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Quantitative Assessment of Mitral Valve Coaptation Using Three-Dimensional Transesophageal Echocardiography

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Background. **Functional mitral regurgitation (FMR) occurs as a consequence of left ventricular remodeling and is an independent predictor of adverse outcome. FMR is assessed qualitatively with two-dimensional echocardiography, but accurate quantitation of the actual degree of mitral valve (MV) coaptation is not possible with this method. We evaluated a novel three-dimensional (3D) approach to quantify the MV coaptation zone in patients with FMR. We hypothesized that measuring the 3D MV coaptation zone is feasible and would correlate with FMR severity when indexed to MV area.**

Methods. **Data were gathered on 25 patients with FMR undergoing cardiac operations, and included a comprehensive two-dimensional and 3D examination with intraoperative transesophageal echocardiography. Using available 3D MV quantification software, offline analysis of end-systolic MV coaptation zone and MV area was performed. A novel MV coaptation index was calculated by the following formula: [3D end-systolic MV coaptation zone/3D MV area]. FMR severity was described as trace, mild, moderate, and severe using the integrative approach recommended by official guidelines.**

Results. **Analysis of variance demonstrated that the coaptation index was associated with the severity of FMR ($F = 20.5$, $r^2 = 0.75$, $p < 0.0001$). There was also a correlation between 2D vena contracta and the coaptation index ($r = -0.74$, $p < 0.0003$).**

Conclusions. **We describe a novel 3D approach to direct assessment of the MV coaptation zone. When indexed to the MV area, the 3D MV coaptation zone is closely associated with FMR severity. Assessment of the mitral coaptation may be a potentially powerful tool in the perioperative evaluation of the competency of the MV.**

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Functional mitral regurgitation (FMR) occurs when a structurally normal mitral valve (MV) is rendered incompetent as a result of local or global left ventricular remodeling. This failure of leaflet coaptation is caused by annular dilatation, leaflet tethering due to papillary muscle displacement, or both [1]. Increasing severity of FMR has been correlated with decreased survival [2, 3]. Although there are established guidelines for the echocardiographic assessment of FMR severity, the evaluation of the leaflet coaptation zone defined by the area of actual leaflet contact is less well established but is nonetheless critical for the intraoperative guidance of MV repair [4–8].

Decreased leaflet coaptation is mechanistically central to the pathophysiology of FMR. Poor leaflet coaptation resulting from residual leaflet tethering after MV repair predicts disease recurrence [9, 10]. Accordingly, surgeons have developed intraoperative techniques to assess leaflet coaptation [11]. The coaptation length index, defined as the ratio of coaptation length to septal-lateral diameter, is a two-dimensional (2D) echocardiographic index that correlates with the degree of residual mitral regurgitation (MR) after annuloplasty [7, 8]. However, all 2D echocardiographic approaches are fundamentally limited to one-dimensional measurements of length, due to the single planar view provided, and are prone to error given the irregular three-dimensional (3D) topography of the coaptation zone.

Improved 3D echocardiographic imaging, together with quantitative analysis software, has led to initial attempts to determine the MV coaptation zone as a 3D surface

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[5, 6, 12]. Using a canine model with staged aortic banding to induce left ventricle pressure overload, Yamada and colleagues [5] produced varying degrees of FMR. They then measured the difference between middle-systolic and end-systolic 3D MV leaflet surface areas, thus calculating a coaptation index that correlated with FMR severity [5]. The same authors applied this index in patients with dilated cardiomyopathy and demonstrated its ability to predict the presence of FMR in humans [6, 12].

An alternative 3D approach described by Gogoladze and colleagues [13] relies on the analysis of leaflet coaptation lengths in three different valve regions along the coaptation line, which correlated with FMR. Differences in coaptation length between MVs of normal vs FMR patients were most pronounced in the A2-P2 region than in the A1-P1 or A3-P3 regions.

Building on these concepts, we describe a novel 3D approach that directly measures the actual area of the mitral leaflet coaptation zone rather than relying on indirect methods of subtracting leaflet areas measured at different times throughout the cardiac cycle. We hypothesized that the mitral leaflet coaptation zone could be measured and would correlate with the severity of FMR when indexed to the total end-systolic MV surface area.

