Defining “Severe” Secondary Mitral Regurgitation
Emphasizing an Integrated Approach

Paul A. Grayburn, MD,* Blasé Carabello, MD,† Judy Hung, MD,§ Linda D. Gillam, MD,|| David Liang, MD,* Michael J. Mack, MD,‡ Patrick M. McCarthy, MD,*** D. Craig Miller, MD,†† Alfredo Trento, MD,‡‡ Robert J. Siegel, MD***

ABSTRACT
Secondary mitral regurgitation (MR) is associated with poor outcomes, but its correction does not reverse the underlying left ventricular (LV) pathology or improve the prognosis. The recently published American Heart Association/American College of Cardiology guidelines on valvular heart disease generated considerable controversy by revising the definition of severe secondary MR from an effective regurgitant orifice area (EROA) of 0.4 to 0.2 cm², and from a regurgitant volume (RVol) of 60 to 30 ml. This paper reviews hydrodynamic determinants of MR severity, showing that EROA and RVol values associated with severe MR depend on LV volume. This explains disparities in the evidence associating a lower EROA threshold with suboptimal survival. Redefining MR severity purely on EROA or RVol may cause significant clinical problems. As the guidelines emphasize, defining severe MR requires careful integration of all echocardiographic and clinical data, as measurement of EROA is imprecise and poorly reproducible. (J Am Coll Cardiol 2014;64:2792–801) © 2014 by the American College of Cardiology Foundation.

In severe primary mitral regurgitation (MR), “it is the abnormal valve that makes the heart sick” (1). Surgical correction of primary MR, ideally by mitral valve repair, corrects left ventricular (LV) volume overload, allowing a normal lifespan (2–4). Conversely, secondary or functional MR is caused by systolic restriction of mitral leaflet motion by tethering and/or annular dilation. Although secondary MR is associated with a poor outcome, it is not clear that correction of MR reverses the underlying LV pathophysiology or improves prognosis. Difficulty in quantifying secondary MR by traditional echocardiographic methods further complicates the issue. The 2014 American Heart Association/American College of Cardiology (AHA/ACC) guidelines for the Management of Patients with Valvular Heart Disease (5) From the *Baylor Heart and Vascular Institute, Dallas, Texas; †Department of Internal Medicine, The Heart Hospital Baylor Plano, Plano, Texas; ‡Department of Internal Medicine, Mount Sinai School of Medicine, New York, New York; §Cardiology Division, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts; ||Cardiovascular Medicine, Morristown Medical Center, Morristown, New Jersey; ¶Department of Internal Medicine, Stanford University Medical School, Stanford, California; ‡Department of Cardiothoracic Surgery, The Heart Hospital Baylor Plano, Plano, Texas; **Bluhm Cardiovascular Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois; ††Department of Cardiovascular Surgery, Stanford University Medical School, Stanford, California; and the |||Cedars-Sinai Heart Institute, Los Angeles, California. Dr. Grayburn has received grant support from Abbott Vascular and Medtronic; has served as a consultant for Abbott Vascular, Tendyne, and Bracco Diagnostics; and has had Echo Core Lab contracts for ValTech Cardio, Guided Delivery Systems, and Tendyne. Dr. Gillam has had Core Lab Research contracts for Edwards Lifesciences and Medtronic. Dr. Liang serves as a consultant for Philips Healthcare. Dr. McCarthy has served as a consultant for Edwards Lifesciences; and is an inventor of IMR ETLogix. Dr. Miller has served on the PARTNER Executive Committee for Edwards Lifesciences; has served as a consultant for Medtronic CardioVascular Division and Abbott Vascular Structural Heart (MitraClip); has served on the scientific advisory board for GenTAC. Dr. Siegel has served as a speaker for Philips and Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Gerald Maurer, MD, served as Guest Editor for this paper. Listen to this manuscript’s audio summary by JACC Editor-in-Chief Dr. Valentin Fuster. You can also listen to this issue’s audio summary by JACC Editor-in-Chief Dr. Valentin Fuster.

