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ORIGINAL RESEARCH

Echocardiographic Evaluation of Chronic Aortic Regurgitation

Comparison With Cardiac Magnetic Resonance and Implications for Guideline Recommendations

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ABSTRACT

BACKGROUND Guidelines for echocardiographic evaluation of aortic regurgitation (AR) have not been validated against an independent quantitative standard.

OBJECTIVES The aim of this study was to evaluate the accuracy of the ASE (American Society of Echocardiography) AR guidelines against cardiac magnetic resonance (CMR) and to develop simplified approaches for detection of significant AR.

METHODS Patients with AR underwent echocardiography and CMR <4 hours apart. AR severity was graded according to ASE guidelines. Quantitation of regurgitant volume (RegV) was performed with pulsed Doppler at the mitral annulus and right ventricular outflow compared with left ventricular (LV) outflow, and with proximal isovelocity surface area.

RESULTS The authors studied 81 patients; median age was 52 years, and 58% had a bicuspid aortic valve. According to echo, 35 (43%) patients had mild AR, 18 (22%) moderate, 12 (15%) moderate to severe, and 16 (20%) had severe AR. The area under the curve (AUC) for detection of severe AR by CMR using ASE grading was 0.9 (82.4% sensitivity and 96.9% specificity). Feasibility of RegV quantitation was >88% using either echo volumetric method, and it was low for proximal isovelocity surface area (37%). The highest accuracy for echo parameters against CMR was seen with vena contracta width, jet width, and LV end-diastolic volume index (AUC: 0.86-0.89); pressure half-time had the lowest accuracy. Without RegV quantitation, a vena contracta width ≥0.5 cm and indexed LV end-diastolic volume ≥82 mL/m^2 had 95.5% positive predictive value and 87.5% negative predictive value for identifying ≥moderate to severe AR by CMR (AUC: 0.89).

CONCLUSIONS The ASE guidelines display very good performance in identifying significant AR. A simplified approach using vena contracta width and LV volumes can be used to reliably identify significant AR. Further validation of the findings in larger cohorts and against clinical outcomes is needed. (JACC Cardiovasc Imaging. 2024;■:■–■)

Echocardiography is the first-line method for evaluation of the etiology and severity of aortic regurgitation (AR). The ASE (American Society of Echocardiography) guideline algorithm recommends identifying specific features of mild and severe AR for grading, and quantitation when feasible.[1] However, these recommendations are not yet supported by rigorous evidence from an

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ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

CMR = cardiac magnetic resonance

LVEF = left ventricular ejection fraction

LVEDV = left ventricular end-diastolic volume

LVESV = left ventricular end-systolic volume

LVOT = left ventricular outflow tract

MA = mitral annulus

PISA = proximal isovelocity surface area

RegF = regurgitant fraction

RegV = regurgitant volume

RVOT = right ventricular outflow tract

SV_{LVOT} = left ventricular outflow tract stroke volume

SV_{MA} = mitral annulus stroke volume

SV_{RVOT} = right ventricular outflow tract stroke volume

TTE = transthoracic echocardiogram

VCW = vena contracta width

independent quantitative standard. The relative accuracy of echo parameters, the respective weight the reader would assign to them, and whether a large number of parameters are needed for a high specificity of AR severity have not been elucidated. Studies that compared echocardiographic quantitation against cardiac magnetic resonance (CMR) have included relatively few patients or did not include the full spectrum of AR severity.[2,3] In addition, CMR has become the reference in quantitating ventricular volumes and aortic flow with good reproducibility in AR quantitation[3-5] and outcome studies in AR.[6-9]

The aims of the current study were as follows: 1) to compare the accuracy of the ASE algorithm in detecting hemodynamically significant AR (≥ moderate to severe) by CMR and its overall concordance with CMR quantitation; 2) to evaluate the feasibility and accuracy of individual quantitative echocardiographic measures of AR severity using CMR as the reference standard; and 3) to identify the relative accuracy of echo parameters in assessing AR and the thresholds that are specific for AR severity to reliably identify hemodynamically significant chronic AR.

METHODS

We prospectively enrolled patients referred to CMR for assessment of chronic AR between 2018 and 2022. Patients underwent a comprehensive transthoracic echocardiogram (TTE) just before or after CMR, in the same suite, with examinations occurring near simultaneously, <4 hours apart. Informed consent was obtained from all patients, and the study was approved by the Institutional Review Board.

Patients with the following factors were excluded: 1) aortic valve prosthesis; 2) > mild aortic valve stenosis (peak velocity by Doppler >2.5 m/s or mean gradient >20 mm Hg) on TTE; 3) the presence of > mild regurgitant lesion other than AR based on TTE; and 4) congenital cardiac disease other than bicuspid aortic valve (**Figure 1**). Patients with acute AR such as AR due to aortic dissection or endocarditis were not included. There were no patients experiencing atrial fibrillation or flutter.

ECHOCARDIOGRAPHIC ACQUISITION AND ANALYSIS. Standard TTE studies were acquired using available ultrasound systems (Siemens Acuson S2000 and Philips Epiq iE33) by an advanced cardiac sonographer (C.A.). Standard 2-dimensional and Doppler imaging views were obtained as per guidelines.[1] Efforts were made to capture the complete AR jet with color Doppler, including the proximal flow convergence zone from the parasternal and apical views, vena contracta from the parasternal views, and jet direction and width in the left ventricular outflow tract (LVOT). Zoomed-in images and baseline shift of the Nyquist limit were used to optimize acquisitions. Pulsed Doppler in the LVOT, right ventricular outflow tract (RVOT), the mitral annulus (MA), proximal descending thoracic aorta, and the abdominal aorta were acquired. The MA diameter was measured from the apical 4-chamber view during diastasis. The RVOT annulus was measured in early systole from the parasternal short-axis view at the site of pulsed wave Doppler interrogation. Continuous wave Doppler interrogation of the AR jet was optimized from the apical and/or parasternal window depending on the eccentricity of the AR jet. Ultrasound enhancing agents were not used.