Material and Methods

After institutional review, we retrospectively identified 25 patients from the Duke perioperative echocardiographic database between June 2008 and November 2010. Patients with varying degrees of FMR and a comprehensive 2D and 3D echocardiographic examination with images of the MV were included. Patients with concomitant MV leaflet prolapse or flail leaflets were excluded. Echocardiographic images were obtained using the 3D transesophageal echocardiography xMatrix transducer (X7-2t and IE33 system; Philips Medical Systems, Andover, MA). 3D mitral valve images reviewed included full-volume and 3D zoom acquisitions. Full-volume images were used preferentially when both were available unless there were stitch artifacts.

Measurement of the Coaptation Zone and the Coaptation Zone Index

Each 3D data set was exported to an offline Image Arena software workstation (4D Mitral Valve assessment software; TomTec Imaging Systems, Unterschleissheim, Germany) for analysis. End-systolic 3D models of the MV were generated following the workflow of the imaging software. Rotational cross-sections centered at the anterior horn of the MV annulus were used to delineate the coaptation line (Figs 1A, 1B). For each model, the atrial and ventricular mitral coaptation lines were defined by using sequential pairs of atrial and ventricular coaptation points. Each pair of coaptation points defined a unique coaptation length. Pairing these coaptation lengths with neighboring coaptation lengths defined the boundaries of coaptation subareas. Excel software (Microsoft, Redmond, WA) was used to compare each subarea individually computed from the x, y, and z coordinates of each point. The entire coaptation zone for each MV then was calculated by summing the individual subareas.

The exact position of each coaptation point was decided upon by visually tracking the MV leaflets as they opened and closed in a magnified view. By using magnification, chordal tissue could generally be differentiated from leaflet tissue by the echodensity of the tissue, leaflets generally being more echodense. Of note, the ventricular coaptation point did not necessarily correspond to the leaflet tips. In cases of tethering and papillary muscle displacement, the leaflet tips appeared to be pulled away from the coaptation zone. The number of subareas created depended on the coaptation zone's topography and the overall size of the valve. More topographically

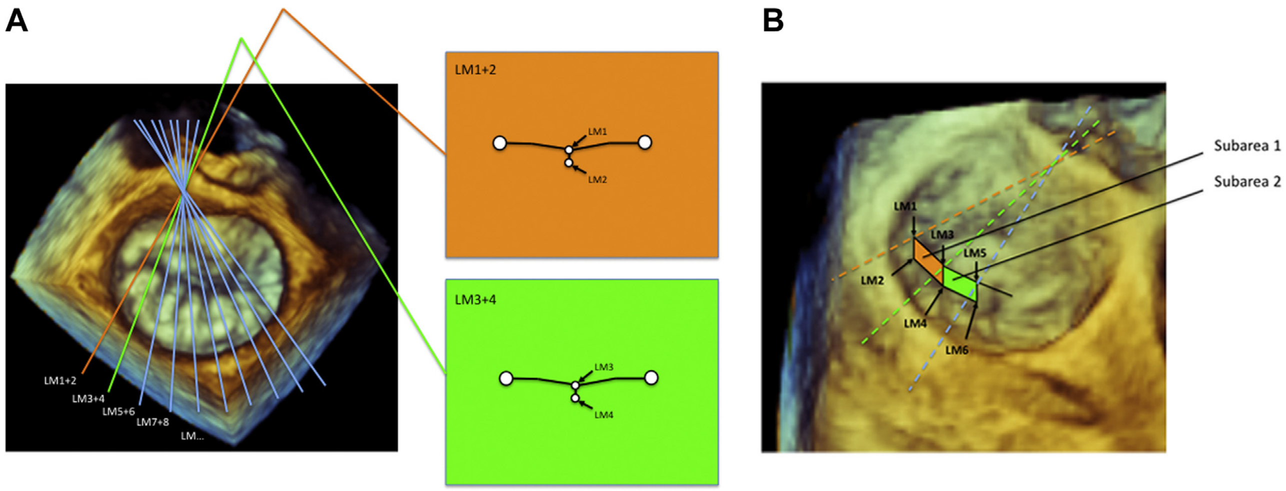

Fig 1. (A) For each valve, the three-dimensional mitral valve coaptation zone was determined by defining a large series of coaptation lengths within rotational cross-sections, centered on the aortomitral junction. (B) These pairs of points in space were used to create individual subareas. The sequential subareas were added to achieve the total mitral valve coaptation zone. (LM = landmark.)

