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ORIGINAL RESEARCH

Optimal Quantification of Functional Mitral Regurgitation: Comparison of Volumetric and Proximal Isovelocity Surface Area Methods to Predict Outcome

Sachiyo Igata, PhD, ACS, RDCS; Bruno R. Cotter, MD; Calvin T. Hang, MD, PhD; Nagisa Morikawa, MD, PhD; Monet Strachan, ACS, RDCS; Ajit Raisinghani, MD; Daniel G. Blanchard, MD; Anthony N. DeMaria, MD

BACKGROUND: Effective orifice area (EOA) ≥0.2 cm^2 or regurgitant volume (Rvol) ≥30 mL predicts prognostic significance in functional mitral regurgitation (FMR). Both volumetric and proximal isovelocity surface area (PISA) methods enable calculation of these metrics. To determine their clinical value, we compared EOA and Rvol derived by volumetric and PISA quantitation upon outcome of patients with FMR.

METHODS AND RESULTS: We examined the outcome of patients with left ventricular ejection fraction <35% and moderate to severe FMR. All had a complete echocardiogram including EOA and Rvol by both standard PISA and volumetric quantitation using total stroke volume calculated by left ventricular end-diastolic volume×left ventricular ejection fraction and forward flow by Doppler method: EOA=Rvol/mitral regurgitation velocity time integral. Primary outcome was all-cause mortality or heart transplantation. We examined 177 patients: mean left ventricular ejection fraction 25.2% and 34.5% with ischemic cardiomyopathy. Echo measurements were greater by PISA than volumetric quantitation: EOA (0.18 versus 0.11 cm^2), Rvol (24.7 versus 16.9 mL), and regurgitant fraction (61 versus 37 %) respectively (all *P* value <0.001). During 3.6±2.3 years' follow-up, patients with EOA ≥0.2 cm^2 or Rvol ≥30 mL had a worse outcome than those with EOA <0.2 cm^2 or Rvol <30 mL only by volumetric (log rank *P*=0.003 and 0.004) but not PISA quantitation (log rank *P*=0.984 and 0.544), respectively.

CONCLUSIONS: Volumetric and PISA methods yield different measurements of EOA and Rvol in FMR; volumetric values exhibit greater prognostic significance. The echo method of quantifying FMR may affect the management of this disorder.

Key Words: functional mitral regurgitation ■ outcome ■ proximal isovelocity surface area (PISA) method ■ volumetric method

See Editorial by Hu and Chen

Functional mitral regurgitation (FMR), whether attributable to ischemic or nonischemic disease, has been characterized by an enlarged left ventricle, tethered mitral leaflets, and a dynamic change of mitral annular geometry.[1–6] Patients with FMR who have an effective orifice area (EOA) ≥0.2 cm^2 or regurgitant volume (Rvol) ≥30 mL have been demonstrated to have a worse clinical outcome.[7] The most commonly applied method to calculate EOA and Rvol uses measurements derived from the proximal isovelocity surface area (PISA) signal. However, this method has a number of limitations including assumption of a hemispherical shape, a flat mitral annulus and an infinitesimally small regurgitant area.[8–11] An alternate quantitative approach uses left ventricular (LV) volumetric measurements to derive total stroke volume (TSV), and the product of LV outflow velocity and area to determine forward stroke volume.[12,13] The volumetric method also has imperfections, including

Correspondence to: Anthony N. DeMaria, MD, Division of Cardiovascular Medicine, University of California, San Diego, Sulpizio Cardiovascular Center, 9434 Medical Center Dr La Jolla, CA. E-mail: ademaria@ucsd.edu

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CLINICAL PERSPECTIVE

What Is New?

- We compared the determination of effective orifice area and regurgitant volume by volumetric and proximal isovelocity surface area echo methods to predict the outcome of patients with functional mitral regurgitation.
- We found that effective orifice area or regurgitant volume obtained by the volumetric method demonstrated greater prognostic significance.

What Are the Clinical Implications?

- Effective orifice area and regurgitant volume obtained by echo are important measures of the severity of functional mitral regurgitation.
- Accurate quantitation of valvular regurgitation has prognostic importance and has implications regarding selection of interventional therapy in patients with functional mitral regurgitation.
- The volumetric method of deriving effective orifice area and regurgitant volume by echo is superior to the proximal isovelocity surface area method in predicting mortality in patients with functional mitral regurgitation and should be the preferred quantitative method.