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highlight the importance of distinguishing primary from secondary MR and emphasize the need for disease staging. Accordingly, assessment of MR severity has changed from mild, moderate, or severe to at risk for MR (Stage A), progressive MR (Stage B), asymptomatic severe MR (Stage C), or symptomatic severe MR (Stage D). “Severe” is defined as the magnitude of valve dysfunction that worsens prognosis, and the guidelines repeatedly emphasize that quantifying the severity of any valvular lesion requires integration of multiple parameters, not a single number. The new guidelines revised the definition of severe secondary MR from an effective regurgitant orifice area (EROA) of 0.4 to 0.2 cm$^2$ and a regurgitant volume (RVol) of 60 to 30 ml; regurgitant fraction (RF) remains unchanged at 50%. This change has already provoked controversy (6,7). We review the hydrodynamic determinants of EROA and RVol and evidence supporting the main reasons for redefining severe secondary MR: association of a lower EROA threshold with suboptimal survival and EROA underestimation due to noncircular orifice geometry. We also discuss clinical problems that may occur if the revised definition is applied without integrating all echocardiographic/Doppler findings into a complete clinical picture.

**QUANTIFYING SEVERE MR**

In 2003, the American Society of Echocardiography published guidelines for evaluation of valvular regurgitation (8), which highlighted the inherent limitations of all echocardiographic measures of MR severity, necessitating use of a matrix of qualitative and quantitative findings, rather than relying on any single measurement. With that important caveat, quantification of MR severity, rather than inaccurate, “eyeball” grading of color Doppler jets, was encouraged. Quantitative parameters for severe MR included RF $\geq$50%, RVol $\geq$60 ml, and EROA $\geq$0.4 cm$^2$. These values were derived from a single-center observational study comparing RVol and EROA calculated by the proximal isovelocity surface area (PISA) method, quantitative Doppler, or the average of both methods to angiographic grading in 180 consecutive patients (9). LV angiography and echocardiography were performed within 3 months of each other. Primary MR was present in 96 patients, secondary MR in 84, and 39 were in atrial fibrillation. EROA, RVol, and RF values overlapped considerably between angiographic 1, 2, and 3+ MR (Figure 1). Because both groups were combined, whether overlaps in primary and secondary MR are similar or different is unclear. Statistical analysis revealed the optimum cutoff value for 4+ MR was EROA $\geq$0.4 cm$^2$, RVol $\geq$60 ml, and RF $\geq$50%. Until recently, these recommended values remained unchanged. The 2014 AHA/ACC guidelines contain a new table redefining severe secondary MR as EROA $\geq$0.2 cm$^2$ or RVol $\geq$30 ml or RF $\geq$50%, with important, but easily missed footnotes (5). The first footnote states that, “categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.” The second footnote states, “measurement of [PISA] by 2D [transthoracic echocardiography] in patients with secondary MR underestimates the true EROA due to the crescentic shape of the proximal convergence.” While the AHA/ACC guidelines did not elaborate the rationale for changing the definition, it appears to be on the basis of: 1) association of secondary MR with a worse prognosis; and 2) underestimation of EROA by PISA. Importantly, theoretical considerations support the concept that lesser degrees of MR could have an adverse hemodynamic effect in secondary MR wherein the LV is already damaged.

**HEMODYNAMIC CONSIDERATIONS**

In primary MR, LV dysfunction/remodeling is due to MR itself and is easier to define. Defining “severe” secondary MR is more problematic because the LV is already damaged. RF $>50\%$ is reasonably assumed to be severe MR because more than one-half the total LV stroke volume is lost backward into the left atrium (LA). The Central illustration plots the relationship between EROA and left ventricular end-diastolic volume (LVEDV; top panel) and between RVol and LVEDV (bottom panel) with severe MR (RF = 50%). An important, underappreciated dependence of both EROA and RVol on LVEDV is evident, such that an EROA of 0.2 cm$^2$ can be associated with RF $>50\%$ when LVEDV is normal, but is typically 0.3 cm$^2$ at moderately dilated LVEDV values (220 to 240 ml) typical of most clinical trials in heart failure. Only at very large LVEDV values is EROA 0.4 cm$^2$ associated with RF $>50\%$. Furthermore, the relationship between EROA and LVEDV is influenced by the mean systolic pressure gradient between the LV and LA, with higher EROA values in decompensated HF patients with hypotension and elevated LA pressure compared with hypertensive patients with normal LA pressure. An EROA $>0.6$ cm$^2$ is nearly impossible in secondary MR (unless the LV is extremely large) because MR cannot exceed 100% of total LV stroke.
volume. Left ventricular ejection fraction (LVEF) influences the relationship between RVol and LVEDV (bottom panel) such that it is virtually impossible to have a 60 ml RVol unless LVEF is 40% or more and the LV is significantly dilated. Conversely, even RVol <30 ml can be associated with RF >50% in smaller ventricles or very low LVEF values. As shown in the Central Illustration, severe MR (RF >50%) at lower levels of EROA and RVol than previously considered is possible, but values defining severe MR in individual patients depend on multiple factors, including LVEDV, LVEF, and the pressure gradient between the LV and LA.