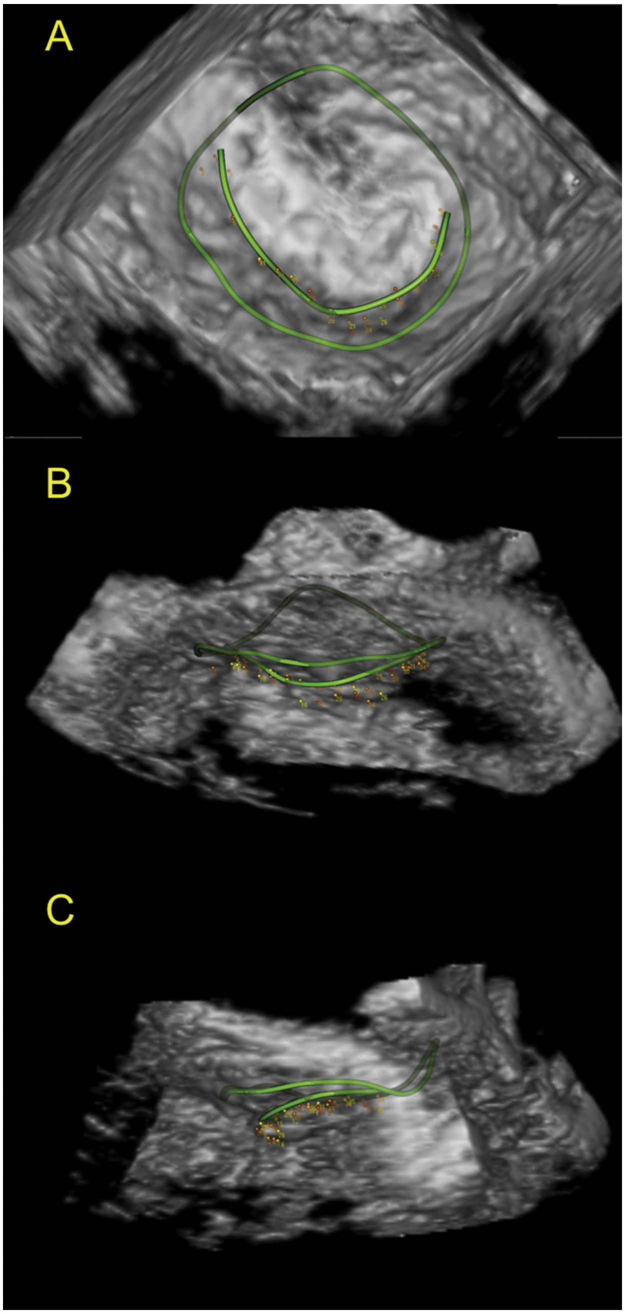

Fig 2. Screen shots show the three-dimensional (3D) model of the mitral valve coaptation zone from the (A) surgical view and (B) from a posterior and (C) a posterior-medial commissural position. The green lines represent the annulus and the coaptation line. The yellow and orange dots depict the multitude of x, y, and z coordinates used to define the individual subareas and the larger coaptation zone.

complex coaptation zones required smaller and, hence, more numerous subareas to capture their unique geometry. Regurgitant orifices were incorporated in the models by reducing the distance between pairs of points to a minimum, thus creating infinitesimal coaptation lengths. For quality assurance and to assess the appropriateness of the coaptation points chosen, the final series of coaptation points in each model was reviewed in 3D before the coaptation zone was calculated (Fig 2A–C).

