Volumetric Measurement of the Anatomic Regurgitant Orifice Area in Mitral Regurgitation: Comparison with Two-Dimensional Flow Convergence Analysis

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Abstract

Mitral effective regurgitant orifice area (EROA) using the flow convergence (FC) method is the current method of choice for quantifying the severity of mitral regurgitation (MR). However, this methodology has limitations, especially in patients with complex mitral valve (MV) pathology. The superior image quality of the transesophageal real-time 3D echocardiography (RT3D-TEE) offers an opportunity for direct visualization and 3D measurement of the anatomic regurgitant orifice area (AROA). Accordingly, we developed a 3D technique to measure AROA from RT3DE-TEE datasets and compared it with the conventional FC derived measurements of EROA. We studied 61 patients, undergoing clinically indicated TEE, with well visualized FC. ROA calculations obtained from TEE images using FC technique (EROA); and zoomed RT3DE-TEE acquisitions using prototype software for direct 3D orifice area measurements (AROA) correlated well (r=0.81) and showed only a non-significant bias (0.05 cm²). In conclusion, visualization of the true, anatomic MV orifice area from RT3DE-TEE images is feasible in most patients. 3D volumetric analysis of AROA may become a useful alternative to quantify MR in patients in whom EROA measurement by FC technique is challenging.

1. Introduction

Effective regurgitant orifice area (EROA) based on vena contracta estimation is currently used to quantify the degree of mitral regurgitation (MR). However, unlike 2D planimetry of mitral and aortic stenotic valves, in patients with MR, planimetry of the regurgitant orifice area is not feasible because of the complex, nonplanar 3D geometry of the regurgitant orifice. Indirect measurements are used to determine the EROA using Doppler measurements of the proximal flow convergence (FC) [1,2]. Unfortunately, these techniques are prone to error because of the assumptions regarding MV geometry and flow, especially in settings of distorted MV geometry [3-5].

In contrast to 2D echocardiography, real-time 3D echocardiography (RT3DE) using matrix 3D transesophageal (MTEE) technology, with its improved spatial resolution, has resulted in enhanced visualization of the valvular pathomorphology. In addition to precisely identifying the location of the prolapsing or restricted scallop and the origin of the regurgitant jet, RT3DE allows direct 3D visualization of the anatomic regurgitant orifice. Accordingly, we hypothesized that MTEE images could provide the basis for accurate and reproducible volumetric quantification of the anatomic regurgitant orifice area (AROA) and may serve as an alternate method to quantify MR in settings of challenging and complex MV anatomy. To test this hypothesis, software was developed for quantitative 3D volumetric measurement of AROA, which takes into account its complex 3D geometry, rather than using planimetry in a single cut-plane. The goals of this study were to: (i) quantify AROA in patients with MR using this software, (ii) compare volumetric AROA values to 2D FC EROA measurements in the same patients, and (iii) compare the reproducibility of these 2 techniques.

2. Methods

2.1. Population

61 patients undergoing clinically indicated TEE were studied (age 59±10 yrs, 36 males). Exclusion criteria were: poor 3D images precluding analysis, prosthetic valves and/or post-MV repair, and poorly visualized FC. Of these 61 patients, 38 had eccentric MR jets, and 23 had central MR of either ischemic or dilated etiology.

2.2. Imaging

The clinical portion of the 2D TEE exam was performed according to standard protocol. The proximal FC zone was optimized by shifting the baseline of color Doppler aliasing velocity. The radial distance (r) between the first aliasing contour (red/blue interface) and the center of the regurgitant orifice was measured at the time of the largest convergence image. Then, RT3DE imaging of the MV was performed using an iE33 ultrasound system (Philips), equipped with an MTEE transducer (X7-2t). Zoomed RT3DE images of the MV were acquired in a single cardiac cycle. Care was taken to include the entire MV apparatus in the scan volume.

2.3. Image analysis

Images were reviewed and analyzed offline on an Xcelera workstation (Philips). The FC was performed using standard methodology. In the presence of multiple MR jets, the best visualized largest jet was used for quantification.

The 3D analysis of maximal AROA was performed using custom software (MVQ, Philips). First, the annulus was manually initialized by defining annular points in multiple planes rotated around the axis perpendicular to the mitral annular plane (figure 1A). Then, the annulus was segmented to identify leaflet geometry and coaptation points by manually tracing the leaflets in multiple parallel long-axis planes spanning the annulus from commissure to commissure (figure 1B). The resultant 3D coaptation line and the reconstructed annulus were displayed on the original 3D image and as a color-coded 3D rendered surface representing a topographical map of the mitral apparatus (figure 1C). In patients with MR, an area of mal-coaptation visualized as an interruption of the leaflet coaptation line (figure 2B) was not traced, resulting in a 3D regurgitant orifice, which was then automatically measured in 3D space. Since the orifice boundary is not planar, a minimal 3D surface area was computed numerically by solving an approximation to the "stretched membrane"- biharmonic equation. In cases of multiple orifices, AROA was automatically calculated as the sum of areas of individual orifices.