**ASSOCIATION OF SECONDARY MR WITH ADVERSE OUTCOMES.** Several studies evaluated the relationship between MR severity and prognosis in secondary MR (10-18) (Table 1). All are observational, most include a mixture of ischemic and nonischemic etiologies, and different methods were used for grading MR. These studies suggest that any degree of MR is associated with increased risk of mortality on multivariate analysis. Of the 5 quantitative studies, 3 showed that a vena contracta width >0.4 cm, or EROA ≥0.2 cm² were associated with higher mortality (10,13,17), 1 showed no association of MR severity with mortality, but did show that vena contracta width ≥0.4 cm predicted the combined endpoint of mortality, heart failure hospitalization, and transplantation (16), and 1 showed no effect of EROA on mortality (14). The latter was a study of 558 patients from an advanced heart failure clinic at the Mayo Clinic. There was no difference in mortality between patients with or without EROA ≥0.2 cm², suggesting that the prognostic influence of MR severity is more important early, and less important later in the course of the disease, when LV dilation is extreme and advanced heart failure is established. However, hemodynamic considerations easily explain differences between the studies (Figure 2). Most studies did not report LVEDV and none reported MR peak velocity. However, if LVEDV is estimated from the reported LV end-diastolic dimension and peak velocity is estimated from the reported systolic blood pressure, each study can be plotted on the hydraulic orifice equation graph, which reveals that all fall closely along the physiologic range. It seems
obvious that EROA should be indexed for LVEDV to determine MR severity.

Another problem with these studies is inherent selection bias: EROA measurement by PISA cannot be done in the absence of a defined proximal convergence zone, such that patients with mild MR were often excluded. In the Rossi et al. (17) study, EROA was measureable in 81% of patients with severe MR...
TABLE 1 Studies Evaluating MR Severity and Prognosis*

<table>
<thead>
<tr>
<th>Study (Ref. #)</th>
<th>N</th>
<th>Type of Study</th>
<th>LVEDV, ml</th>
<th>LVEDV Cutoff</th>
<th>Etiology of MR</th>
<th>Echo Core Lab</th>
<th>Method of Grading MR</th>
<th>MR as Independent Predictor of Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grigioni et al. (10)</td>
<td>303</td>
<td>Single center, observational</td>
<td>NR</td>
<td>NR</td>
<td>Post-MI</td>
<td>No</td>
<td>QD, PISA</td>
<td>EROA ≥0.2 cm² and EROA &lt;0.01-0.19 cm²</td>
</tr>
<tr>
<td>Koelling et al. (11)</td>
<td>1,421</td>
<td>Single center, observational</td>
<td>NR</td>
<td>&lt;0.35</td>
<td>Secondary MR</td>
<td>No</td>
<td>Jet area</td>
<td>Moderate/severe vs. none/mild</td>
</tr>
<tr>
<td>Trichon et al. (12)</td>
<td>2,057</td>
<td>Single center, observational</td>
<td>NR</td>
<td>&lt;0.40</td>
<td>59% ischemic</td>
<td>No</td>
<td>LV angiogram</td>
<td>Graded worsening for all degrees of MR</td>
</tr>
<tr>
<td>Lancellotti et al. (13)</td>
<td>98</td>
<td>Single center, observational</td>
<td>146±18</td>
<td>&lt;0.45</td>
<td>Ischemic</td>
<td>No</td>
<td>PISA</td>
<td>EROA ≥0.2 cm²</td>
</tr>
<tr>
<td>Patel et al. (14)</td>
<td>558</td>
<td>Single center, observational</td>
<td>NR</td>
<td>&lt;0.35</td>
<td>Secondary MR</td>
<td>No</td>
<td>PISA</td>
<td>No difference for EROA ≥ or 0.2 cm²</td>
</tr>
<tr>
<td>Cioffi et al. (15)</td>
<td>175</td>
<td>Single center, observational</td>
<td>NR</td>
<td>&lt;0.40</td>
<td>Secondary MR</td>
<td>No</td>
<td>Jet area</td>
<td>Moderate/severe vs. none/mild</td>
</tr>
<tr>
<td>Grayburn et al. (16)</td>
<td>336</td>
<td>Substudy of multicenter RCT</td>
<td>229±77</td>
<td>&lt;0.35</td>
<td>Secondary MR</td>
<td>Yes</td>
<td>VCW, QD, PISA</td>
<td>MR not predictive of death; VCW ≥0.4 cm</td>
</tr>
<tr>
<td>Rossi et al. (17)</td>
<td>1,256</td>
<td>Multicenter, observational</td>
<td>NR</td>
<td>NR</td>
<td>Secondary MR</td>
<td>No</td>
<td>VCW, PISA</td>
<td>VCW &gt;0.4 cm and EROA &gt;0.2 cm²</td>
</tr>
<tr>
<td>Deja et al. (18)</td>
<td>1,209</td>
<td>Substudy of multicenter RCT</td>
<td>222±69</td>
<td>&lt;0.35</td>
<td>Ischemic</td>
<td>No</td>
<td>ASE grading</td>
<td>Graded worsening for all degrees of MR</td>
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</table>