A level III echocardiographer (R.A.) independently interpreted studies, blinded to CMR and clinical data. Measurements included vena contracta width (VCW), AR jet width to LVOT diameter ratio, pressure half-time, and proximal isovelocity surface area (PISA) from the apical window. The presence of holodiastolic flow reversal in the descending and abdominal aortas was assessed. In the descending thoracic aorta, the end-diastolic aortic reversal velocity, velocity time integral of the reversed diastolic flow, and the ratio of velocity time integral of the reversed flow to forward flow were measured and derived. Biplane LV volumes and linear dimensions were quantitated per guidelines.[10] Regurgitant volume (RegV) was calculated as the difference between LVOT stroke volume and MA stroke volume (SV_{LVOT}-SV_{MA}) and as the difference between LVOT and RVOT stroke volume (SV_{LVOT}-SV_{RVOT}). The regurgitation volume derived with PISA ($RegV_{PISA}$) was calculated by using the standard formula. Regurgitant fraction (RegF) was calculated as $RegV/SV_{LVOT}$. The intraobserver and interobserver variability of LV volumes, RegV, and VCW measures by echo were evaluated in 15 randomly selected patients (intraobserver variability was done on measurements performed by 1 of the authors [C.A.] at 2 separate time points; interobserver variability done on measurements was performed by 2 of the authors [R.A and C.A.] who were blinded to the other's measurements).

AR severity was first graded based on the ASE guidelines. If ≥4 specific criteria for mild or severe AR were present, AR was then considered mild or severe, respectively. In patients without ≥4 specific criteria for either mild or severe AR, quantitation was used to

grade AR severity per guidelines. We used RegV quantitation obtained by the SV_{LVOT}-SV_{MA} method given that it had the highest feasibility in this study (see results below). Patients were considered to have mild AR if RegV was <30 mL, moderate AR if RegV was 30 to 44 mL, and moderate to severe AR if RegV was 45 to 59 mL.[1] For determination of severe AR, either RegV ≥60 mL or RegF ≥50% was used to grade AR as severe. We followed the same approach of grading AR severity for both echo and CMR, recognizing that RegV and RegF can place patients in different categories depending on LV size and function (eg, moderate AR by RegV and moderate to severe AR by RegF).

CMR ACQUISITION AND ANALYSIS. CMR studies were acquired using either 1.5-T or 3.0-T clinical scanners (Siemens) with a phased-array coil system. A CMR examination for aortic valve assessment began with cine-CMR for anatomical and functional assessment in a short-axis stack and standard 2-, 3-, and 4-chamber views using a steady-state free-precession sequence. Phase contrast CMR was performed at the level of the sinotubular junction, LVOT, ascending aorta, and the pulmonary artery. Scan parameters are detailed in the Supplemental Methods.

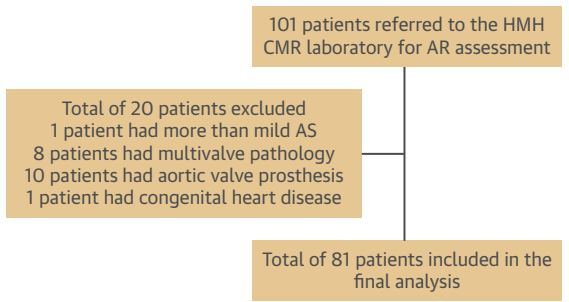
Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), LVEF, and LV mass were measured consistent with guidelines.[11] The regurgitation volume by CMR ($RegV_{CMR}$) was calculated by using the direct method from phase contrast imaging at the level of the sinotubular junction. Phase contrast imaging in the ascending aorta and the difference between aortic and net pulmonic forward stroke volume were used as secondary checks for $RegV_{CMR}$ quantitation. The regurgitant fraction was calculated as (reverse volume/forward volume × 100%).

All analyses were performed by using the same software (Precession, Heart Imaging Technologies). Analysis of CMR findings was performed in a blinded fashion to echocardiography findings. The interobserver variability of RegV measures by CMR was evaluated in the same 15 randomly selected patients in whom variability was assessed by echo.

The severity of AR was graded similar to grading by echocardiography. Mild AR was present if RegV was <30 mL, moderate AR was present if RegV was 30 to 44 mL, moderate to severe AR was present if RegV was 45 to 59 mL, and severe AR was present if RegV was ≥60 mL or RegF was ≥50%.

STATISTICAL ANALYSIS. Descriptive data are reported as median (IQR) for continuous variables and as frequencies and proportions for categorical variables. Scatter plots with Pearson correlation coefficients and regression lines were used to present the correlation in parameters between TTE and CMR. Agreement plots were used to assess the agreement in measurements by using the Bland-Altman plot. Agreement between TTE and CMR in classifying AR severity was determined by using Cohen's kappa statistic. Variability of echocardiographic parameters compared with $RegV_{CMR}$ was evaluated using the intraclass correlation coefficient (ICC). The ICC was used to evaluate the interobserver and interobserver variability measures of LV volumes and RegV. The diagnostic performance of different combinations of

FIGURE 1 Patient Enrollment



Patient flow diagram of patients referred for assessment of aortic regurgitation (AR). AS = aortic stenosis; CMR = cardiac magnetic resonance; HMH = Houston Methodist Hospital.

TABLE 1 Baseline Patient Characteristics (N = 81)

Age, y	52.0 (40.0-62.0)
Female	21 (25.9)
White	69 (85.2)
Body surface area, m^2	2.0 (1.8-2.1)
Body mass index, kg/m^2	25.3 (20.9-29.1)
Heart rate, beats/min	69.0 (61.0-77.0)
SBP, mm Hg	131.0 (118.0-143.0)
DBP, mm Hg	68.0 (61.0-77.0)
Coronary artery disease	7 (8.6)
Diabetes	3 (3.7)
Hyperlipidemia	27 (33.3)
Hypertension	36 (45.0)
Current or prior smoking	16 (20.8)
History of myocardial infarction	1 (1.2)
Heart failure symptoms	
No	75 (92)
Yes	6 (7.4)

Values are median (IQR) or n (%).
DBP = diastolic blood pressure; SBP = systolic blood pressure.

TABLE 2 Baseline Findings on Echocardiography and CMR (N = 81)

