Evaluation of the Integrative Algorithm for Grading Chronic Aortic and Mitral Regurgitation Severity Using the Current American Society of Echocardiography Recommendations: To Discriminate Severe from Moderate Regurgitation

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Background: The recently published integrative algorithms for echocardiographic grading of native aortic regurgitation (AR) and mitral regurgitation (MR) by the American Society of Echocardiography are consensus based and have not been evaluated. Thus, the aims of the present study were to investigate the feasibility of individual parameters and to evaluate the ability of the algorithms to discriminate severe from moderate regurgitation.

Methods: This prospective study comprised 93 patients with chronic AR ($n = 45$) and MR ($n = 48$). All patients underwent echocardiography and cardiovascular magnetic resonance within 4 hours. The algorithms were evaluated using two different definitions for severe regurgitation: (1) a cardiovascular magnetic resonance standard indicating future need for valve surgery and (2) a clinical standard using patients who underwent valve surgery with proven postoperative left ventricular reverse remodeling and improved functional class (AR/MR, $n = 26/26$).

Results: The feasibility of the criteria in the first step of the algorithm was higher (AR/MR, 95%/91%) compared with the second step using quantitative Doppler parameters (74%/57%). For the AR algorithm, sensitivity was 95% and specificity 44%, whereas for the MR algorithm, sensitivity was 73% and specificity 92%. Among patients with benefit of surgery, the algorithms correctly identified 77%, misclassified 8%, and were inconclusive in 15% of the patients with AR; the corresponding figures were 73%, 15%, and 12% in the patients with MR.

Conclusions: Using cardiovascular magnetic resonance as reference, the recommended algorithms for grading of regurgitation have the ability to rule out severe AR and rule in severe MR. The quantitative Doppler methods are hampered by feasibility issues, and our findings suggest that the decision regarding surgical intervention in symptomatic patients with discordant or inconclusive echocardiographic grading should be based on a consolidated assessment of clinical and multimodality findings. (J Am Soc Echocardiogr 2018;■:■-■.)

Keywords: Aortic regurgitation, Mitral regurgitation, ASE recommendations, ASE algorithm, Echocardiography, Cardiovascular magnetic resonance

Echocardiography is the primary diagnostic tool for the assessment of chronic valvular regurgitation, including elucidation of mechanism as well as quantification of severity and impact on cardiac function. Accurate evaluation of chronic aortic regurgitation (AR) and mitral regurgitation (MR) severity, particularly to discriminate severe from moderate regurgitation, is crucial for appropriate clinical decision making and optimal timing of surgery. The recommendations for the evaluation of valvular regurgitation from the American Society of Echocardiography (ASE; 2003) and the European Association of Echocardiography (2010) have been the core documents guiding the assessment of native valvular regurgitation severity in clinical practice.[1-3] These recommendations emphasize a comprehensive evaluation with

Abbreviations
Ao FF = Aortic forward flow
AR = Aortic regurgitation
ASE = American Society of Echocardiography
CMR = Cardiovascular magnetic resonance
EDV = End-diastolic volume
EROA = Effective regurgitant orifice area
LV = Left ventricular
LVSV = Left ventricle stroke volume
MR = Mitral regurgitation
PHT = Pressure half-time
PISA = Proximal isovelocity surface area
RF$_{CMR}$ = Regurgitant fraction by cardiovascular magnetic resonance
RF = Regurgitant fraction
RVol = Regurgitant volume
RVol$_{CMR}$ = Regurgitant volume by cardiovascular magnetic resonance
VC = Vena contracta
VTI = Velocity-time integral
VTI$_{RegJet}$ = Velocity-time integral of the regurgitant jet