Nonstandard Abbreviations and Acronyms

ASE	American Society of Echocardiography
EOA	effective orifice area
FMR	functional mitral regurgitation
MR	mitral regurgitation
PISA	proximal isovelocity surface area
RF	regurgitant fraction
RvoI	regurgitant volume
TSV	total stroke volume

the fact that the assessment of endocardial detection depends upon the quality of the recording, and that the accuracy of LV outflow measures rely upon the precision of aortic annulus and outflow velocity identification. Both methods also use velocity measurements from the mitral regurgitant jet. The outcome of FMR quantified by these two methods remains uncertain, as is their ability to risk-stratify patients. It is anticipated that a more accurate method of quantifying mitral regurgitation (MR) would enable greater risk stratification and prognostic ability. Therefore, we compared PISA and volumetric quantitation of FMR and examined patient outcomes to determine the ability of these 2 methods to identify high-risk patients with FMR. In the past, MR in patients with severe LV dysfunction was considered a disease of the ventricle, and it was believed that repair of the valve would not be of benefit. Two recent studies have yielded divergent results as to the benefit of interventional therapy.[14,15] It is likely that the relative risks of the patients included in the studies played a role in the different results. Therefore, accurate risk stratification will be of particular importance for patients with FMR with severe LV dysfunction.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

This is a retrospective single-center study of patients undergoing echocardiography between January 1, 2010, and December 31, 2015. We identified the echocardiograms of all patients with left ventricular ejection fraction (LVEF) ≤35% and moderate (147; 83%) to severe (30; 17%) FMR according to American Society of Echocardiography (ASE) guidelines.[13] Also, we considered additional findings such as pulmonary vein systolic flow reversal (39; 22%) and MR jet directed toward left atrial posterior wall (115; 65%) for MR grading. For consistency, if a patient had multiple echocardiograms in the study period, we selected the first echo that showed LVEF ≤35% and moderate to severe FMR. All patients had an echocardiogram performed as indicated clinically. A total of 316 patients met LVEF ≤35% and moderate to severe FMR; among them, we included 177 patients, 67% men, with an average age of 59±13 years. We excluded patients with suboptimal 2-dimensional image quality (35; 11%), atrial fibrillation or frequent arrhythmia (21; 7%), moderate to severe aortic regurgitation (7; 2%), and missing data (76; 24%) (Figure 1). Comorbidities and outcome were documented by a review of medical records. Our study complies with the Declaration of Helsinki and is approved by the ethics committee of the University of California, San Diego. Written informed consent was waived given the retrospective nature of the study.

Echocardiography

All patients underwent a comprehensive echocardiogram as part of routine clinical care. Registered cardiac sonographers performed the echocardiograms using commercial ultrasound machines: Philips iE33 (Philips Medical Systems, Bothell, WA), Siemens SC2000 (Siemens Medical Solutions, Malvern, PA), and General Electric Vivid E9 (GE Medical Systems, Milwaukee, WI). Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume and LVEF were calculated

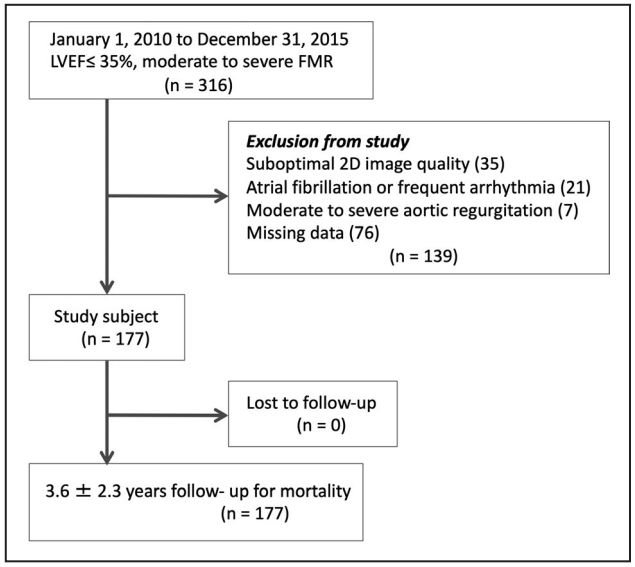

Figure 1. Flow diagram of study subjects.
2D indicates 2-dimensional; FMR, functional mitral regurgitation; and LVEF, left ventricular ejection fraction.

using 2-dimensional Simpson's method.[16] Transmitral E/A velocity ratio, the ratio of transmitral and mitral annular early diastolic velocities as E/e′, left atrial volume index, tricuspid annular plane systolic excursion, and tricuspid regurgitation peak gradient were measured according to the ASE guidelines.[16] All echocardiographic data were stored in a workstation (Syngo, Siemens Medical USA, Malvern, PA) for offline measurement and analysis of EOA, Rvol, and regurgitant fraction (RF) by both volumetric and PISA methods.[13] All measurements and analysis were performed blinded to the outcome of the patients. For the volumetric method, TSV is computed from LVEDV×LVEF, forward stroke volume is calculated by the Doppler method using the LV outflow tract area×velocity time integral of left ventricular outflow tract, and EOA was derived as (TSV–forward stroke volume)/velocity time integral of the MR jet. PISA was calculated in the standard fashion in accordance with ASE guidelines.[13] The primary outcome was all-cause death or heart transplantation. We followed the patients from 2010 to 2015 (mean, 3.6±2.3 years) and compared the EOA, Rvol and RF and outcome in patients with and without EOA ≥0.2 cm^2 or Rvol ≥30 mL between the volumetric and PISA methods.