2.4. Inter-technique comparisons

3D volumetric AROA measurements were compared with the 2D FC values using linear regression and Bland-Altman analyses. These comparisons were performed for the entire group of 61 patients with MR, and separately for the two subgroups of eccentric and central MR.

2.5. Reproducibility analysis

For both techniques, reproducibility was assessed in 20 patients, including 10 patients from each subgroup. Intra-observer variability was assessed using repeated measurements performed by the same observer a month later. Inter-observer variability was evaluated by repeating the analysis by a second independent observer, blinded to the results of prior measurements. Variability was defined as the absolute difference between repeated measurements in percent of their mean.

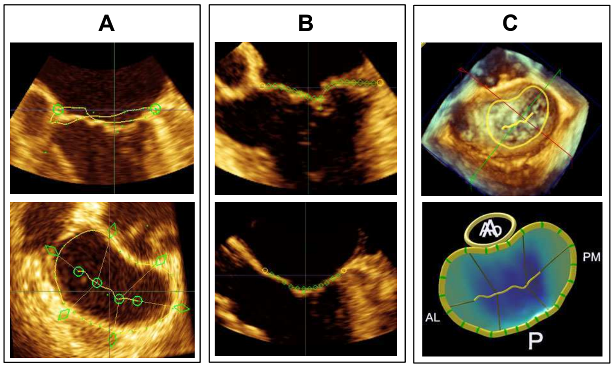

Figure 1. Volumetric analysis of maximal anatomic AROA (MVQ software) in a patient with normal mitral valve. (A) after mitral annulus is manually initialized in multiple rotated planes and interpolated (top), the resultant 3D contour is superimposed on the en-face view of the valve (bottom) to allow visual assessment of annular shape and adjustments; (B) MV leaflets are manually traced from commissure to commissure in multiple parallel planes; (C) the coaptation line is then generated from these tracings and displayed on the original 3D image (top) and as a color-coded 3D rendered valve surface (bottom).

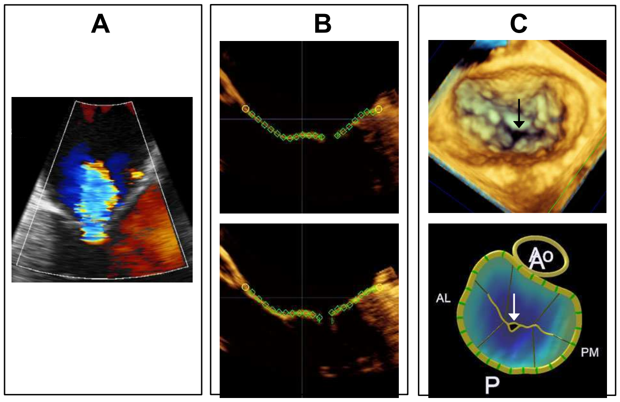

Figure 2. Volumetric analysis of AROA in a patient with in a patient with central MR: (A) Flow convergence. (B) MR is a result of an area of leaflet mal-coaptation visualized as an interruption of the leaflet coaptation line, yielding a 3D regurgitant orifice as seen on en-face 3D view of the valve from the left atrial perspective (C, top). This interrupted coaptation line as well as the reconstructed annulus were displayed as a color-coded 3D rendered surface representing a topographical map of the mitral apparatus (C, bottom).

3. Results

Figure 2 shows an example of a patient with central MR. In this patient, the FC demonstrated a single central MR jet, likely secondary to annular dilatation, which was confirmed visually by the 3D images and quantitatively by the 3D volumetric analysis of AROA. Figure 3 shows an example of a patient with eccentric MR, including the FC, the en-face 3D view of the valve and the color-coded 3D rendered valve surface. While 2D Color Flow Doppler allowed high quality visualization of the eccentric MR jet, the 3D images allowed the determination of a flail leaflet as the cause of MR and the 3D volumetric analysis increased the level of confidence in determining its severity. Figure 4 shows an example of a patient with Barlow's disease, in whom 2D color-Doppler showed two regurgitant jets, originating from two separate orifices clearly visualized in the 3D images. Volumetric AROA measurement reflected the contribution of both orifices, which was challenging with 2D FC technique.

