 vs ERO 2DTTE	−0.28 to 0.20	.78
ERO 2DTTE vs AVC* 3DTEE	−0.897 to 0.218	.30
ERO 2DTTE vs AVC av AVC	−0.825 to 0.074	.20
Total AVC planimetry cm^2 vs ERO TTE 2D	−0.887 to −0.011	.23

VC, vena contracta; 2DTTE, two-dimensional transthoracic echocardiography; 2DTEE, two-dimensional transesophageal echocardiography; 3DTEE, three-dimensional transesophageal echocardiography; AVC, area of vena contracta; ERO, effective regurgitant orifice; AVC, area of vena contracta planimetry; av AVC, average orthogonal diameters

variable angulation and thereby, it is difficult to define by theoretical models.

Probably one of the most useful findings during MR assessment with 3D color flow reconstruction is the display of more than one jet with its corresponding and independent proximal convergence flow. In those cases, the VCA was accurately measured separately by mapping each area. The summation of these areas determined the total VCA. We believe that such degree of precision is not feasible by 2D methods and it is likely the cause for underestimation.[9,12]

Defining a gold standard for MR quantification constitutes a major challenge. In the present study, ERO by PISA as well as the 2D VC diameter was not taken as a reference owing to the theoretical error of assuming a circular orifice.

In this population, a large proportion of patients underwent surgical valve repair/replacement (77%), showing severe remodeling of the left atrium, LV, and mitral ring, which reflects the degree of MR severity and chronicity. On the other hand, only 19% of patients had a 2D VC diameter >7 mm, highlighting how the use of a single VC assessment will likely reduce the echocardiographic sensitivity. In that venue, ERO measured by PISA (both TTE and TEE) performed better than VC, identifying 69% of patients with severe MR (ERO>0.4).

There was also no agreement between the direct VCA measurement by 3DTEE and the 2D ERO. As previously stated, 3D technique should be more precise as it does not assume geometries in their calculation. Currently, there are no 3DTEE cutoff values for MR severity; direct VCA measurement is likely to be more useful for surgical decision making. Such decision is typically the result of the interplay of imaging and clinical findings along with therapeutic strategies.

Other investigators have also measured the 3D VCA, but they have used TTE. In the study by Zeng et al., an VCA cutoff value of 0.41 cm^2 was identified in patients with moderate to severe MR, demonstrating optimal sensitivity and specificity. Nonetheless, that study used 2D echo as gold standard. Kahlert et al. found significant VC asymmetry by TTE, while they did not measure multiples VCA as we found with TEE. TTE requires an optimal acoustic window and only allows measurement of single VC.

Currently, there is no standardization of MR grading by 3DTEE, this methods appears more reliable and should be used to base therapeutic decisions.

6.1 | Limitations

Spatial resolution and temporary capture of color 3DTEE is still suboptimal, which could overestimate MR quantification. The presence of atrial fibrillation, high in this patient subset, impairs the ability to perform 3D color volume capture.

7 | CONCLUSIONS

Mitral valve assessment by 3DTEE was feasible and demonstrated poor agreement with 2D echo. The use of 3DTEE allowed evaluation of multiple VCA, defining in greater detail the morphology of the regurgitant orifice. Such detailed assessment may change surgical indications as well as its approach (mitral valve replacement versus repair, surgical versus catheter-based).

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How to cite this article: Lombardero, M., Henquin, R., Perea, G., Corneli, M. and Izurieta, C. (2016), True morphology of mitral regurgitant flow assessed by three-dimensional transesophageal echocardiography. Echocardiography, 1–7. doi: 10.1111/echo.13395