Statistical Analysis

Continuous data were presented as mean±SD or medians with the interquartile range. We performed the Kolmogorov-Smirnov test to evaluate the assumption of normality. We compared echocardiographic factors between the volumetric and PISA methods using a paired t test for parametric data or the Mann-Whitney U-test for nonparametric data. The correlations between the volumetric and PISA methods were performed using Pearson's correlation coefficient and Spearman's rank correlation coefficient for parametric and nonparametric data. The correlation between EOA and LVEDV was assessed using linear regression analysis. We compared clinical outcome of patients with EOA ≥0.2 cm^2 versus EOA <0.2 cm^2 (or Rvol ≥30 mL versus Rvol <30 mL) as calculated by the PISA and volumetric methods using the Kaplan-Meier log-rank test. To analyze the impact of EOA on mortality risk, we performed Cox proportional hazards regression analysis for the group of patients with EOA ≥0.2 cm^2 by the volumetric method, to those with EOA ≥0.2 cm^2 by PISA. To assess the concordance of the risk, we analyzed Harrell's concordance index. Interobserver variability of EOA and Rvol by both the volumetric and PISA methods were evaluated by intraclass correlation coefficients (ICC) analysis. Statistical analyses were performed with the use of the SPSS system (IBM, Chicago, IL) or SAS software (SAS Institute, Cary, NC).

RESULTS

We identified 316 patients with an LVEF ≤35% and FMR; among them, 177 patients were evaluated by EOA, Rvol, and RF by both the volumetric and PISA methods. The primary reasons for patient exclusion were poor image quality, undetectable PISA radius, or arrhythmia. Patients' characteristics are shown in Table 1; an ischemic cardiomyopathy was present in 61 (34.5%) patients with FMR. Mean LVEF was 25.2±7.7%, median LVEDV and LV end-systolic volume were 186.0 mL and 135.5 mL. Median TSV and forward stroke volume obtained from the volumetric method were 45.9 mL and 27.6 mL.

We compared the values of EOA, Rvol, and RF between the volumetric and PISA methods. Values were smaller by the volumetric method (EOA, 0.11 [0.06–0.19] cm^2; Rvol, 16.9 [9.5–24.8] mL; and RF, 36.9±16.8%) than by PISA (0.18 [0.10–0.29] cm^2; 24.7 [14.1–38.6] mL; and 60.9±41.8%, respectively; all P<0.001) (Figure 2). The correlation between values by the volumetric and PISA methods were r=0.314, 0.246, and –0.012 for EOA, Rvol, and RF, respectively (EOA, Rvol: P<0.01, RF: P=0.878). EOA by the volumetric method had a modest correlation with LVEDV (r=0.510; P<0.001), while EOA by PISA had weaker correlation with LVEDV (r=0.303; P<0.001) (Figure 3).

During 3.6±2.3 years' follow-up, 49 patients died, 18 patients had heart transplantation, and 10 patients had mitral valve repair surgery.

The number of deaths/transplants in patients with EOA ≥0.2 cm^2 or Rvol ≥30 mL when calculated by volumetric quantitation was 61% (23/38) and 59% (17/29), respectively. When calculated by the PISA method, the numbers were 41% (33/80) and 43% (29/68), respectively.

Table 1. Patient Characteristics

Parameters	Values
Age, y	58.9±13.3
Male, n	119 (67.2)
BSA, m^2	1.89±0.28
Hispanic, n	39 (22.0)
Non-Hispanic White, n	84 (47.5)
Non-Hispanic Black, n	39 (22.0)
Non-Hispanic Asian, n	9 (5.1)
Non-Hispanic Mix, n	6 (3.4)
Nonischemic FMR, n	116 (65.5)
Ischemic FMR, n	61 (34.5)
LVEF, %	25.2±7.7
LVEDV, mL*	186.0 (143.5–249.0)
LVESV, mL*	135.5 (100.0–193.8)
E/A ratio*	2.19 (1.53–2.68)
E/e′ ratio*	15.2 (11.5–20.6)
LAVI, mL/m^{2*}	47.8 (39.5–58.3)
TRPG, mm Hg	34.1±12.2
TAPSE, cm*	1.49 (1.18–1.80)
TSV, mL*	45.9 (36.3–57.3)
LVOT FSV, mL*	27.6 (21.5–36.1)
EOA by volumetric method, cm^{2*}	0.11 (0.06–0.19)
Rvol by volumetric method, mL*	16.9 (9.5–24.8)
RF by volumetric method, %	36.9±16.8
Pulmonary venous flow reversal, n	39 (22.0)
MR jet reached LA posterior wall, n	115 (64.9)
Wide MR jet or 2 MR jets, n	119 (67.2)
EOA by PISA method, cm^{2*}	0.18 (0.10–0.29)
Rvol by PISA method, mL*	24.7 (14.1–38.6)
RF by PISA method, %	60.9±41.8

Values are number (%), mean±SD, or *median (interquartile range). BSA indicates body surface area; EOA, effective orifice area; FMR, functional mitral regurgitation; FSV, forward stroke volume; LAVI, left atrial volume index; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVOT, left ventricular outflow tract; PISA, proximal isovelocity surface area; RF, regurgitant fraction; Rvol, regurgitant volume; TAPSE, tricuspid annular plane systolic excursion; and TRPG, tricuspid regurgitation peak gradient.