In the group of 61 patients with MR, FC measurement of EROA ranged from 0.07 to 0.98 cm² (mean: 0.41±0.20 cm²). Volumetric AROA measurements resulted in a range of 0.08 to 0.96 cm² (mean: 0.46±0.21 cm²). Measurements correlated well between the two techniques (r=0.81) and showed a small positive bias (0.05 cm²). In the 38 patients with eccentric MR, FC measurements of EROA ranged from 0.10 to 0.90 cm² (mean: 0.47±0.21 cm²), and in the 23 patients with central MR from 0.07 to 0.56 cm² (mean: 0.31±0.14 cm²). AROA measurements resulted in a range of 0.08 to 0.96 cm² (mean: 0.53±0.22 cm²) in the patients with eccentric MR, and from 0.11 to 0.63 cm² (mean: 0.35±0.15 cm²) in the patients with central MR. Comparing both groups, AROA and FC measurements correlated better in patients with central MR (r=0.76 for eccentric MR and r=0.86 for central MR). In addition, the bias was larger in the eccentric (0.06 cm²) than central MR group (0.04 cm²), and the limits of agreement were almost twice as wide in patients with eccentric MR (figure 5).

Table 1 summarizes the results of the reproducibility analysis in the two subgroups of patients with central and eccentric MR jets. First, as expected, in both groups, for both techniques, the inter-observer variability was higher than the intra-observer variability. Second, the reproducibility of the 2D FC measurements was lower (higher variability) than that of the 3D volumetric AROA. In addition, the reproducibility was lower in the eccentric compared to central MR group, as reflected by higher variability levels in the former group, with the exception of inter-observer variability of the FC technique.

		Central MR	**Eccentric MR**
Inter-observer	**2D FC**	19±11	19±15
	3D AROA	14±12	11±6
Intra-observer	**2D FC**	16±11	14±8
	3D AROA	12±9	9±5

Table 1. Reproducibility of effective regurgitant orifice area (EROA) using the 2D flow convergence (FC) technique and 3D analysis in two subgroups of patients with central and eccentric MR jets (N=10 each).

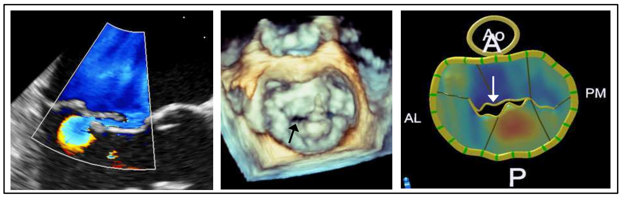

Figure 3. Patient with eccentric MR with a flail P2 scallop showing the FC (left), en-face 3D view of the valve from the left atrial perspective (middle) and the color-coded 3D rendered surface (right), both depicting the anatomic regurgitant orifice (arrows) and the flail leaflet partially covering the orifice in the 3D view.

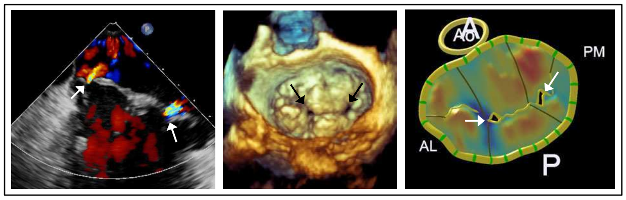

Figure 4. Patient with Barlow's disease and multi-segmental prolapse, depicting two separate regurgitant jets (left, arrows). Individual orifices are noted in 3D (middle) and quantified by the 3D volumetric analysis (right).

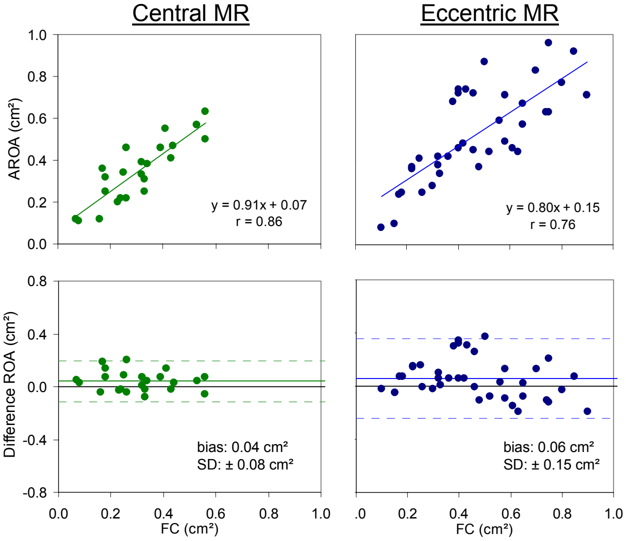

Figure 5. Results of the comparisons between the measurements of AROA and EROA. Linear regression (top) and Bland Altman analyses (bottom) for the 23 patients with central (left) and 38 patients with eccentric (right) MR jets. Solid horizontal lines show the mean difference (bias), dashed horizontal lines show the limits of agreement (±2SD around the mean).