CMR findings	
Leaflet morphology	
Trileaflet	34 (42.0)
Bicuspid	47 (58.0)
LVEDV, mL	206.7 (166.0-247.8)
Indexed LVEDV, mL/m^2	102.8 (88.7-127.7)
LVESV, mL	76.0 (60.0-97.0)
Indexed LVESV, mL/m^2	39.1 (32.3-48.4)
LV SV, mL	125 (104-151.5)
Aortic valve forward SV, mL	117.9 (92.8-137)
LVEDD, cm	5.4 (4.7-6.0)
LVESD, cm	3.5 (3.1-4.2)
LVEF, %	61.1 (57.0-66.0)
Indexed LV mass, mg/m^2	71.7 (61.1-90.6)
Indexed left atrial volume, mL/m^2	46.5 (37.2-58.9)
Anteroseptal wall thickness, cm	0.9 (0.7-1.0)
Inferolateral wall thickness, cm	0.8 (0.7-1.0)
AR severity on CMR	
RegV CMR, mL	30.0 (14.0-52.0)
RegF CMR, %	26.0 (15.0-37.0)
AR severity	
Mild	41 (50)
Moderate	16 (20)
Moderate to severe	7 (9)
Severe	17 (21)
TTE findings	
Aortic valve morphology	
Unicuspid	1 (1.2)
Bicuspid	61 (75.3)
Tricuspid	17 (21.0)
Unclear	2 (2.5)
AR mechanism	
Focal prolapse	60 (74.1)
Calcific	8 (9.9)
Leaflet perforation	1 (1.2)
Flail	2 (2.5)
Aortic root dilation	3 (3.7)
Restricted cusp motion	2 (2.5)
Mixed	3 (3.7)
No mechanism defined	2 (2.5)
LVEDV, mL	158.0 (126.0-199.0)
Indexed LVEDV, mL/m^2	79.0 (63.0-94.0)
LVESV, mL	51.0 (36.0-72.0)
Indexed LVESV, mL/m^2	27.0 (19.0-35.0)
LVEDD, cm	5.5 (4.9-6.0)
LVESD, cm	3.3 (3.0-3.7)
LVSV, mL	100.0 (85.0-123.0)
LVEF, %	65.0 (61.0-72.0)
LV mass index, g/m^2	106.0 (86.0-126.0)
LVOT SV, mL	99.0 (86.0-120.0)
MA SV, mL	66.0 (57.0-77.0)
RVOT SV, mL	63.0 (54.0-75.0)
VCW, cm	0.48 (0.30-0.72)
Jet width to LVOT diameter, %	25.0 (17.0-40.0)
AV pressure half-time, ms	526.0 (402.0-746.0)
Diastolic flow reversal in the abdominal aorta, present	14 (20.6)
AR severity on TTE based on ASE guidelines[a]	
AR severity	
Mild	35 (43)
Moderate	18 (22.0)
Moderate to severe	12 (15.0)
Severe	16 (20.0)
RegV (LVOT – MA method), mL	33.5 (19.5-50.0)
RegF (LVOT – MA method), %	35.0 (22.0-41.5)
RegV (LVOT – RVOT method), mL	36.0 (21.0-57.0)
RegF (LVOT – RVOT method), %	35.0 (22.5-50.0)
PISA RegV, mL	51.0 (26.0-69.0)
PISA RegF, %	40.5 (29.0-55.0)

Continued in the next column

TABLE 2 Continued

Values are n (%) or median (IQR). [a]Aortic regurgitation (AR) severity based on American Society of Echocardiography (ASE) guidelines. If ≥4 specific criteria for mild or severe AR were present, AR was then considered mild or severe, respectively. In patients without ≥4 specific criteria, quantitation of regurgitant volume (RegV) by left ventricular outflow tract (LVOT) stroke volume (SV) – mitral annulus (MA) SV was used to further quantify AR.

AV = atrioventricular; CMR = cardiac magnetic resonance; LV = left ventricular; LVEDD = left ventricular end-diastolic diameter; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; LVESV = left ventricular end-systolic volume; LVSV = left ventricular stroke volume; PISA = proximal isovelocity surface area; RegF = regurgitant fraction; RVOT = right ventricular outflow tract; TTE = transthoracic echocardiogram; VCW = vena contracta width.

TTE parameters was presented by the sensitivity, specificity, positive and negative predictive values, and the area under the curve (AUC). Optimal cutoffs for TTE parameters in predicting severe AR or ≥ moderate to severe AR by CMR were determined by using the receiver-operating characteristic curve analysis with Youden index.[12]

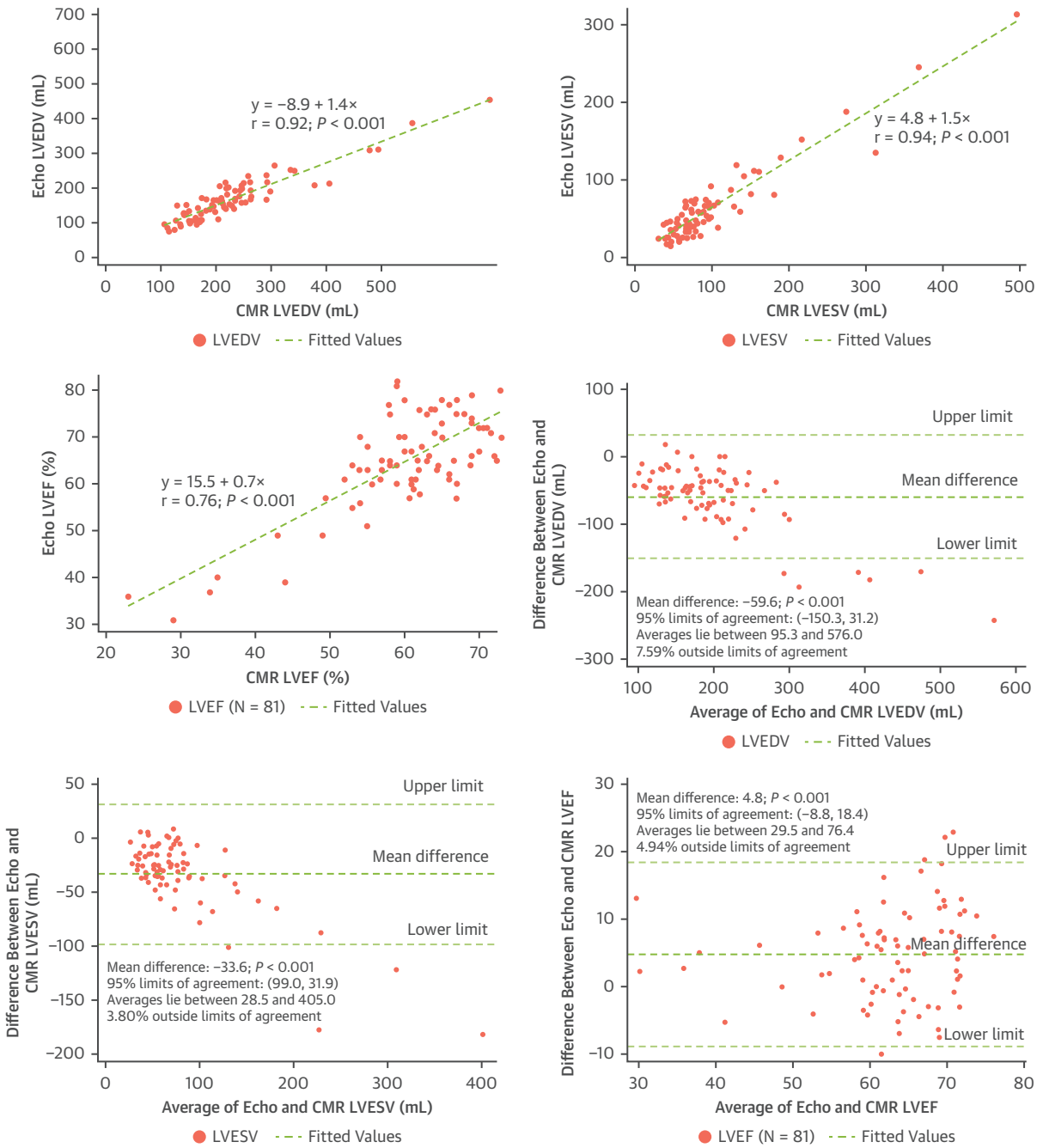
All analyses were performed on Stata version 17.0 (StataCorp LLC). A value of $P < 0.05$ was considered statistically significant.