By the volumetric method, patients with EOA ≥0.2 cm^2 or Rvol ≥30 mL had more adverse outcomes compared with those with EOA <0.2 cm^2 (log rank P=0.003) or Rvol <30 mL (log rank P=0.004) (Figure 4, 5). By the PISA method; however, the outcome was similar for both the patients with and without EOA ≥0.2 cm^2 (log rank P=0.984) or Rvol ≥30 mL (log rank P=0.544) (Figure 4, 5). We also analyzed the association between EOA, LVEDV, and mortality risk. Hazard ratio of EOA ≥0.2 cm^2 by the volumetric method (hazard ratio, 2.411; 95% CI, 1.410–4.125; P=0.001) was statistically significant compared with EOA ≥0.2 cm^2 by the PISA method (hazard ratio, 1.018; 95% CI, 0.625–1.658; P=0.942) (Table 2).

We performed receiver operating characteristic curve analysis of EOA and Rvol to determine the cutoff value for predicting death and heart transplant (Figure 6). The area under the curve of EOA and Rvol by the volumetric method were 0.62 and 0.61with P = 0.007 and 0.013, but by PISA were 0.56 and 0.54 with P = 0.193 and 0.425. Also, we analyzed the concordance index on the basis of the Cox model. The concordance index of EOA by the volumetric method (0.581) was higher than that by PISA (0.498) (volumetric versus PISA, P=0.247). Concordance index of Rvol by volumetric (0.573) was also higher than that by PISA (0.481) (volumetric versus PISA, P=0.179). Although there is no statistical difference of concordance index between PISA and volumetric method, concordance indexes of volumetric method were higher than those of PISA methods.

Interobserver Variability

We analyzed ICC of EOA and Rvol by both the volumetric and PISA methods. Two investigators (S.I and C.H.) measured EOA and Rvol by both the volumetric and PISA methods in 15 cases. The ICC of EOA by volumetric or PISA method was 0.90 (95% CI, 0.660–0.970) and 0.78 (95% CI, 0.393–0.928), respectively. The ICC of Rvol was 0.87 (95% CI, 0.550–0.962) and 0.86 (95% CI, 0.606–0.956), respectively. The ICCs of volumetric were less variability than those of PISA method.

DISCUSSION

We compared echocardiography measurements of the severity of functional mitral regurgitation by the PISA and volumetric methods and related them to the hard outcomes of all-cause mortality and heart transplantation over a mean of 3.6 years. The major findings of our study were: values of FMR differed by the 2 methodologies; PISA yielded larger values of EOA and Rvol than volumetric; and importantly, high-risk classification by volumetric was superior to that of PISA in predicting outcome. The differences in quantitation of FMR by the PISA and volumetric methods may be of significance in the management of patients with FMR.

PISA is the most common and useful method employed to quantify the severity of primary MR. However, the PISA method has several critical limitations, especially in patients with FMR or secondary MR. For example, PISA has many assumptions, such as that the mitral valve is a flat plane, the regurgitant orifice is central and infinitely small and that the PISA signal conforms to the geometry of a hemispheric shell. However, the mitral leaflet plane is clearly not flat, and of a greater significance, the PISA signal shape