*Excluding acute myocardial infarction (MI) studies. LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; NR = not reported; PISA = proximal isovelocity surface area; QD = quantitative Doppler; RCT = randomized clinical trial; VCW = vena contracta width.

but only in 34% with mild or moderate MR. In the Patel et al. (14) study, EROA was measureable in 72% with moderate or severe MR, but in only 14% with mild MR. Missing data in patients with mild MR could have confounded the results. In a recent large multicenter trial of ischemic heart failure (19), the echocardiography core laboratory graded MR severity in 1,852 patients (92.3% of available echocardiograms), but EROA by PISA was only measureable in 169 (8%). Reasons include failure to properly perform PISA and inability to measure PISA when there is no or only mild MR. While the studies in Table 1 are generally accepted evidence that secondary MR is associated with poor prognosis, they do not constitute sufficiently strong evidence for a guideline document to change the definition of severe MR. Further studies are needed to evaluate whether indexing EROA or RVol for LVEDV would improve prognostic value.

The guidelines all emphasize the lack of strong evidence that MR repair or replacement improves prognosis in secondary MR, despite the apparent prognostic significance of lower EROA and RVol values. Beigel and Siegel (7) elaborate, invoking the Cardiac Arrhythmia Suppression Trial as the quintessential example of failure of treatment of an established risk factor (frequent ventricular ectopy post-acute MI) to improve mortality. Unlike ventricular ectopy, which is easily and accurately quantified, quantification of MR severity is an imperfect art, most commonly done by calculating EROA and RVol using the PISA method by 2D echocardiography. However, PISA has many limitations (Table 2) and should not be the sole criterion for determining MR severity.

**FIGURE 2 Relationship Between EROA and LVEDV at Different Hemodynamic States With Studies Reporting EROA’s Prognostic Value**

Studies reporting left ventricular end-diastolic volume (LVEDV) are bolded and studies estimating LVEDV from left ventricular (LV) end-diastolic diameter are in italics. None reported MR peak velocity. Therefore, systolic blood pressure was used as a surrogate (except for Cioffi et al. [15] and Rossi et al. [17], which did not report blood pressure). The Patel et al. (14) study, which did not find that EROA 0.2 cm² predicted prognosis, lies on the upper right part of the EROA/LVEDV relationship, where severe MR would be expected at a EROA value of 0.4 cm². Abbreviations as in Figure 1.
Moreover, very little data supports isolated use of or reproducibility of 2D PISA for differentiating mild, moderate, or severe MR.