RESULTS

A total of 81 consecutive patients were studied. Median age was 52 years (IQR: 40-62 years); 74% were male, and 58% had a bicuspid aortic valve. Patient characteristics are presented in Table 1. The predominant mechanism of AR was focal leaflet prolapse (74.1%). Findings on TTE and CMR are summarized in Table 2. The majority of patients had a normal LVEF of >50% (90%). According to TTE, 35 (43%) patients had mild AR, 18 (22%) moderate AR, 12 (15%) moderate to severe AR, and 16 (20%) severe AR. According to CMR, 41 (50.6%) patients had mild AR, 16 (19.8%) moderate AR, 7 (8.6%) moderate to severe AR, and 17 (21%) severe AR.

By CMR grading, the RegV and RegF values were in different categories according to ASE guidelines

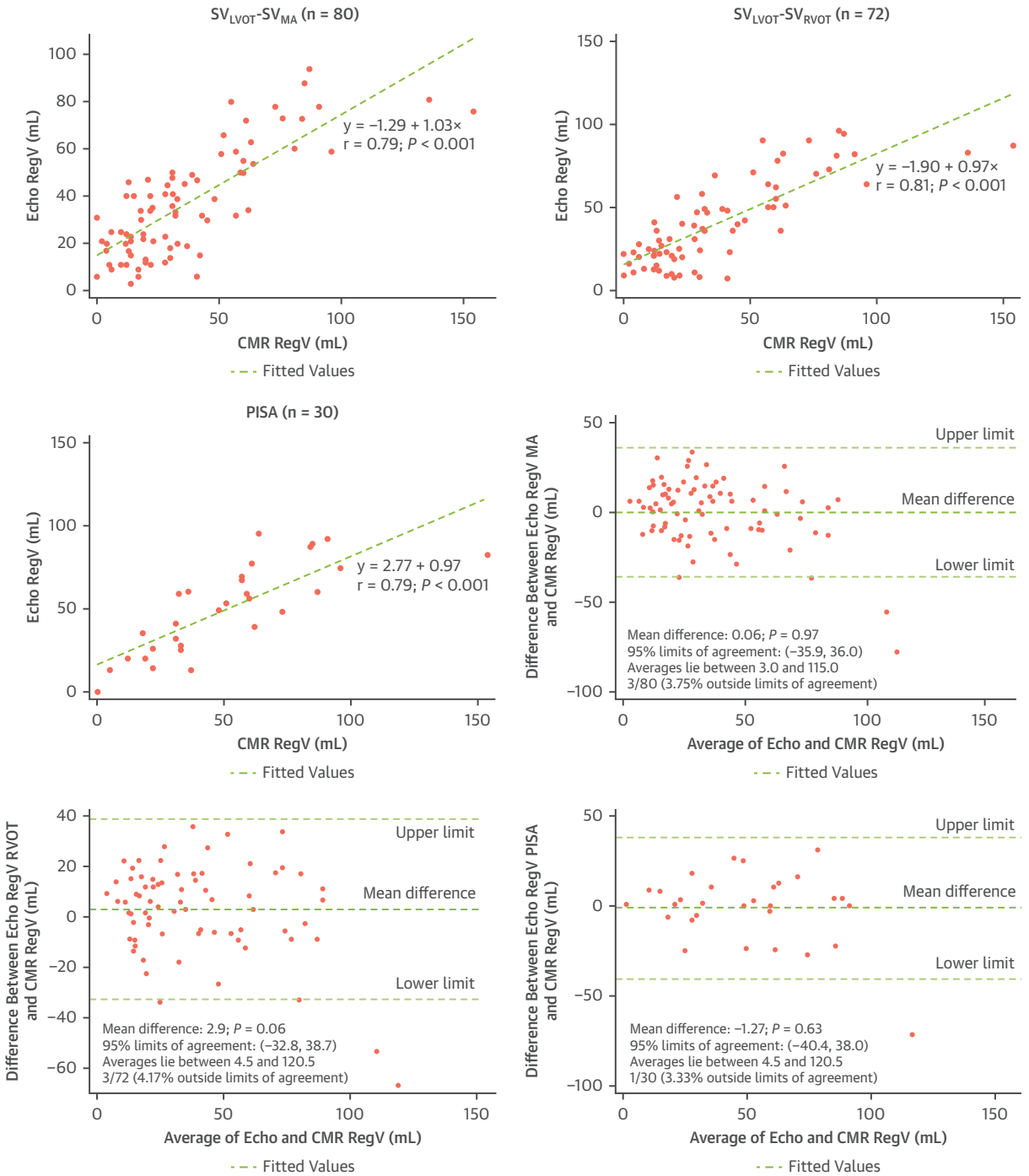
FIGURE 2 **Comparison of Echocardiography and CMR Measures of LV Volume and Function**



Scatter plots and Bland-Altman figures for comparison of echocardiography vs cardiac magnetic resonance (CMR) measurement of left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and left ventricular ejection fraction (LVEF).