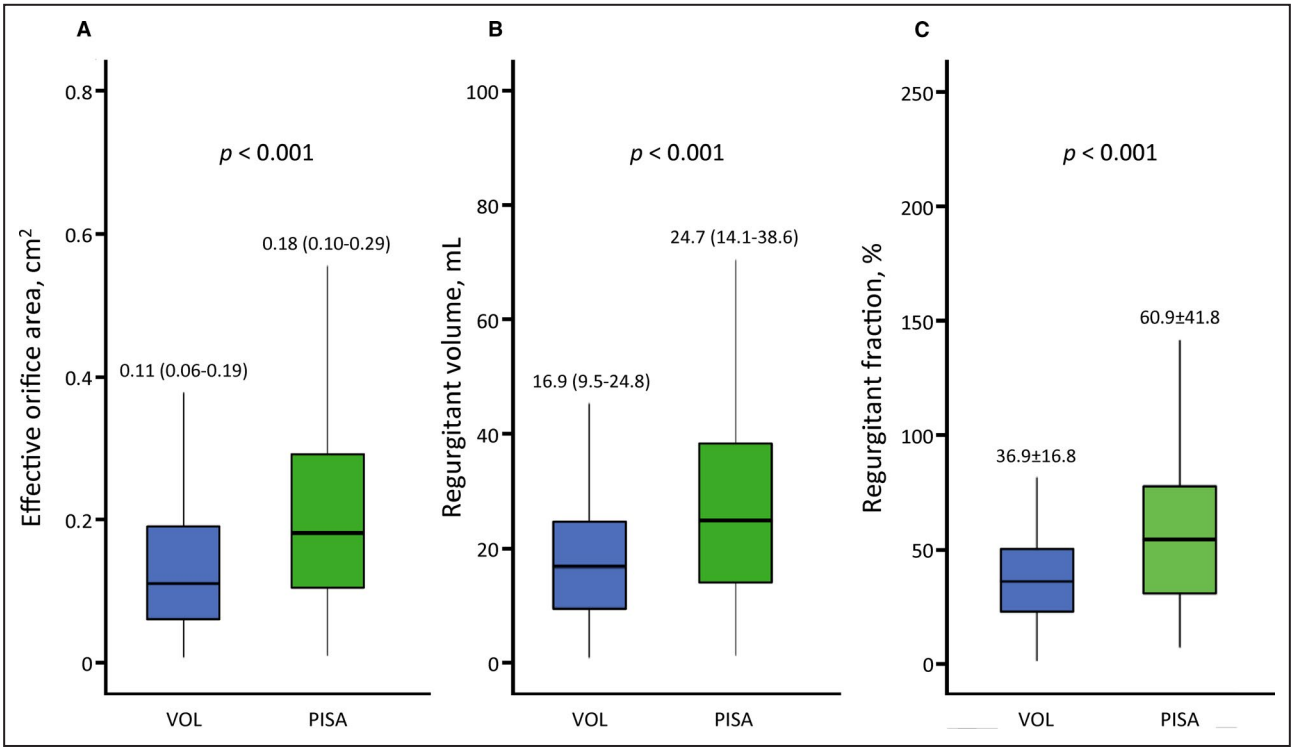

Figure 2. Comparison of the (A) effective orifice area, (B) regurgitant volume (Rvol), and (C) regurgitant fraction (RF) between the volumetric (VOL) and proximal isovelocity surface area (PISA) method.

is often crescentic and nonhemispherical.[8] The geometry of the proximal convergence zone in FMR is complex and often asymmetrical in shape.[9] Although the PISA radius is measured at only 1 point in the cardiac cycle, the magnitude of the MR jet often varies during systole and frequently shows a biphasic temporal pattern.[10] Usually, the PISA method is widely used for assessment for primary MR in patients with normal EF. Given many limitations by the PISA method in FMR, or secondary MR, it is uncertain if PISA is useful for assessment of severity in this patient population. In fact, we found that only the value by the volumetric method predicted worse outcome in patients with FMR. Prior studies have shown that the reproducibility of PISA

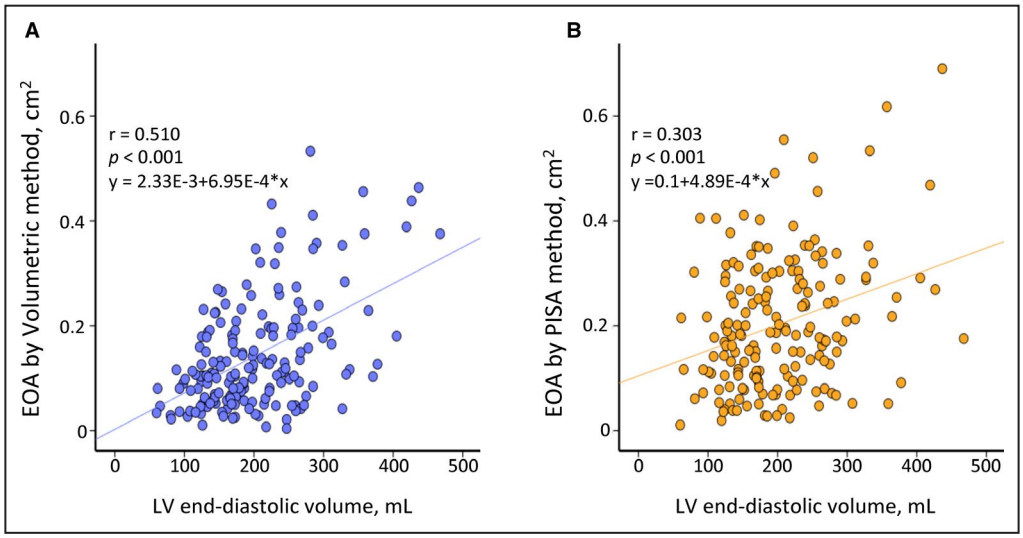

Figure 3. Correlation of effective orifice area (EOA) and left ventricular (LV) end-diastolic volume. **A**, EOA obtained from volumetric method. **B**, EOA obtained from proximal isovelocity surface area (PISA) method.

