Structural Heart

The Journal of the Heart Team

ISSN: 2474-8706 (Print) 2474-8714 (Online) Journal homepage: https://www.tandfonline.com/loi/ushj20

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To cite this article: Paul A. Grayburn, Robert C. Stoler & Michael J. Mack (2017) The 2017 ACC/AHA Updated Valve Guidelines Regarding Mitral Regurgitation: The Guidelines Get it Right, Structural Heart, 1:1-2, 31-33, DOI: 10.1080/24748706.2017.1326648

To link to this article: https://doi.org/10.1080/24748706.2017.1326648

Accepted author version posted online: 04 May 2017.
Published online: 19 May 2017.

STRUCTURAL HEART
2017, VOL. 1, NOS. 1–2, 31–33
https://doi.org/10.1080/24748706.2017.1326648

OPINION

The 2017 ACC/AHA Updated Valve Guidelines Regarding Mitral Regurgitation: The Guidelines Get it Right

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Introduction

When the ACC/AHA Guidelines for Valvular Heart Disease were first published in 1998, they were based primarily on expert opinion and observational studies, as randomized controlled trials (RCTs) were sparse. Fortunately, that situation has improved dramatically such that the 2014 guidelines[1] have recently been updated[2] to include new information from RCTs on transcatheter aortic valve replacement (TAVR) and the Cardiothoracic Surgery Network (CTSN) trials in secondary mitral regurgitation (MR). New or modified recommendations in the 2017 guideline update focus on three primary areas: (1) new indications for TAVR; (2) revised definition of severe secondary MR and recommendations for management of MR; and (3) management of patients with prosthetic valves. Of these, the most provocative, yet welcome, changes are those regarding MR.

Primary MR

Primary MR is a condition in which pure volume overload on the left heart eventually leads to progressive dilation of the left ventricle (LV) and left atrium (LA), LV systolic dysfunction, pulmonary hypertension, and atrial fibrillation. Because "the valve makes the heart sick," surgical correction of MR is curative.[3] The most common cause of severe primary MR in developed countries is degenerative MR (mitral valve prolapse or flail leaflet) and fortunately, such valves can usually be repaired in the hands of experienced mitral valve surgeons. The guidelines strongly recommend mitral valve repair in degenerative MR, particularly when the lesion is limited to the posterior leaflet, where repair is almost always feasible. In fact, it is contraindicated to perform valve replacement for isolated posterior leaflet flail or prolapse unless repair has been attempted and failed (Class III Harm), a rare event in experienced hands. Unfortunately, we have encountered many such patients that were not referred to experienced mitral valve surgeons (or centers) and were treated with replacement. It remains a challenge for some hospitals/administrators/physicians to refer their patients to mitral centers of excellence. Incentives need to be realigned to put the patient's best interest first, particularly when minimally invasive approaches to mitral valve repair have outstanding results,[4–6] but are not universally available.

Because primary MR eventually leads to decreased LV ejection fraction (LVEF), the Class I recommendation to perform mitral valve repair in Stage D (symptomatic severe) MR with LVEF > 30% remains unchanged. Interestingly, in a registry of 1875 patients with flail leaflet, LVEF < 30% was rare (0.3%); and LVEF was 45–60% in only 23% of patients.[7] This is largely due to the favorable loading conditions of primary MR; such that LVEF does not accurately reflect underlying LV myocardial dysfunction. Observational studies document that patients with LVEF < 60% have a worse prognosis after mitral valve repair.[7,8] Thus, a decrease in LVEF on longitudinal studies toward the threshold value of 60% or an increase in LV end-systolic diameter toward 4.0 cm is now considered a Class IIa recommendation to perform mitral repair.

Secondary MR

In the 2014 version of the guidelines,[1] the definition of severe secondary (also known as functional) MR was lowered from the traditional values of calculated effective regurgitant orifice area (EROA) ≥ 0.4 cm^2, regurgitant volume ≥ 60 ml, and regurgitant fraction ≥ 50% to new thresholds of EROA ≥ 0.2 cm^2, regurgitant volume ≥ 30 ml with regurgitant fraction remaining ≥ 50%. The 2014 change was prompted by observational data showing that the lower values were associated with an adverse prognosis[9–12] in secondary MR. However, this change generated considerable controversy within the cardiology community.[13–15] The reasons have been elaborated in detail,[15] but include single frame measurement of EROA that may not reflect dynamic changes during systole, use of a formula that assumes round orifice geometry when the orifice is crescent-shaped in secondary MR, dynamic changes in MR with loading conditions, ischemia or dyssynchrony, and the squaring of small errors in measurement. Although echocardiography can underestimate MR severity, it has a general tendency to overestimate it, as shown in a recent comparison of echocardiography to cardiac magnetic resonance imaging.[16] Importantly, there has never been convincing evidence that surgical or catheter-based correction of secondary MR improves survival. Therefore, lowering the threshold values for severe MR could lead to unnecessary surgical or transcatheter intervention. The updated 2017