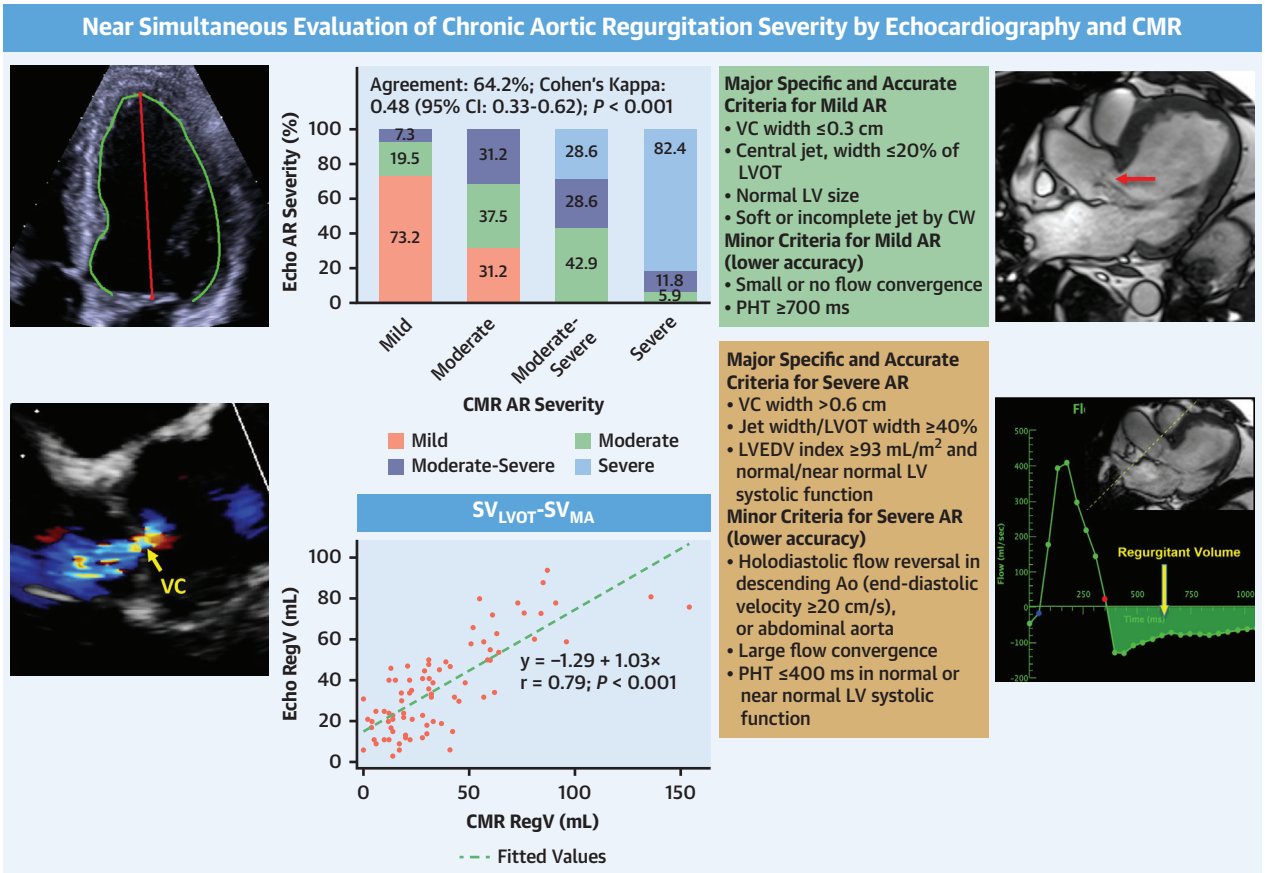
in 22 (27%) of 81 cases. There were 10 cases with RegV ≥30 mL but RegF in the 20% to 29% range, and they were graded as moderate AR. There were 5 cases of RegV ≥45 mL but RegF of 30% to 39%, and they were graded as moderate to severe AR. There were 7 severe AR cases with discordance, 1 had a RegV of 57 mL and RegF of 61% (was considered severe), and 6 patients had RegV ≥60 mL but

FIGURE 3 **Comparison of Echocardiography and CMR Measures of Regurgitation Volume**



Scatter plots and Bland-Altman figures for comparison of echocardiography vs cardiac magnetic resonance (CMR) measurement of regurgitant volume (RegV). Comparisons were made for 3 methods: the stroke volume (SV) difference between the left ventricular outflow tract (LVOT) and mitral annulus (MA), difference of SV between the LVOT and right ventricular outflow tract (RVOT), and by the proximal isovelocity surface area (PISA) method.

CENTRAL ILLUSTRATION **Overview of Echocardiography and CMR Assessment of AR**



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Agreement between transthoracic echocardiogram and CMR in overall assessment of AR severity and correlation of regurgitant volume (RegV) by CMR and transthoracic echocardiogram. Yellow arrow indicates the vena contracta (VC). The red arrow indicates the AR jet seen on CMR. Ao = aortic valve; AR = aortic regurgitation; CMR = cardiac magnetic resonance; LV = left ventricular; LVEDV = left ventricular end-diastolic volume; LVOT = left ventricular outflow tract; MA = mitral annulus; PHT = pressure half-time; SV = stroke volume.

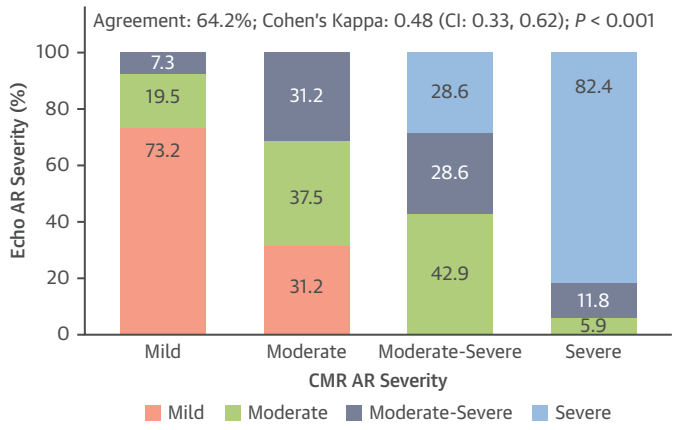
RegF <50% (range: 40%-49%) and were also considered severe AR.

FEASIBILITY OF ECHOCARDIOGRAPHY MEASURES AND AGREEMENT WITH CMR. LVEDV and LVESV with echo correlated well with CMR volumes ($r = 0.92$ for LVEDV, $r = 0.94$ for LVESV); the correlation of LVEF was moderate ($r = 0.76$). There was underestimation of LVEDV and LVESV by TTE compared with CMR with a negative bias of 59.6 mL for LVEDV, 33.6 mL for LVESV, and overestimation of LVEF by TTE (positive bias of 4.8%) (Figure 2).

Assessment of VCW and jet width/LVOT diameter was feasible in 77.8% of patients. In the remaining patients, these measures could not be performed accurately, mostly because of severe eccentricity of the AR jet by color Doppler. Feasibility of TTE quantitative volumetric measures of AR RegV was highest (98.8%) using the SV_{LVOT}-SV_{MA} method, followed by the SV_{LVOT}-SV_{RVOT} method (88.9%). The lowest feasibility (37%) of TTE quantitative volumetric measures was using the PISA method.