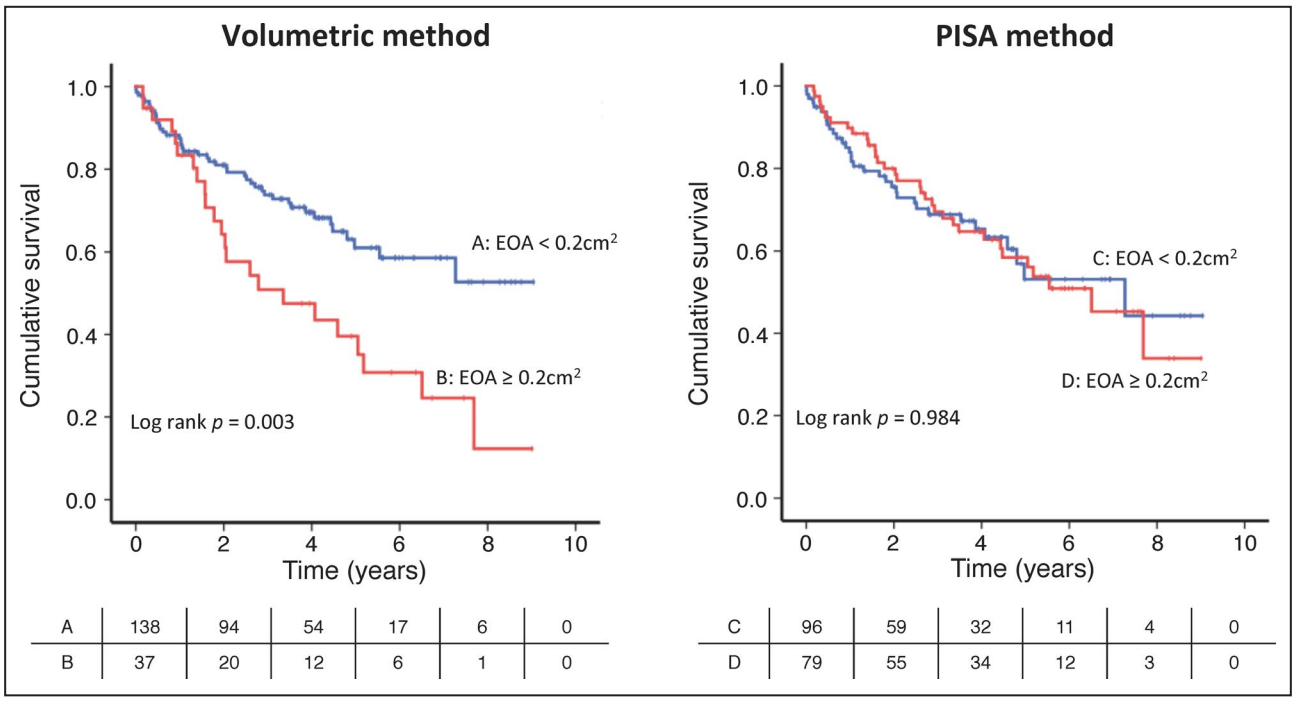

Figure 4. Outcome in patients with and without effective orifice area (EOA) ≥0.2 cm² by volumetric or proximal isovelocity surface area (PISA) method.

measurements is modest and associated with suboptimal interobserver agreement.[11] In our study, ICC of EOA by PISA was less than those by the volumetric method. The calculation of PISA radius may affect this variability. These factors clearly contribute to the difference between volumetric and PISA measurements. In this regard, our study found that 24 patients had Rvol greater than TSV (ie, RF >100%) by the PISA method.

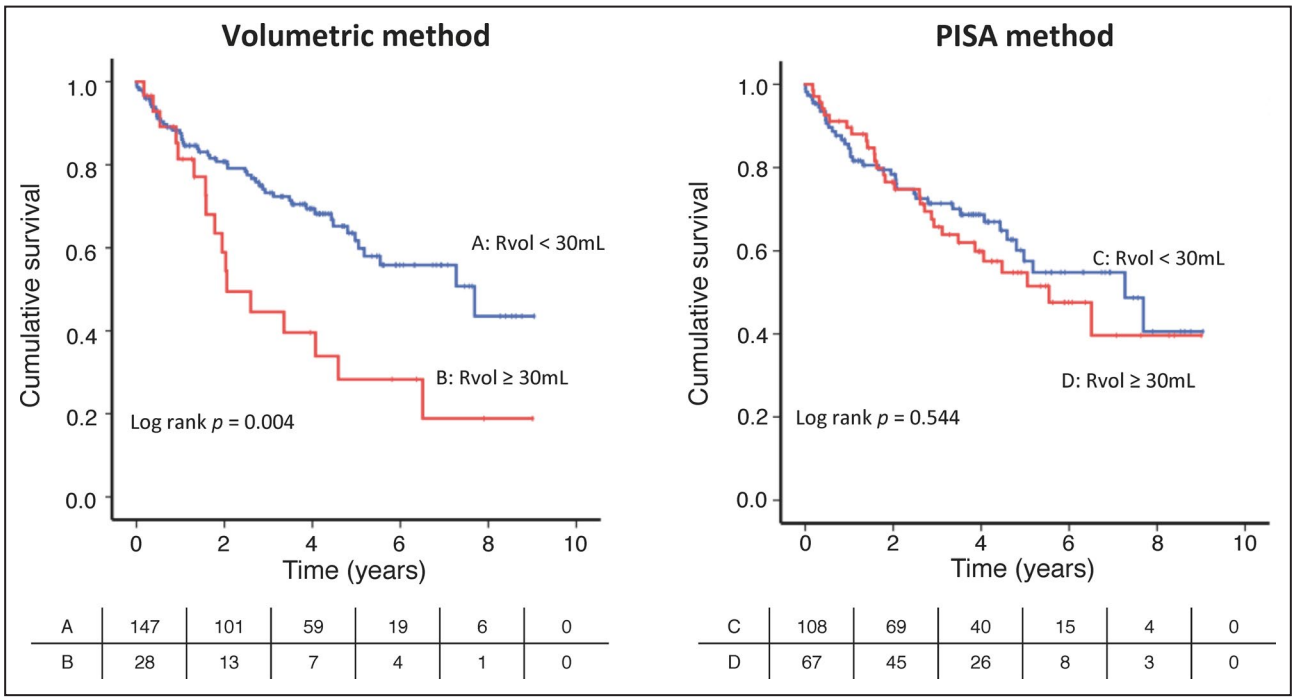

Figure 5. Outcome in patients with and without regurgitant volume (Rvol) ≥30 mL by volumetric or proximal isovelocity surface area (PISA) method.