We then measured the end-systolic MV area as viewed from the left atrial perspective using dedicated MV software (MVQ, QLAB 7.0; Philips Medical Systems) for each of the 25 valves. This software enabled us to independently measure the anterior and posterior MV leaflet areas for the same end-systolic frame that was used to determine the coaptation zone (Figs 3A, 3B). Anterior and posterior MV leaflet areas were summed to obtain a total MV area. By dividing the previously measured coaptation zone by the MV area, we produced a dimensionless coaptation zone index that could then be used to compare individual valves.

Grading Severity of Mitral Regurgitation

A certified echocardiographer, blinded to the coaptation zone index, graded the severity of MR in the 25 patients by using all available American Society of Echocardiography criteria [4]. At a minimum, jet area and, when available, 2D vena contracta width (VCW) were used. The coaptation zone and the coaptation zone index were compared with the overall severity grade of MR and the VCW.

Statistical Methodology

The association between the coaptation zone index and the MR severity score was assessed with a one-way analysis of variance. MR severity was graded according to the standard categories of trace, mild, moderate, and severe. The association between the coaptation zone index and VCW was assessed with a Pearson correlation because both are continuous variables. An identical analysis was done for the coaptation zone without it being indexed. All analyses were conducted using SAS 9.1.3 software (SAS Inc, Cary, NC). Significance was assessed at a p value of less than 0.05.

Results

Baseline preoperative characteristics of the studied patients are outlined in Table 1. Data for the 2D VCW were missing for 6 of 25 patients in this data set. These are patients in whom the degree of intraoperative MR was trace ($n = 5$) or mild ($n = 1$), and thus, the intraoperative TEE did not include a designated assessment of the 2D VCW based on color Doppler. In the remaining set of 19 patients, VCW ranged from 0.1 to 0.9 cm. End-systolic 3D models of the MV were successfully generated in all 25 patients, and all 4 MR severity grades were represented. Our approach used rotational cross-sections centered at the anterior horn of the MV and proved suitable to delineate the coaptation zone by identifying a large number of atrial and ventricular coaptation points. The number of subareas used to describe the coaptation zones in the 25 patients ranged from 15 to 25. Generation of the 3D model and assessment of the coaptation zone of an individual MV took a minimum of 3 hours. Given the labor-intensive and time-consuming process,

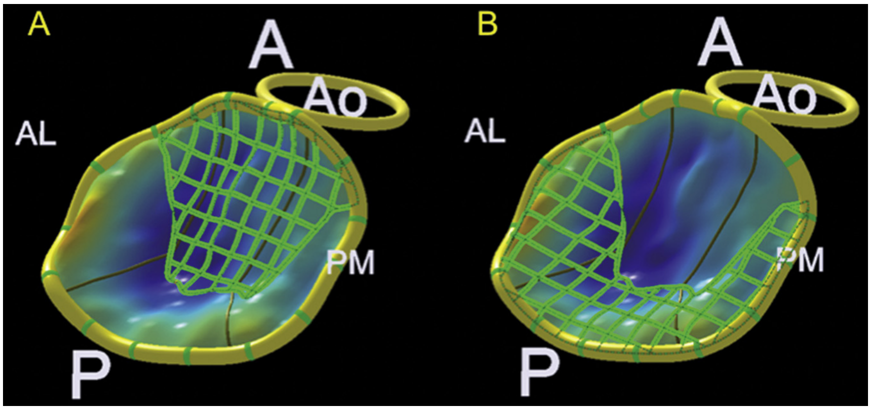

Fig 3. Three-dimensional model of a mitral valve demonstrates the calculation of the total valve area used to produce the dimensionless coaptation zone index. (A) The exposed leaflet area of the anterior mitral valve leaflet and (B) the exposed leaflet area of the posterior mitral valve leaflet, both at end systole, are illustrated. (A = anterior; AL = anterolateral commissure; Ao = aortic valve; P = posterior; PM = posteromedial commissure.)

assessments were not done in replicates, and intraobserver or interobserver variability was not assessed.