Marwick et al. (6) argue that the redefinition of severe MR is problematic because the increased risk of secondary MR is not clearly "purely attributable to MR severity." Although increasing MR severity is associated with mortality, even when adjusted for comorbidities, this may be related to secondary MR patients being older and having larger ventricles, more fibrosis/infarction, other major comorbidities, or unmeasured variables.

**PROBLEMS WITH THE USE OF PISA FOR GRADING MR SEVERITY**

EROA shape in secondary MR is usually crescentic (20–26) (Figure 3). Calculation of EROA by PISA assumes a round orifice through a flat surface, such that the proximal flow convergence region is hemispheric and flow can be calculated from the product of the aliasing velocity and the surface area of a hemisphere (2\pi r^2). If the shape of the proximal flow convergence region were a symmetric hemiprolate ellipsoid (i.e., football shaped), calculation of a corrected EROA would be possible; however, the geometry of the proximal convergence zone in secondary MR is complex and often asymmetrical. Fortunately, 3D echocardiography allows direct measurement (20–26). The product of EROA and the velocity-time integral of the MR jet by continuous-wave Doppler is the RVol. One study comparing RVol by 3D echocardiography to magnetic resonance imaging in patients with secondary MR showed a ±8 ml 95% confidence interval (23). Three-dimensional echocardiography, whether by transthoracic or transesophageal imaging, potentially allows more accurate EROA and RVol calculations (26); however, the new guidelines, which appear to partially rely on systematic underestimation of EROA (and hence RVol) by the PISA method, do not address the abundant literature that 3D echocardiography may avoid this problem.

Secondary MR has a characteristic biphasic pattern during systole. MR is generally greatest in early systole, has a nadir in midsystole, and then increases just before mitral valve opening (27). As the PISA method only uses a single time point, overestimation of MR can occur if the operator picks the largest radius at early systole. Conversely, if PISA is measured during midsystole EROA will be underestimated. Moreover, the hydrodynamic concept of EROA refers to the mean EROA occurring over the MR time course, which is not always holosystolic. Single-frame EROA measurements by either traditional 2D PISA or 3D imaging do not necessarily reflect the mean EROA.

PISA radius measurement is difficult because although the aliasing line is clear, the exact point of flow convergence on the anatomical orifice is not.

**TABLE 2 Limitations of the PISA Method**

<table>
<thead>
<tr>
<th>Limitation</th>
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<tr>
<td>Limited accuracy in eccentric jets</td>
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<td>Difficult to judge precise location of mitral valve orifice</td>
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<td>Errors in measurement are squared, resulting in large variance in effective regurgitant orifice area</td>
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<tr>
<td>Must be angle-corrected in nonplanar flow convergence geometry</td>
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<tr>
<td>Assumes hemispheric flow convergence geometry, which is rarely the case in secondary mitral regurgitation</td>
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<tr>
<td>Regurgitant flow changes during systole</td>
</tr>
<tr>
<td>Assumes that measured proximal isovelocity surface area radius corresponds temporally to peak velocity of the mitral regurgitation jet by continuous Doppler</td>
</tr>
<tr>
<td>Not validated for multiple jets</td>
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<tr>
<td>Shape is affected by aliasing velocity and adjacent structures</td>
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<tr>
<td>Interobserver variability and poor agreement among experienced observers</td>
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PISA = proximal isovelocity surface area.

**FIGURE 3 Example of EROA Underestimation by PISA Due to Crescentic Orifice Shape**

(A) Proximal isovelocity surface area (PISA) radius (left) and continuous-wave Doppler (right) resulting in a calculated EROA of 0.18 cm². (B) Direct measurement of the EROA in the same patient at 0.35 cm² by 3D color Doppler (left). EROA is crescentic on 3D imaging, with its major and minor axes shown at right. Abbreviations as in Figure 1.
therapy. LVEF improved from 30% to 50%, LV and LA volumes improved, and the patient became asymptomatic. In the left panel, PISA radius was measured at 7 mm, giving a calculated EROA of 0.16 cm² and RVol of 30 ml, consistent with other findings of mild MR, including an A-wave-dominant mitral inflow pattern, normal pulmonary venous flow velocities, and a LA volume index of 24 ml/m². The right panel shows that an 8 mm radius would result in EROA of 0.26 cm² and RVol of 42 ml, which could be considered severe MR under the new guidelines. Because typical baseline-shifted aliasing velocities are around 30 cm/s and typical peak mitral velocities are around 500 cm/s, the difference between an EROA above or below the new 0.2 cm² threshold is strictly on the basis of the PISA radius being 7 mm versus 8 mm. Biner et al. (28) showed that expert observers disagree substantially on classification of MR severity by PISA, largely because of small differences in radius measurement. Given this issue, confirmation of MR severity by other parameters is needed when EROA and RVol are determined using PISA.