Table 2. Cox Proportional Hazards Regression Analysis for Mortality

	HR	95% CI	*P* Value
EOA ≥0.2 cm^2 by volumetric method	2.411	1.410–4.125	0.001
EOA ≥0.2 cm^2 by PISA method	1.018	0.625–1.658	0.942

EOA indicates effective orifice area; HR, hazard ratio; and PISA, proximal isovelocity surface area.

Our results suggest that PISA may overestimate EOA and Rvol in patients with FMR. Hagendorff et al[17] also reported this pitfall of the PISA method for EOA and Rvol measurements.

There are 2 approaches for calculation of TSV by volumetric methods. One is the Doppler method comparing the mitral inflow to the aortic outflow calculated as the product of cross-sectional area and integrated velocity; the other is Simpson's method. In the former, mitral annulus geometry, sample volume position and angulation, and the precision of pulsed Doppler tracing can all affect the accuracy of TSV as derived by mitral inflow.[18,19] These variables can also affect measurement of aortic outflow. TSV by Simpson's method is derived as LVEDV–LV end-systolic volume or LVEDV×LVEF, and has been shown to have a good correlation with similar measurements by cardiovascular magnetic resonance imaging (CMR).[20] Thus, we used Simpson's rule to calculate Rvol as TSV (LVEDV×LVEF)–forward stroke volume. It has been shown that LV volumes obtained from 2-dimensional echocardiography underestimate those obtained from CMR and 3-dimensional echocardiography in patients with normal LVEF.[21,22] Accordingly, while both volumetric methods are subject to limitation of measurement precision, the number of potential variables appear a bit less with Simpson's approach, and that was chosen as the volumetric technique for this study.

Uretsky et al[23] compared Rvol between the PISA method by echocardiography and CMR assay by volumes. In agreement with our findings, they determined that Rvol obtained by PISA was larger than that by CMR. They included degenerative and flail mitral regurgitation, only 18% of subjects had FMR. Lopez-Mattei et al[24] compared Rvol between a volumetric method using transmitral flow by echocardiography and CMR. They found statistically significant discrepancies between the 2 methods, although no systematic overestimation existed. LVEF of both studies varied widely. In our study, LVEF/stroke volume was very low, and we included only moderate to severe FMR. Direct comparison of our study with theirs is complicated by differences in MR, cause of FMR, calculation method, characteristics of study population such as LVEF, and, of course, comparison standard.

Severe MR is defined as EOA ≥0.4 cm^2, Rvol ≥60 mL, and RF ≥50% in the ASE guideline.[13] Although the European Society of Cardiology guideline is similar to that of ASE for patients with primary MR,[25] for patients with FMR they state that EOA ≥0.2 cm^2 and Rvol ≥30 mL is the threshold for increased risk of cardiac events.[13,25,26] LV function is impaired and cardiac output is reduced in patients with FMR, so regurgitation of even lesser degree than severe by ASE criteria may be sufficient to affect patient outcome. In fact, although our subjects were diagnosed as having moderate or severe MR by virtue of a large vena contracta or jet area or the presence of pulmonary vein flow reversal, most did not yield a calculated EOA ≥0.4 cm^2 or Rvol