Analysis of variance for the 25 patients demonstrates that the coaptation zone index was associated with the severity grade of FMR ($F = 20.5$, $r^2 = 0.75$, $p < 0.0001$; Fig 4A). The coaptation zone index and the VCW were also significantly correlated ($r = –0.74$ $p < 0.0003$; Fig 4B). In contrast, the coaptation zone, when not indexed to the MV area, was neither associated with the severity grade of MR ($F = –1.06$, $p = 0.39$) nor with the VCW ($r = –0.34$, $p = 0.15$).

Table 1. Demographics[a]

Pt	Age (y)	Sex	Operation	Ejection Fraction[b]	Carpentier Classification	Vena Contracta (cm)	Severity of Mitral Regurgitation (1–4)
1	85	M	CABG	0.25–0.35	I	0.44	3
2	73	M	MVR	0.35–0.45	III	0.62	4
3	71	F	MVP/TVP	0.45–0.55	I	0.66	4
4	51	M	CABG	0.45–0.55	I	0.28	2
5	68	F	CABG/MVP	0.45–0.55	III	0.77	4
6	63	F	CABG	0.45–0.55	I	NA	1
7	70	F	CABG	0.25–0.35	III	0.6	4
8	72	M	CABG	0.45–0.55	I	0.16	1
9	48	F	MVR/TVP	0.15–0.25	III	0.86	4
10	70	F	CABG	0.45–0.55	I	NA	1
11	61	M	CABG	0.45–0.55	I	NA	2
12	61	F	CABG	0.45–0.55	I	NA	1
13	66	F	CABG	0.15–0.25	III	0.3	2
14	67	M	AVR	0.25–0.35	III	0.35	3
15	79	M	AVR	0.45–0.55	I	0.31	2
16	48	M	CABG	<0.15	III	0.24	2
17	64	M	CABG	0.35–0.45	I	0.31	2
18	63	M	Lead removal	0.25–0.35	III	0.29	2
19	55	M	CABG	>0.55	I	NA	1
20	73	M	CABG	>0.55	I	0.15	2
21	74	M	MVP	0.25–0.35	III	0.51	4
22	58	F	MVR	0.25–0.35	III	0.29	4
23	54	F	AVR	0.45–0.55	I	0.14	1
24	73	F	MVP/TVP	0.45–0.55	III	0.32	3
25	71	M	CABG	0.45–0.55	I	NA	1

[a] The study evaluated 25 patients (10 women, 15 men), their average age was 65.5 years. [b] Patients with Carpentier classification type III valves had statistically significant lower ejection fractions than those with type I, which included normal valves ($p < 0.01$).

AVR = aortic valve replacement; CABG = coronary artery bypass grafting; F = female; M = male; MVP = mitral valve plasty (repair); MVR = mitral valve replacement; NA = not available; TVP = tricuspid valve plasty (repair).