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guidelines now offer the same definition of MR severity for primary and secondary MR, and reiterate the American Society of Echocardiography guideline recommendations[17] that multiple echocardiographic parameters be integrated to determine MR severity rather than sole reliance on a single measurement. Furthermore, there is an emphasis on "the understanding that [EROA] cutoff of >0.2 cm^2 is more sensitive and >0.4 cm^2 is more specific for severe MR." This latter point merits emphasis because an EROA of 0.2 cm^2 could be severe MR, particularly when the LV is not very dilated. Consider a patient with an LV end-diastolic volume of 150 ml and LVEF 30%. Total LV stroke volume is 45 ml (150 ml × 30%). It would be impossible to have a regurgitant volume ≥ 45 ml. If the true (not measured) EROA were 0.2 cm^2 and the velocity-time integral of the MR jet by continuous wave Doppler were 150 cm, regurgitant volume would be 30 ml. Thus, forward stroke volume would be 15 ml and the regurgitant fraction 67%. This patient has severe MR; emphasizing the need to consider EROA, regurgitant volume and regurgitant fraction in relation to LV total stroke volume when assessing MR severity.[15]

The other major changes in secondary MR are recommendations for surgery. Based on the recently published CTSN trials, a new recommendation states that "it is reasonable to choose chord-sparing mitral valve replacement over downsized annuloplasty if operation is considered for severely symptomatic patients (NYHA Class III to IV) with chronic severe ischemic MR (Stage D) and persistent symptoms despite guideline-directed medical therapy (Class IIa, Level of evidence B-R)." The CTSN severe trial showed no difference between mitral valve repair (undersized annuloplasy) or replacement in the primary endpoint of LV remodeling. There was also no difference in mortality at 1 or 2 years,[18,19] although the trial was not powered for a mortality difference. However, there was a higher rate of recurrent moderate or severe MR in the annuloplasty group (58.8 vs. 3.8% at 2 years, $p < 0.001$), with associated higher rates of hospitalization and heart failure. Post-hoc analysis showed that patients with posterobasal aneurysms were most likely to have recurrent MR after annuloplasty due to severe tethering of the posterior leaflet toward the apex, which cannot be corrected by an annuloplasty ring.[20] Patients with durable repairs had better outcomes than those with recurrent MR. Remaining questions include how to best select patients who would benefit from annuloplasty, and whether additional repair techniques (e.g. chordal cutting, chordal lengthening, papillary muscle repositioning) should be added to annuloplasty in selected patients. Until such issues are resolved, the current guideline is appropriate and the decision to perform MVR versus downsized annuloplasty should be individualized carefully.

A previous recommendation for surgical repair of secondary moderate MR has been modified in the updated guidelines from a Class IIb, level of evidence C (limited data or expert opinion) to level of evidence B-R (moderate quality evidence from one or more RCT) due to the information from the CTSN randomized trials. The recommendation states that "in patients with chronic, moderate ischemic MR (Stage B) undergoing CABG, the usefulness of mitral valve repair is uncertain." This is based on the CTSN moderate trial which randomized 301 such patients to CABG only or CABG plus a downsized annuloplasty ring. There was no difference in the primary outcome of LV remodeling, nor in secondary clinical outcomes, despite a higher rate of moderate or severe MR in the CABG only group (32.3% vs. 11.2%, $p < 0.001$).[21,22]

Transcatheter mitral valve interventions

The updated guidelines did not change the indication for MitraClip in patients with primary degenerative MR, favorable anatomy and prohibitive risk for surgery. This remains the only FDA-approved indication for MitraClip. Despite a RCT and multiple observation studies showing benefit in this patient population (level of evidence B), the class of recommendation remains IIb. Many cardiologists expected this to change to IIa based on proven device safety in a worldwide experience of over 45,000 patients and clinical benefit in terms of MR reduction, LV remodeling, and functional capacity. Ongoing trials of MitraClip for secondary MR are awaited,[23] but cannot be addressed in the guidelines until the results have been published. Early feasibility trials of transcatheter mitral valve repair and replacement are underway and preliminary results have been published,[24,25] but it is far too soon to include them in the guidelines.

Overall, the updated guidelines are a welcome addition, especially as they relate to MR. Ongoing RCTs and early feasibility trials with various transcatheter technologies are underway. Because the criteria for intervention in MR depend on demonstration of safety and efficacy, future updates to the guidelines will be based on the outcomes of these studies.

Disclosure Statements

Paul A. Grayburn, MD, has received research grants from Edwards, Medtronic, Abbott Vascular, Tendyne, Boston Scientific, Echo Core Lab, Neochord, and ValTech Cardio, and is a consultant for Abbott Vascular, Neochord, and ValTech Cardio. Robert C. Stoler, MD, has received research grants form Edwards, Medtronic, Abbott Vascular, Tendyne, and Boston Scientific, and is a consultant for Medtronic and Boston Scientific. Michael J. Mack, MD, has received research grants from Edwards, Medtronic, and Abbott Vascular.

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