**FIGURE 4** 4-Chamber View From a Patient With Secondary MR

Identical images taken 3 months after optimization of guideline-directed medical therapy and cardiac resynchronization. (Left) PISA radius is measured at 7 mm, giving a calculated EROA of 0.16 cm² and RVol of 30 ml. (Right) PISA radius is measured at 8 mm, giving a calculated EROA of 0.26 cm² and RVol of 42 ml. This patient had an A-wave-dominant mitral filling pattern, normal pulmonary venous flow velocities, and a normal left atrial volume of 24 ml/m². If the definition is changed, a small error in radius measurement by PISA (7 mm vs. 8 mm) makes the difference between mild (Stage B) and severe (Stage C or D) secondary MR. Abbreviations as in Figures 1 and 3.

**FIGURE 5** 4-Chamber Echocardiographic Images From a Patient With Severe Secondary MR

Baseline (left) and 1 month later, after optimizing medical therapy (right). (Top) Changes in color-Doppler mitral regurgitation (MR) jet. (Bottom) Change from systolic flow reversal (blue arrow, left) to normal (blue arrow, right). This case illustrates secondary MR’s dynamic nature, which improves or worsens substantially depending on volume status, blood pressure, heart failure exacerbation, ischemia, or medication changes.

**CLINICAL DILEMMAS CREATED BY THE NEW GUIDELINES**

**DISPARATE RESULTS FROM 2D AND 3D ECHOCARDIOGRAPHY.** A patient with an EROA of 0.25 cm² by PISA will commonly have EROA >0.4 cm² on 3D echocardiography. Such patients usually have severe MR substantiated by other echocardiographic findings and clinical decision making is straightforward; however, discrepancies between 2D- and 3D-derived EROA can be problematic. For example, if the EROA by PISA is 0.15 cm² and the patient is determined to have mild MR on the basis of the totality of echocardiographic and clinical findings, what happens if the EROA is 0.25 cm² by 3D imaging? Unfortunately, the new AHA/ACC guidelines could be misinterpreted to classify the patient as having severe MR. Although increasingly used to measure EROA and RVol in secondary MR without assuming round orifice geometry, it is typically a single-frame measurement of a dynamic orifice and is subject to overestimation of EROA because the pulsed-Doppler color flow technique includes lower velocity signals from turbulent eddies outside of the high-velocity jet core emerging from the orifice (29). Note that the studies in Table 1 showing a mortality risk for any degree of MR used either subjective grading or PISA. The ability of 3D planimetry of EROA to predict outcomes has not been validated.

**THE DYNAMIC NATURE OF SECONDARY MR.** Figure 5 is from a patient seen for evaluation of severe secondary MR due to an underlying nonischemic cardiomyopathy. The patient has New York Heart
Association functional class III heart failure symptoms and a recent admission for heart failure exacerbation. EROA by PISA was 0.35 cm² with a restrictive mitral filling pattern and systolic flow reversal in the right upper pulmonary vein. Blood pressure was 138/78 mm Hg. The patient was determined to have severe MR, but was not on optimal medical therapy. Losartan was increased from 25 to 50 mg and furosemide from 20 to 40 mg daily. One month later, the patient was asymptomatic and clinically euvoletic. Blood pressure was now 108/64 mm Hg. Two-dimensional Doppler echocardiography demonstrated an EROA by PISA of 0.15 cm²; the mitral inflow pattern showed impaired relaxation, and the right upper pulmonary vein flow pattern was normal. This patient illustrates the dynamic nature of secondary MR. EROA also varies notoriously with loading conditions, commonly seen during hypertensive crises and heart failure exacerbations. Functional MR severity changes over time with medical therapy, revascularization, and cardiac resynchronization therapy. The guidelines do not address how to approach the dynamic nature of secondary MR. It seems prudent not to label patients as having severe MR until they are on optimally tolerated doses of guideline-directed medical therapy, and, if clinically indicated, have undergone revascularization and/or cardiac resynchronization therapy.

