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LETTERS TO THE EDITOR

Should the Guidelines for the Assessment of the Severity of Functional Mitral Regurgitation Be Redefined?

The 2012 guidelines for the management of valvular heart disease by the European Society of Cardiology (ESC) (1) recommend that for functional mitral regurgitation (MR), an effective regurgitant orifice area (EROA) of >20 mm^2 should be considered severe; however, an EROA of >40 mm^2 is used as the cutoff for degenerative MR.

Several nonrandomized studies have shown that cardiac mortality is increased in the presence of functional MR and reduced left ventricular (LV) ejection fraction (2). Patients with an EROA of ≥20 mm^2 have a lower 5-year survival rate and a higher risk of congestive heart failure. This same association is present for lesser degrees of MR; with an EROA of 1 to 19 mm^2, there is an increased 5-year mortality rate and a high risk of congestive heart failure. Current American College of Cardiology/American Heart Association (ACC/AHA) (3) and ESC guidelines (1) use a matrix of criteria for the diagnosis of severe MR, as shown in Table 1. No single criterion in isolation is sufficient to establish a diagnosis of severe MR. EROA can be calculated by the proximal isovelocity surface area (PISA) or by measuring the MR volume or regurgitant volume by assessing the LV volume and LV forward stroke volume. Most echocardiography laboratories do not use the latter volumetric technique because it is time-consuming and can be associated with significant errors due to unreliable endocardial edge detection. In addition, calculations of forward stroke volume may be inaccurate because they are generally based on the assumption that the LV outflow tract is circular, whereas, in fact, recent 3-dimensional echocardiography and computed tomography data have shown that it is generally oval.

Thus, most clinical laboratories rely on flow convergence assessment or the PISA method to assess the EROA. However, the use of the PISA to assess the EROA has also been shown to be highly problematic: Table 2 lists >10 substantial limitations to the PISA method. In addition to these limitations, reliance on a single method to assess MR severity in functional MR deviates from the wisdom of using multiple criteria to grade MR severity, which was supported by the initial ACC/AHA guideline committees and the American and the European echocardiography societies.

Unlike degenerative MR, especially in the setting of a flail leaflet where MR severity is relatively fixed, functional MR varies with the patients' hemodynamic status. Because functional MR severity may be highly variable, patients should be assessed while on optimal therapy (including revascularization and/or cardiac resynchronization therapy) before classifying them as severe.

The rationale for the ESC recommendations to lower the threshold for grading MR severity in the setting of functional MR is in part related to the adverse prognosis associated with MR in patients with LV dysfunction. However, associations do not always equal causation, therapeutic indications, or therapeutic benefit. CAST (Cardiac Arrhythmia Suppression Trial) serves as an example of why associated phenomena should not be used as targets for treatment. For years, "it was known" that ventricular ectopy in the setting of reduced LV function was associated with a worse prognosis as well as being associated with a higher incidence of sudden death. However, the CAST clearly showed that treating this associated variable (premature ventricular contractions) with antiarrhythmic agents increased all-cause mortality and also serves as an example of why associated phenomena should not be used as targets for treatment.

Table 1. Multiparameter Approach for Defining Severe Mitral Regurgitation

Qualitative
Color Doppler jet area >40% of the left atrium, wall-hugging jet of any size, swirling in the left atrium
Doppler vena contracta width ≥0.7 cm
Systolic flow reversal in the pulmonary veins
Quantitative
Regurgitant volume ≥60 ml/beat
Regurgitant fraction ≥50%
Effective regurgitant area >0.4
Additional supportive parameters
Left atrial size: enlarged
Left ventricular size: enlarged
E-wave dominant mitral flow >1.2 m/s
Holosystolic Doppler signal

Table 2. Limitations of the Proximal Isovelocity Surface Area Method

Limited accuracy for eccentric jet
Difficult to judge
Precise location of mitral valve orifice
Flow convergence shape
Assumes a hemispheric jet
Jet usually noncircular and often slit like
Shape affected by aliasing velocity
Shape affected by adjacent structures
Errors in measurement are amplified due to squaring in equation
Regurgitant flow changes during systole
Not valid for multiple jets
Great interobserver variability and poor agreement, even among experienced echocardiologists

Multiple trials demonstrate that for functional MR (ischemic or nonischemic), surgery with revascularization or mitral valve repair or replacement does not improve the 5-year survival rate (4). The only therapies that are beneficial for functional MR are those that improve ventricular function such as beta-blockers and angiotensin-converting enzyme inhibitors. Until now, moderate MR has been defined by an EROA of 0.20 to 0.39 mm^2. Patients with 3+ to 4+ MR who have moderate (2+) residual MR after placement of a MitraClip (Abbott Vascular, Abbott Park, Illinois) have reverse remodeling, a decrease in LV end-diastolic volume from 159 ml to 141 ml ($p < 0.001$), a trend toward a decrease in end-systolic volume from 82 ml to 77 ml ($p = 0.07$), and improvement in symptoms after 1 year (5). However, according to the recent ESC criteria, patients with moderate functional MR would be classified inappropriately as having severe MR and would be candidates for further intervention.