multiple echocardiographic parameters followed by an integrative interpretation of the findings in the specific clinical context. However, no detailed information addressing feasibility issues or discordant findings was provided. In the real-world practice of echocardiography, these issues are challenging and may generate inconclusive results and thereby delay treatment. Recently, the ASE published new recommendations for grading AR and MR severity with suggestions for further refined diagnostic procedures and introduced, among others, cardiovascular magnetic resonance (CMR) as a complementary diagnostic tool.[4] The current recommendations present an algorithm consisting of a first step with several specific (structural, qualitative, and semi-quantitative) criteria indicating severe regurgitation and, in indeterminate cases, a second step using quantitative Doppler methods. The thresholds and findings indicating severe regurgitation are unaltered compared with the previous recommendations, but the number of parameters required for each grade is now clearly defined. The proposed diagnostic algorithms are based on published literature and expert consensus, but importantly, the diagnostic accuracy of the suggested algorithms has so far not been evaluated. In studies evaluating the diagnostic accuracy of valvular regurgitation, lack of a "true" reference standard is a problem that is generally acknowledged. In the present study, we strived to approach a reference standard for severe regurgitation using two different surrogates. First, we evaluated the algorithms using CMR as reference (CMR standard). The thresholds of regurgitant fraction (RF) by CMR (RF$_{CMR}$) were based on recently published clinical outcome data indicating future need for valve surgery.[5,6] Second, we evaluated the algorithms in subgroups of patients operated for severe chronic AR or MR with documented benefit of the valve surgery confirmed by reverse remodeling of the left ventricle and/or postsurgical symptom alleviation (clinical standard).

Thus, the aims of the present study were twofold: (1) to assess the usefulness of the individual echocardiographic parameter in terms of feasibility, applicability, and reproducibility as well as their relationship to CMR findings and (2) to evaluate the overall diagnostic performance of the recommended algorithms of the current ASE recommendations.

METHODS

Study Population

This prospective study comprised 93 patients with chronic moderate or severe AR ($n = 45$) and MR ($n = 48$). Baseline patient characteristics are presented in Table 1. A comprehensive echocardiographic examination performed by an experienced investigator was followed by a CMR scan within 4 hours. The exclusion criteria were moderate or greater regurgitation in any other valve, any other significant cardiac disease or arrhythmia, and contraindications to CMR imaging. Echocardiography was performed either as part of routine follow-up (AR, $n = 17$; MR, $n = 20$) or as a study before aortic or mitral valve surgery (AR, $n = 28$; MR, $n = 28$). A second echocardiographic and/or CMR examination was performed 10 ± 1 months after surgery in 26 patients with AR and 26 patients with MR. Two patients with MR were unwilling to participate in any follow-up examination after the surgery. Eight patients with AR and eight with MR underwent only a postsurgical echocardiographic examination, because of newly obtained relative contraindications to CMR imaging (permanent pacemaker, mechanical valve) or unwillingness to undergo a second CMR scan. There was one patient with moderate regurgitation operated due to a dilated ascending aorta and one due to symptoms, as well as four asymptomatic patients with severe regurgitation not proceeding to valve surgery (AR, $n = 2$; MR, $n = 2$). These six patients together with the two patients who were unwilling to participate in the postsurgical follow-up examinations were excluded from the evaluation of the algorithms using the clinical standard but are included in the analysis using the CMR standard. The feasibility and applicability of individual echocardiographic parameters and the relationship to regurgitant volume (RVol) by CMR (RVol$_{CMR}$) and RF$_{CMR}$ were evaluated in the entire patient groups (AR, $n = 45$; MR, $n = 48$).

The study was conducted according to the Declaration of Helsinki. The Regional Ethics Review Board in Gothenburg gave ethical approval for the study protocol, and written informed consent was obtained from all participants.

Reference Standards for Evaluation of the ASE Algorithms

CMR Standard. The RF$_{CMR}$ thresholds indicating future need for surgery are defined in two recent publications on the basis of clinical outcome data.[5,6] Threshold of RF$_{CMR}$ for AR was >33% and for MR was >40%. Thus, patients with RF$_{CMR}$ above the thresholds are classified as having severe regurgitation and below as having moderate regurgitation.

Clinical Standard. In the present study, 26 patients with chronic AR and 26 with chronic MR underwent surgery for severe regurgitation. Evaluation of the indication and decision for surgery was based on the initial clinical and echocardiographic findings without knowledge of the CMR scan results. The hemodynamic significance of regurgitation was confirmed by surgical benefit indicated by improvement of either symptoms or significant reverse remodeling of left ventricular (LV) volume. Symptoms and New York Heart Association functional class were assessed by personal interview with each patient by the same investigator at the time of presurgical and follow-up examination.

Echocardiographic Acquisition and Measurements

The echocardiographic examination was performed using a commercially available imaging system (Vivid E9; GE Healthcare, Milwaukee, WI). The investigator was blinded to results of the