**IMPLICATIONS FOR SURGICAL MANAGEMENT**

Current European Society of Cardiology and AHA/ACC guidelines are consistent in management recommendations for secondary MR. Mitral valve surgery is indicated for a patient with severe MR undergoing cardiac surgery for coronary revascularization or other reasons; however, mitral valve surgery purely to address secondary MR is generally a Class IIb recommendation because the preponderance of current evidence has not shown a mortality benefit. The recent Cardiacoracic Surgery Network trial of severe MR randomized patients to mitral valve repair with a rigid complete annuloplasty ring versus chord-sparing mitral valve replacement. The primary outcome of LV end-systolic volume reduction was no different, but 30-day and 1-year survival were similar, and moderate or greater MR had a 32% recurrence rate at 1 year. Under the new definition, this would be a 32% rate of severe MR at 1 year. A Cardiothoracic Surgery Network trial of moderate MR randomized to bypass surgery alone or without annuloplasty showed no benefit in terms of mortality or LV remodeling at 1 year.

According to the new guidelines, the patients in this trial could now be redefined as having “severe” MR. Although the new guidelines recommend mitral valve surgery for severe symptomatic secondary MR only at a Class IIb level, the definition change poses problems. Clinical trial sites of new mitral valve device therapies may now advocate enrolling patients on the basis of PISA-derived EROA of 0.2 cm². Lower entry thresholds could dilute any observed benefit by making improvements in LV or LA remodeling, or quality-of-life measures more difficult to identify. Interesting, recent data from the MitraClip device clinical trials show significant LV and LA remodeling in secondary MR when MR is reduced from severe (as previously defined) to either mild or moderate (“severe” under the new guidelines). If a patient undergoes a surgical or percutaneous mitral valve procedure that reduces EROA from 0.4 to 0.2 cm², and hemodynamics, heart failure symptoms, quality-of-life scores, and LV and LA remodeling improve, does this patient still have severe MR? The conundrum raised by changing the EROA cutoff value from 0.4 to 0.2 cm² for severe secondary MR highlights the importance of an integrative approach to assessing MR severity, which all published guidelines continue to advocate. An integrated approach incorporates multiple Doppler parameters without relying on any single parameter, thereby minimizing the limitations inherent in each.

**CONCLUSIONS**

Proposed changes to the partial definition of severe secondary MR from an EROA of 0.4 to 0.2 cm² and an RVol of 60 to 30 ml should be applied cautiously in clinical practice. The evidence for changing these cutoffs comes from retrospective analyses of observational studies using a flawed method that underestimates EROA and RVol in secondary MR.

Redefining severe MR may create confusion in clinical practice. Although not intended to do so, guidelines can and often do influence reimbursement decisions, quality metrics, and medicolegal issues. Thus, a major change should require strong evidence, explanation of its necessity and ideally, broad expert consensus substantiated by Level of Evidence: A. Table 16 in the expert guidelines appears to recommend a change in definition of secondary MR severity; however, careful reading of the entire document supports continuing an integrative approach that discounts poor quality data (e.g., EROA underestimation by PISA) and incorporates clinical judgment.
Specifically, we propose the following:

1. The integrative approach using multiple echocardiographic and clinical variables should continue to be used to grade secondary MR severity;
2. The new definition of severe secondary MR with RVol ≥ 30 ml and EROA ≥ 0.2 cm² depends on LV size and on the LV-LA pressure gradient and must be used in that context;
3. The quantification method must be specified (2D PISA, 3D planimetry, volumetric);
4. Classification of a patient as having severe secondary MR (Stage C or D) should be deferred until guideline-directed medical therapy, resynchronization, and revascularization are optimized.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Paul A. Grayburn, Baylor Heart and Vascular Institute, 621 North Hall Street, Suite H030, Dallas, Texas 75226. E-mail: paulgr@baylorhealth.edu.

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KEY WORDS echocardiography, guidelines, hemodynamics, mitral valve, mitral valve insufficiency