With the development of percutaneous techniques, there may be an inclination to treat less severe degrees of MR in an attempt to improve the status of patients with impaired LV function. However, this approach is likely to be problematic. It will be difficult to assess improvement or treatment success (a decrease in MR) if patients with an EROA of 20 to 30 mm^2 are treated. Clinical follow-up and assessment of improvement will be complicated by the patients' underlying LV dysfunction. At present, if the criteria for MR severity are to be reduced in the setting of functional disease, an EROA threshold of 30 mm^2 would be more amenable to determining whether the intervention reduced MR severity. With an EROA between 20 and 30 mm^2, it will be difficult to discern whether the intervention actually decreased MR severity, and even more so if the EROA is 20 to 25 mm^2. It is also important not to use a single variable but to maintain the matrix of echocardiographic Doppler parameters listed in Table 1, which have been the standard used to define MR severity.

Any degree of MR worsens patient prognosis; however, mitral valve surgery does not improve prognosis unless LV function is improved. MitraClip patients with a 2+ (moderate) MR result have an improvement in symptoms, functional capacity, and ventricular size. These findings suggest that moderate MR (EROA of >0.20 and <0.30 cm^2) does not adversely affect either the left ventricle or patient prognosis and should not be classified as severe, despite the most recent ESC guideline/recommendations (1).

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REFERENCES

1. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur J Cardiothorac Surg 2012;42:S1–44.
2. Grigioni F, Enriquez-Sarano M, Zehr KJ, Bailey KR, Tajik AJ. Ischemic mitral regurgitation: long-term outcome and prognostic implications with quantitative Doppler assessment. Circulation 2001;103:1759–64.
3. Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. J Am Coll Cardiol 2006;48:e1–148.
4. Kim Y-H, Czer LSC, Soukiasian HJ, et al. Ischemic mitral regurgitation: revascularization alone versus revascularization and mitral valve repair. Ann Thorac Surg 2005;79:1895–901.
5. Auricchio A, Schillinger W, Meyer S, et al. Correction of mitral regurgitation in nonresponders to cardiac resynchronization therapy by MitraClip improves symptoms and promotes reverse remodeling. J Am Coll Cardiol 2011;58:2183–9.

Physical Exercise Reduces Aortic Regurgitation

Exercise Magnetic Resonance Imaging

In patients with aortic regurgitation (AR), exercise testing plays a pivotal role in clinical decision making according to American College of Cardiology/American Heart Association guidelines. However, it is unclear exactly how AR behaves during exercise, as it has only been estimated but not measured so far. Using cardiac magnetic resonance (CMR), it is theoretically possible to measure AR and cardiac volume changes during exercise. Studies in patients with other cardiac diseases have combined exercise and CMR by using complex, cumbersome, and expensive ergometers (1–3).

Therefore, the first aim of this study was to establish a simple and adequate form of exercise during CMR studies. We designed a steady-state submaximal exercise test, because it is known that most hemodynamic changes occur at submaximal exercise levels (4). Additionally, acquiring blood-flow and cardiac-volume data by CMR requires a certain amount of time during a hemodynamic steady-state.

The second aim of this study was to investigate the change of AR and left ventricular (LV) volumes during steady-state submaximal exercise in patients with asymptomatic isolated AR without any cardiac medication.

To this end, we designed and built an exercise apparatus (patent utility no. 202013006749.7) to easily enable steady-state submaximal exercise over longer periods of time during CMR scanning. The apparatus is intrinsically auto-normative, as the workload depends only on the length and weight of the subject's legs, which are attached to a rope passing over a pulley fixed to a specially designed aluminum frame mounted onto the magnetic resonance table. The patients stroke their legs 72 times/min as directed by a metronome.

Healthy volunteers underwent 2 cardiopulmonary tests to determine steady-state submaximal and peak oxygen uptake (VO_2) by the new submaximal exercise apparatus and by routine symptom-limited maximal bicycle exercise. Submaximal VO_2 was median 24% (range 17% to 37%) of peak VO_2 (8.6 ml/kg/min [range 7.2 to 13.7 ml/kg/min] and 40 ml/kg/min [range 33 to 54 ml/kg/min]).