The ICC for $RegV_{TTE}$ measures against $RegV_{CMR}$ was 0.68 for the SV_{LVOT}-SV_{MA} method, 0.78 for the SV_{LVOT}-SV_{RVOT} method, and 0.94 for PISA. The correlations and Bland-Altman analyses for the 3 TTE methods against $RegV_{CMR}$ are presented in Figure 3. The

FIGURE 4 Agreement Between Echocardiography and CMR in Evaluating AR Severity



Abbreviations as in Figure 1.

correlations were good overall (r = 0.79-0.81). There was no negative or positive bias of any of the 3 TTE quantitation methods against $RegV_{CMR}$ ($P \geq 0.06$). The 95% confidence limits of agreement in the Bland-Altman analysis for $RegV_{TTE}$ by the SV_{LVOT}-SV_{MA} method were −35.9 to 36 mL, the 95% limits for $RegV_{TTE}$ by the SV_{LVOT}-SV_{RVOT} method were −32.8 to 38.7 mL, and the limits were −40.4 to 38 mL for PISA.

OVERALL CONCORDANCE IN AR SEVERITY BETWEEN ECHO AND CMR. Overall concordance of AR severity assessment between TTE and CMR using the ASE guidelines was moderate (64.2%; kappa 0.48 [95% CI: 0.33-0.62]; $P < 0.001$) (Central Illustration, Figure 4). For detection of severe AR, the AUC of the current ASE algorithm was 0.9 (82.4% sensitivity and 96.9% specificity). The AUC of the current ASE algorithm was 0.85 for detection of ≥ moderate to severe AR by CMR (83.3% sensitivity and 86% specificity). A patient example is presented in Figure 5.

The exact grade concordance between echo and CMR was seen in 52 patients (64.2%); a discrepancy of 1 grade was seen in 25 patients (30.9%), and a 2-grade discordance was observed in 4 patients (4.9%) (Table 3). In patients with discordance, TTE overestimated AR severity by 1 grade in 15 patients (18.5%) and by 2 grades in 3 patients (3.7%). AR by TTE was underestimated by 1 grade in 10 patients (12.3%) and by 2 grades in 1 patient (1.2%). The specifics of the patients with a 2-grade discordance are detailed in Supplemental Table 1. All 4 patients were asymptomatic and did not undergo aortic valve surgery; they are being followed up in the clinic.

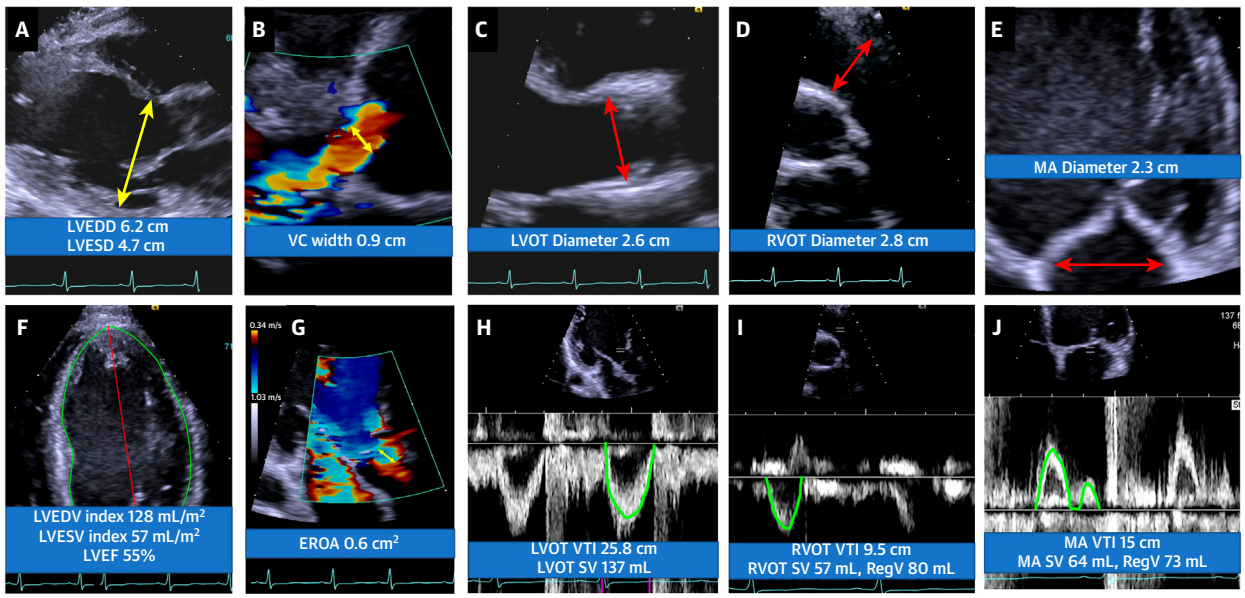
ECHOCARDIOGRAPHIC PARAMETER THRESHOLDS FOR SIGNIFICANT AR AND MILD AR. The accuracy of conventional TTE parameters in addition to the AR volumetric parameters in the assessment of significant AR as determined by CMR is shown in Table 4. The AUCs and the corresponding optimal cutoff values are displayed for each parameter. We evaluated values for identification of both severe AR and ≥ moderate to severe AR, as both grades are important clinically, considering the new data on prognosis.[6,7,9] Among the echo parameters that did not involve RegV volumetric calculations, the highest accuracy for assessing either severe or moderate to severe AR based on CMR findings was seen with VCW followed by jet width/LVOT ratio, indexed LVEDV, and presence of diastolic flow reversal in the abdominal aorta (AUC: 0.93-0.83). Pressure half-time was the least accurate (AUC: 0.36) in the overall evaluation of AR according to CMR findings.

We wanted also to evaluate echo parameters that provide high specificity (>85%) with enough accuracy (AUC >0.7) for assessment of AR severity relative to CMR findings, as used clinically and proposed in the ASE guidelines.[1] These select parameters, with their cutoffs for high specificity, are presented in Table 5 for severe AR and in Table 6 for ≥ moderate to severe AR. VCW was the most accurate parameter, with a cutoff value of 0.64 cm for severe AR and 0.5 cm for moderate to severe AR by CMR. The jet width/LVOT diameter cutoff was 40% for severe AR and 30% for moderate to severe AR. The indexed LVEDV had overall good accuracy (AUC: 0.84), with a cutoff of 93 mL/m^2 for severe AR and 82 mL/m^2 for moderate to severe AR. Holodiastolic flow reversal in the abdominal aorta was 100% specific for ≥ moderate to severe AR, with 60.9% sensitivity (AUC: 0.8). Lastly, pressure half-time and end-diastolic velocity in the descending aorta had a lower accuracy and sensitivity.