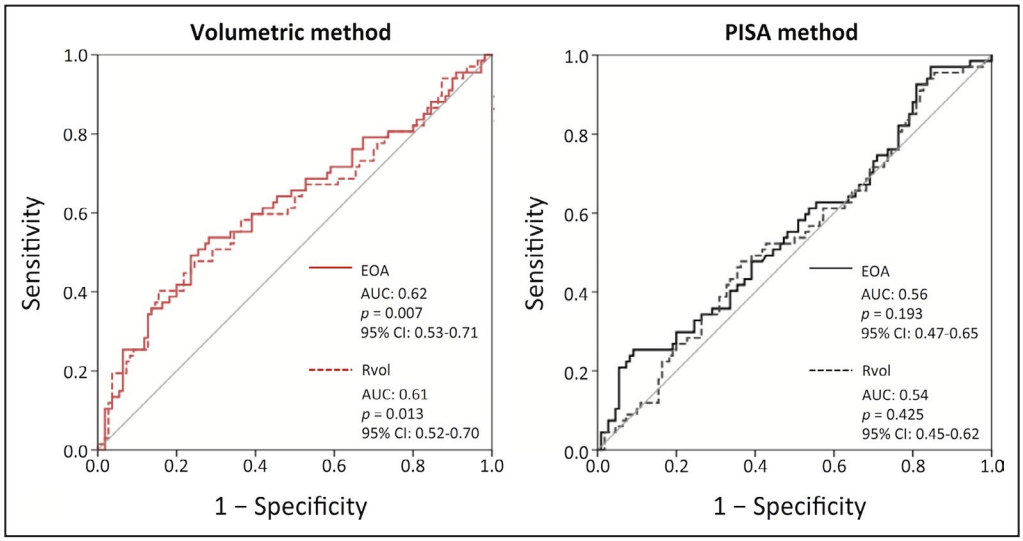

Figure 6. The receiver operating characteristic curves of effective orifice area (EOA) and regurgitant volume (Rvol) for predicting of death and heart transplant.
AUC indicates area under the curve.

≥60 mL. The outcomes did not differ in patients with and without EOA ≥0.2 cm^2 by PISA in our study, consistent with the findings of Patel et al.[27] On the other hand, Rossi et al[7] reported that the patients with EOA ≥0.2 cm^2 by PISA did have adverse outcomes. Ischemic cardiomyopathy of FMR is an independent predictor of cardiovascular death,[28] and the prevalence of ischemic FMR in our study (35%) may explain the variant findings of Rossi (62%).

The most important finding of our study was that patients with values for EOA and Rvol that met European Society of Cardiology criteria for increased risk by volumetric quantitation did have a reduced transplant-free survival, while those by PISA did not. The explanation for this disparity remains uncertain. While PISA has many limitations in the precision of measurement of EOA and Rvol, the volumetric technique also has imperfections. Unfortunately, we do not have an independent standard by which to assess the relative accuracy of the measurements by the 2 techniques. However, the fact that a number of patients had Rvol greater than TSV by PISA supports the overestimation of measurements by this method. By virtue of the inclusion of LV volumes and EF in its algorithm, the volumetric method is more subject to the influence of LV dysfunction than is PISA. The potential influence of LV function upon FMR assessment may contribute to the better prognostic performance of volumetric quantitation. Perhaps the most likely explanation for the lesser prediction of outcome by PISA is the fact that the method appears to overestimate metrics for the severity of FMR. Values for EOA and Rvol were substantially higher by PISA than the volumetric method, likely related to the lack of hemispheric geometry of the PISA signal. It is likely that many patients with low-risk FMR were included in the high-risk group by this method. The inclusion of lower-risk patients in the high-risk category would, of course, blunt the prognostic accuracy of the PISA method. We found that values for EOA, Rvol, and RF by the volumetric method did not show a good correlation with those by PISA. Thus, not only did these 2 methods differ in quantitative metrics, but they also lacked correlation.

Patients with moderate and severe FMR had worse outcome than those with mild or no FMR.[29] Two recent studies yielded divergent results as to the benefit of interventional therapy.[14,15] It is likely that the relative risks of the patients included in the studies played a role in the different results. Therefore, accurate risk stratification will be of particular importance for patients with FMR with severe LV dysfunction.

Limitations

This is a single-center study in a group of patients with severe LV dysfunction (LVEF ≤35%). Our findings may not apply to patients with FMR with a lesser degree of LV dysfunction. In addition to patients with severe FMR, our study also included patients with moderate FMR who did not meet severe criteria by echocardiography (EOA ≥0.2 cm^2 or Rvol ≥30 mL). In our study, TSV and forward stroke volume were low, which likely reflects severe LV dysfunction. Also, we did not compare outcome according to RF. Currently, 3-dimensional echocardiographic software enables the assessment and quantification of complex MR with multiple and eccentric jets.[30,31] However, our study was retrospective, we did not have available 3-dimensional echocardiograms, computed tomography, or magnetic resonance imaging, which was not then and is not now routinely performed in these patients. However, we planned the analysis and reviewed the echocardiographic data prospectively. We did not take into account comorbidities or the therapy applied since each patient served as their own control. We recognize that measurement of LV volumes and EF by 2-dimensional echocardiography may underestimate TSV compared with angiography.

CONCLUSIONS

Measures of the severity of FMR by echocardiography or any other modality are of greatest value in assessing prognosis and guiding therapy. With the advent of evidence that catheter intervention is of value in certain patients with FMR,[14,15] accurate methods to not only assess the severity of FMR but also predict outcome are of great clinical value. Echocardiography is an excellent modality to quantitate FMR and follow its progression. Our data indicate that traditional ultrasound metrics of MR, including EOA and Rvol, can be of value in predicting risk of mortality or heart transplant if derived by a volumetric method. In addition, this volumetric method is superior to the more commonly applied PISA technique. These data may be of value in the management of patients with functional MR.

ARTICLE INFORMATION

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Affiliations

The Division of Cardiology, Department of Medicine, University of California, San Diego, Sulpizio Cardiovascular Center, San Diego, CA (S.I., B.R.C., C.T.H., M.S., A.R., D.G.B., A.N.D.); and The Division of Cardiovascular Medicine, Department of Medicine, Kurume University School of Medicine, Fukuoka, Japan (S.I., N.M.).

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