4. Discussion and conclusions

EROA is widely used in clinical laboratories as a measure of MR severity. FC, which correlates well with other measures of severity of MR obtained with quantitative Doppler echocardiography or angiography [2,6], is currently the method of choice for calculating EROA. However, the FC method is known to be limited by geometric and technical factors particularly, in the presence of distorted mitral valvular geometry. FC calculation is based on the geometric assumption that the isovelocity shell is hemispherical. This is usually true for a point source of regurgitation in axisymmetric flow. Indeed, the results of our study supported this principle by demonstrating a higher correlation between 3D and FC measurements in patients with central MR jets. Also, FC requires operator expertise to setup the machine and to find the spherical shell, which is at times difficult.

This study demonstrated that volumetric quantitative measurement of AROA is feasible even in patients with complex MV pathology, including those with flail, overlapping leaflets and eccentric jets. Overall, these measurements correlated well with the 2D FC values, but the correlation was higher in patients with central MR jets. Our results showed that 3D volumetric quantification of AROA resulted in a positive bias, with slightly larger orifice area values compared to FC. This probably reflects the physical differences between the two methods. The potential advantage of the AROA technique is that it directly measures the true anatomic orifice in 3D, whereas the FC method relies on the quantification of the narrowest flow emerging from the orifice, which is expected to be smaller by the coefficient of contraction [7]. In addition, there can be significant variability in repeated FC measurements, particularly in cases of eccentric jets. In contrast, the 3D measurements can be expected to be less affected by the aforementioned constraints. Indeed, our study demonstrated this added advantage of improved reproducibility of the AROA measurements compared to the FC measurements in patients with both central and eccentric jets.

One of the limitations of this study is the lack of a “gold standard” reference technique for the measurement of the regurgitant orifice area in humans. With the advantages of high spatial resolution and real-time acquisition, MTEE may become an additional method for quantification of AROA in cases of distorted MV geometry. While at the current phase of development, this analysis relies on manual tracing in multiple planes and is time-consuming, a larger degree of automation is expected to further reduce analysis time as well as inter-measurement variability. Another limitation of our RT3DE TEE in its current phase of development is its relative low frame rates.

In summary, this is the first study to demonstrate the feasibility of 3D volumetric quantification of regurgitant orifice area from MTEE images in patients with both central and eccentric MR jets. The improved reproducibility of 3D volumetric AROA measurements compared to FC method, suggest that in certain cases, this new methodology may be a useful alternative to quantify the severity of MR. This may prove particularly useful in patients with multiple orifices and in patients with grossly distorted FC patterns in whom the standard geometrical assumptions may not be applicable. Future automation of the 3D AROA measurements will enhance the clinical potential of this methodology.

References

[1] Bargiggia GS, Tronconi L, Sahn DJ, 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

[2] Enriquez-Sarano M, Miller FA, Jr., Hayes SN, Bailey KR, Tajik AJ, Seward JB. Effective mitral regurgitant orifice area: clinical use and pitfalls of the proximal isovelocity surface area method. J Am Coll Cardiol 1995;25:703-9

[3] Deng YB, Shiota T, Shandas R, Zhang J, Sahn DJ. Determination of the most appropriate velocity threshold for applying hemispheric flow convergence equations to calculate flow rate: selected according to the transorifice pressure gradient. Digital computer analysis of the Doppler color flow convergence region. Circulation 1993;88:1699-708

[4] Schwammenthal E, Chen C, Giesler M, et al. New method for accurate calculation of regurgitant flow rate based on analysis of Doppler color flow maps of the proximal flow field. Validation in a canine model of mitral regurgitation with initial application in patients. J Am Coll Cardiol 1996;27:161-72

[5] 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

[6] Braunberger E, Deloche A, Berrebi A, et al. Very long-term results (more than 20 years) of valve repair with carpentier's techniques in nonrheumatic mitral valve insufficiency. Circulation 2001;104:I8-11

[7] Breburda CS, Griffin BP, Pu M, Rodriguez L, Cosgrove DM, III, Thomas JD. Three-dimensional echocardiographic planimetry of maximal regurgitant orifice area in myxomatous mitral regurgitation: intraoperative comparison with proximal flow convergence. J Am Coll Cardiol 1998;32:432-7

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