Using volumetric quantitation of AR by echo, the optimal thresholds for RegV with high specificity (>85%) for detecting severe AR ranged between 47 and 67 mL for the 3 quantitative methods (AUC: 0.74-0.94; lowest AUC was for the PISA method). The RegV cutoffs for detection of ≥moderate to severe AR are listed in Table 6.

For mild AR, VCW was the most accurate parameter, with a cutoff value of 0.3 cm (AUC: 0.93). The jet width/LVOT diameter cutoff was 20% (AUC: 0.88). The indexed LVEDV threshold associated with mild AR on CMR was <71 mL/m^2 (AUC: 0.8); pressure half-time had a lower accuracy (AUC: 0.71), a sensitivity of 54.8%, and a specificity of 87% at a high threshold of ≥700 milliseconds for mild AR. The optimal

FIGURE 5 Case Example of AR Evaluation and Quantitation with Echocardiography



An example of a 23-year-old man with bicuspid aortic valve and severe AR. Overview of echocardiography findings and quantitation for left ventricular (LV) diameters and vena contracta (VC) width (yellow double-headed arrows) (A and B), valvular annular diameters (red double-headed arrows) (C to E), LV volumes (F), PISA radius measurement (yellow double-headed arrow) (G) and annular pulsed wave Doppler findings (H to J). CMR findings were: LVEDV index, 174 mL/m^2; LVESV, 82 mL/m^2; LVEF, 53%; RegV, 84 mL; and regurgitant fraction 54%. EROA = effective regurgitant orifice area; LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter; VTI = velocity time integral; other abbreviations as in Figures 2 and 3.

thresholds for RegV with high specificity (>85%) for detecting mild AR ranged between 28 and 31 mL for the 3 quantitative methods (AUC: 0.90-0.96) (Supplemental Table 2).

TTE ALGORITHMS TO EVALUATE AR WHEN RegV QUANTITATION IS NOT FEASIBLE. Given that not all TTE parameters for AR can be assessed in clinical practice, we evaluated various combinations of TTE findings based on receiver-operating characteristic curve analysis to predict severe AR and ≥ moderate to severe AR by CMR (Table 7). The use of only 2 independent parameters (VCW ≥0.64 cm and indexed LVEDV ≥93 mL/m^2) had a sensitivity of 86.7% and a specificity of 93.6% for severe AR (AUC: 0.90 [the same AUC as the current ASE algorithm]). This approach decreased the need for AR quantitation compared with current guidelines. Using VCW and LVEDV identified 13 (76%) of 17 patients with severe AR on CMR without necessitating quantitation, whereas the current ASE algorithm (requiring ≥4 specific parameters for severe AR) identified only 4 patients (the remaining 13 required quantitation). Combining VCW and jet width parameters also achieved excellent discrimination (AUC: 0.87). Incorporating other echo findings, although supportive, did not yield higher AUCs.

Similar observations were found for assessing ≥ moderate to severe AR. The use of only 2 independent parameters (VCW ≥0.5 cm and indexed LVEDV ≥82 mL/m^2) had a sensitivity of 80.8% and a specificity of 97.2% for ≥ moderate to severe AR with

TABLE 3 Frequency and Proportion of Each Category of the AR Severity on Echo, Stratified by CMR AR Severity

	CMR AR Severity				
	Mild	Moderate	Moderate to Severe	Severe	Total Echo
Echo AR severity (ASE algorithm)					
Mild	30 (73.2)	5 (31.2)	0 (0.0)	0 (0.0)	35 (43.2)
Moderate	8 (19.5)	6 (37.5)	3 (42.9)	1 (5.9)	18 (22.2)
Moderate to severe	3 (7.3)	5 (31.2)	2 (28.6)	2 (11.8)	12 (14.8)
Severe	0 (0.0)	0 (0.0)	2 (28.6)	14 (82.4)	16 (19.8)
Total CMR	41 (50.6)	16 (19.8)	7 (8.6)	17 (21.0)	81 (100)

Values are n (%).
Abbreviations as in Table 2.

TABLE 4 Optimal Cut-Point of Echocardiographic Parameters and Diagnostic Performance in Predicting Significant AR by CMR

	Optimal Cut-Point Determined by Youden Index			
	Optimal Cut-Point	Sensitivity, %	Specificity, %	AUC
Cut-point to predict severe AR				
AR parameters (nonvolumetric)				
VCW, cm	0.64	100	85	0.93
Jet width/LVOT ratio, %	28	100	74	0.87
AV pressure half-time, ms	675	12	60	0.36
VTI reversal in descending thoracic aorta, cm	14	82	53	0.68
Ratio of VTI reversal to forward flow in descending thoracic aorta	0.48	100	16	0.58
End-diastolic velocity of reversed flow in the descending thoracic aorta, cm/s	18	77	77	0.77
Presence of reversed flow in the abdominal aorta	Yes/no	80	96	0.88
LVEDV, mL	168	100	76	0.88
Indexed LVEDV, mL/m^2	88	94	79	0.87
LVESV, mL	65	71	74	0.72
Indexed LVESV, mL/m^2	34	65	81	0.73
AR volumetric quantitation				
RegV (mL) (LVOT - MA) [method 1]	50	94	92	0.93
RegV (mL) (LVOT - RVOT) [method 2]	50	100	88	0.94
RegV (mL) (PISA) [method 3]	40	100	67	0.83
Average echo RegV [methods 1 + 2]	49	100	89	0.95
LVEDV - LVESV, mL	109	94	76	0.85
(LVEDV - LVESV) - MA SV, mL	44	100	85	0.93
(LVEDV - LVESV) - RVOT SV, mL	60	87	90	0.89
Cut-point to predict moderate to severe or severe AR				
AR parameters (nonvolumetric)				
VCW, cm	0.46	100	84	0.92
Jet width/LVOT ratio, %	28	85	87	0.86
AV pressure half-time, ms	1,421	3	100	0.52
VTI reversal in descending thoracic aorta, cm	12	83	47	0.65
Ratio of VTI reversal to forward flow in descending thoracic aorta	0.54	83	29	0.56
End-diastolic velocity of reversed flow in the descending thoracic aorta, cm/s	12	100	50	0.75
Presence of reversed flow in abdominal aorta	Yes/no	61	100	0.80
LVEDV, mL	168	83	86	0.85
Indexed LVEDV, mL/m^2	83	87	88	0.87
LVESV, mL	47	87	61	0.74
Indexed LVESV, mL/m^2	25	93	61	0.77
AR volumetric quantitation				
RegV (mL) (LVOT - MA) [method 1]	41	87	92	0.89
RegV (mL) (LVOT - RVOT) [method 2]	45	93	96	0.94
RegV (mL) (PISA) [method 3]	40	94	92	0.93
Average echo RegV [methods 1 + 2]	41	93	92	0.93
LVEDV - LVESV, mL	109	83	88	0.86
(LVEDV - LVESV) - MA SV, mL	40	83	92	0.88
(LVEDV - LVESV) - RVOT SV, mL	49	88	95	0.92

AUC = area under the curve; VTI = velocity time integral; other abbreviations as in Table 2.

an AUC of 0.89 (compared with AUC of 0.85 for the ASE algorithm).