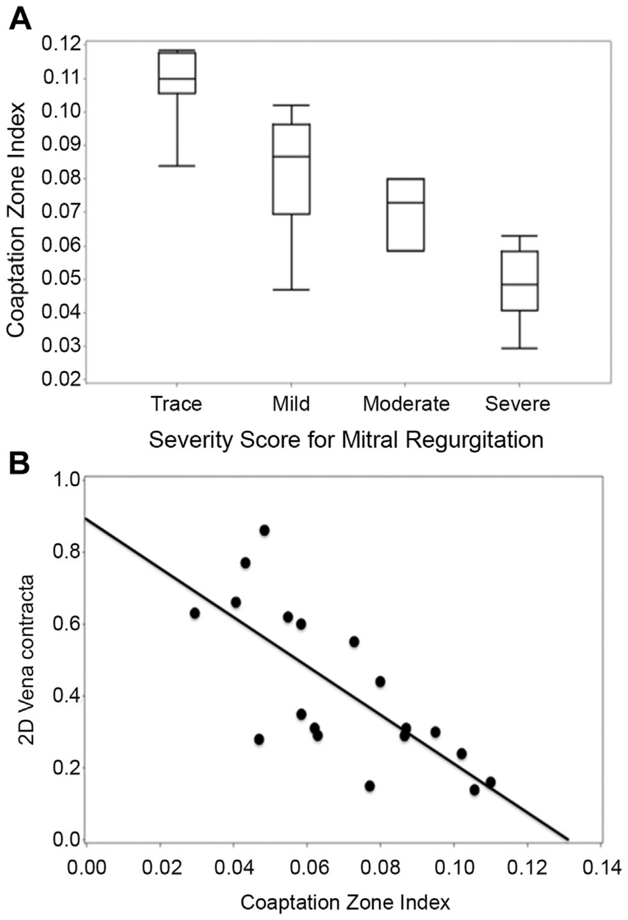

Fig 4. (A) Association between the three-dimensional (3D) coaptation zone index and the severity grade of functional mitral regurgitation as assessed with analysis of variance ($r^2 = 0.75$, $p < 0.0001$). The horizontal line in the middle of each box indicates the median; the top and bottom borders of the box mark the 75th and 25th percentiles, respectively; and the whiskers mark the 90th and 10th percentiles. (B) Association between the two-dimensional vena contracta width and the 3D coaptation zone index using a scatter plot and a best fit line as assessed with Pearson correlation ($r = -0.74$, $p < 0.0003$).

Comment

Advances in 3D echocardiography provide the perioperative echocardiographer with spectacular images and enhanced diagnostic accuracy and facilitate communication with surgeons to provide real-time procedural guidance. This study aimed to use 3D information obtained with intraoperative TEE to quantify the severity of MR and better define its anatomy by measuring the MV coaptation zone in patients with FMR. Our results illustrate the successful implementation of a 3D approach that quantifies the MV coaptation zone area. Although anatomically interesting, the absolute area of the MV coaptation zone may add information of little physiologic importance when seen in isolation but gains relevance once evaluated in relationship to the overall MV area. When indexed to the overall MV area, the MV coaptation zone correlates with the severity of FMR. This finding is consistent with 2D studies of the MV coaptation length that showed improved correlation with severity of MR when coaptation length was indexed to MV dimensions [7, 8]. Conceptually, a given coaptation zone that is sufficiently large to prevent regurgitation for a small MV may be insufficient for a MV of a much larger area.

This work introduces a novel index that describes the extent of MV coaptation in its relationship to the overall MV area. This coaptation zone index is different from other coaptation indices because it is determined from direct measurements of the MV 3D coaptation zone. Still, the overall consistency of our data with those of others who have studied mitral leaflet coaptation lends credence to our results. In a small study of 11 patients, MR was present when the 2D coaptation length index was approximately 0.2 or less [14]. In another study of 23 patients using the same 2D coaptation index, MR was present with an index of 0.11 or less [8, 15]. Using 3D technology in canine model, Yamada and colleagues [5] reported that an index of less than 0.12 relates to a sharp increase in MR severity. These experimental data are supported by similar work in humans, demonstrating that patients with dilated cardiomyopathies had a coaptation index of 0.11, which was significantly lower than that of patients with normal MV anatomy [6]. Compared with these studies, our data suggest that effectively normal valves with trace MR have indices of approximately 0.10, whereas valves with a coaptation index of less than 0.05 are associated with severe MR.

There are potential strengths and weaknesses to our approach and that of others. The approach proposed by other authors of subtracting leaflet dimensions at different time periods in the cardiac cycle may be technically easier, with fewer steps involved than the method we present [5–7, 12, 13]. However, posterior annular calcification frequently can cast acoustic shadows, thus obscuring the posterior leaflet and preventing accurate measurements. Quantification of leaflet dimensions can also be particularly troublesome in the commissural regions because there is no clear echocardiographic demarcation between the anterior and posterior leaflets because they are continuous and because current software programs do not provide appropriate cropping planes to map these areas in diastole. To mitigate some of these problems, other investigators have used the early systolic frame when the leaflets initially touch as the reference area representing the whole leaflet area [5–7, 12, 13]. However, obtaining an echocardiographic frame that captures this exact moment is rare due to the poor temporal resolution of 3D echocardiography. Furthermore, regional leaflet loitering results in the leaflets coming together in different regions at various moments in time. For example, even though A1-P1 may be coapting at a given point in time, A3-P3 may be tethered apart. Finally, the mitral leaflet elasticity means that the leaflet length may increase with tension up to 15% and introduces the possibility of error [13, 16].

Fundamentally, the approach measures leaflet tissue available for coaptation or the “leaflet reserve” rather than then amount of leaflet functionally involved in coaptation [13]. On the contrary, the coaptation zone index we present is different from the other proposed indices because it is based on a direct measurement of the MV 3D coaptation zone. Although not specifically evaluated in the current study, our strategy should be sufficiently granular to recognize the potential asymmetry of the anatomically complex MV coaptation zone rather than limiting the assessment to a single measure of the coaptation length along the line of coaptation.

In the absence of an established standard against which to validate our measurement of the coaptation zone, we chose instead to demonstrate that the coaptation zone index correlates with the degree of MR. Although published guidelines exist to evaluate the degree of MR, a noninvasive gold standard for MR quantitation does not exist [4, 17]. Most echocardiographic techniques are able to reliably distinguish between mild and severe MR, but there is significant overlap between “mild and moderate” and “moderate and severe” echocardiographic grades [18]. This ambiguity of grades occurs because of the largely subjective nature of MR echocardiographic assessment and, importantly, because MR is a continuous variable.

Recognizing this, the American Society of Echocardiography guidelines advocate using multiple criteria when evaluating the severity MV regurgitation and the assignment of “mild-moderate” and “moderate-severe” when appropriate [4]. Our data similarly lack resolution between severity grades. However, it is impossible to discern whether the degree of overlap between MR severity grades in our study presents a fundamental flaw of our approach or simply reflects the recognized fallibility of current echocardiographic techniques that we used as standard for validation [18, 19]. For this reason we compared our index with the VCW, a continuous variable, and found a good correlation. Although our results demonstrate that the 3D coaptation zone index is associated with the degree of FMR and thus supports our ability to measure the coaptation zone as an anatomic entity, the accuracy of our methodology cannot be definitely appraised without further study.

We expect that with continued technologic improvements in 3D echocardiographic imaging and associated quantitative software, future work on the MV coaptation zone will be more streamlined, if not largely automated. Further work should include the cross-sectional area of the proximal regurgitant jet (3D vena contracta) because this has been shown to correlate better with FMR than traditional color mapping techniques [20]. Magnetic resonance imaging of MR might also provide another robust alternative standard against which our 3D coaptation zone index can be evaluated [17, 21]. After such further evaluation, we are hopeful that our 3D coaptation zone index can be applied clinically to further evaluate mechanism of FMR and to guide surgical planning and assessment in MV repair.

This study has some limitations. The design of this study was targeted to demonstrate feasibility and an initial proof of concept with the focus on the methodologic aspects of how to measure the MV coaptation from 3D data sets. Although the small sample of 25 patients included valves with various etiologies of FMR, the study intentionally disregarded these differences and used the available 3D data sets to build computer models of different coaptation zones. In the absence of a gold standard for comparison, we validated our findings by correlating the 3D coaptation zone with the severity of MR.

Another limitation of this preliminary work relates to the lack of interobserver and intraobserver analysis. Given the large number of measurements per patient (frequently 100 per patient when 50 sequential coaptation lengths were measured), the assessment of interobserver and intraobserver variability was not realistically possible. Importantly, our 3D approach to the MV coaptation zone was static in that it uses only the end-systolic frame. MV closure has been described as a dynamic bimodal pattern that can be represented mathematically as quadratic [22–24]. Although FMR is influenced by changes in loading conditions that were not incorporated in this study, the coaptation index and severity of MR were measured at a single time point. Future developments of automated dynamic 3D quantification software will likely be important in streamlining what admittedly is a very cumbersome technique [25, 26].

In summary, this study describes a novel 3D approach to direct assessment of the MV coaptation zone. When indexed to the total MV area, the 3D MV coaptation zone is closely associated with FMR severity. Once automated and validated against appropriate standards, our method may constitute a valuable tool in the perioperative evaluation of the competency of the MV before and after surgical repair.

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