For detection of mild AR by CMR, the use of the 2 independent parameters (VCW ≤0.3 cm and indexed LVEDV ≤71 mL/m^2) had a sensitivity of 81% and a specificity of 95.1% (AUC: 0.88). Use of VCW ≤0.3 cm and jet width/LVOT diameter ≤20% had a sensitivity of 90.9% and a specificity of 92.5% for mild AR (AUC: 0.92). This approach also decreased the need for AR quantitation compared with current guidelines (Supplemental Table 3). Using VCW and indexed LVEDV identified 13 (32%) of 41 patients with mild AR on CMR without necessitating quantitation, while the current ASE algorithm (requiring ≥4 specific

parameters for mild AR) identified 10 (24%) of 41 patients (the remainder required quantitation). Thus, for the population studied, the simplified approach identified either mild or severe AR from specific criteria in 26 (49%) of 58 patients, whereas the current ASE guidelines identified 14 (24%) of 58 patients ($P < 0.001$); the rest necessitated AR quantitation.

REPRODUCIBILITY OF ECHOCARDIOGRAPHIC AND CMR QUANTITATIVE PARAMETERS. The interobserver and intraobserver variability for LV volumes, RegV, and VCW are shown in Supplemental Table 4. For interobserver variability, the ICC for RegV-TTE by SV_{LVOT}-SV_{MA} was 0.72 ($P < 0.001$), and the ICC for RegV-TTE by the SV_{LVOT}-SV_{RVOT} method was 0.72 ($P < 0.001$). The intraobserver variability for RegV-TTE was higher for both methods (ICC of 0.89 for the SV_{LVOT}-SV_{MA} method and 0.87 for the SV_{LVOT}-SV_{RVOT} method; both; $P < 0.001$). The ICCs for interobserver and intraobserver variability of VCW were 0.78 and 0.96 ($P < 0.001$), respectively. The interobserver variability for RegV-CMR was 0.99 ($P = 0.01$).

TABLE 5 Select Echocardiographic Parameters With High Specificity (>85%) and AUC >0.7 in Predicting Severe AR on CMR

	Association With Severe AR on CMR			
	Cut-point	Sensitivity, %	Specificity, %	AUC
AR parameters (nonvolumetric)				
VCW, cm	≥0.64	100.0	85.4	0.93
Jet width/LVOT ratio, %	≥40	78.6	87.8	0.83
Presence of flow reversal in the abdominal aorta	Yes/no	80.0	96.2	0.88
Indexed LVEDV, mL/m^2	≥93	82.4	85.5	0.84
AV pressure half-time, ms	<405	76.5	86.7	0.79
End-diastolic velocity of reversed flow in the descending thoracic aorta, cm/s	≥20	64.7	88.5	0.77
AR volumetric quantitation				
RegV (mL) (LVOT – MV) [method 1]	≥47	94.1	85.7	0.90
RegV (mL) (LVOT – RVOT [method 2]	≥50	100.0	87.5	0.94
RegV (mL) (PISA) [method 3]	≥67	58.3	88.9	0.74
Average echo RegV (mL) [methods 1 + 2]	≥47.5	100.0	85.9	0.93
(LVEDV – LVESV) – MA SV, mL	≥45	100.0	85.3	0.93
(LVEDV – LVESV) – RVOT SV, mL	≥55	86.7	86.5	0.87

Parameters given in *italics* are less accurate (AUC <0.8, low sensitivity at a high specific cutoff).
Abbreviations as in Table 2.

DISCUSSION

When performed near-simultaneously, echo and CMR have overall good concordance in assessing AR severity. Exact concordance or 1 grade discordance on a 4-grade scale was seen in 95.1% and discordance by 2 grades in 4.9% of patients. Feasibility of Doppler quantitation of RegV was high, except for the PISA method, with a good correlation with CMR quantitation. Among other echo parameters, the most accurate in assessing AR was VCW, and the least accurate was pressure half-time. We developed simplified algorithms using combinations of echocardiographic parameters to reliably evaluate hemodynamically significant (≥ moderate to severe) and mild AR. The simplest and most accurate combination was VCW and the LVEDV index. Although other parameters were supportive, they did not add further to the accuracy of AR assessment. Using these thresholds of jet characteristics in conjunction with LV volumes exhibited very good performance for detection of hemodynamically significant AR, similar to the current ASE algorithm. However, it is simpler, provides a hierarchical strength of the echocardiographic parameters, and likely leads to a lesser need for quantitation.

AR SEVERITY. Current guidelines on AR severity rely on thresholds that were primarily derived from angiography at cardiac catheterization. However, recent CMR studies have shown that patients with AR may be at risk for adverse events or require valve replacement at lower degrees of AR than currently established; AR fraction >35% and RegV >40 mL are associated with adverse events.[6-9] Thus, we evaluated echocardiographic predictors of both traditionally severe AR as well as ≥ moderate to severe

TABLE 6 Select Echocardiographic Parameters With High Specificity (>85%) and AUC >0.7 in Predicting Significant AR (Moderate to Severe or Severe AR)

	Association With Moderate to Severe or Severe AR on CMR			
	Cut-Point	Sensitivity, %	Specificity, %	AUC
AR parameters (nonvolumetric)				
VCW, cm	≥0.5	92.3	86.5	0.89
Jet width/LVOT ratio, %	≥30	84.6	86.5	0.86
Indexed LVEDV, mL/m^2	≥82	86.7	85.7	0.86
Presence of reversed flow in the abdominal aorta	Yes/no	60.9	100.0	0.80
AV pressure half-time, ms	<455	66.7	85.1	0.74
End-diastolic velocity of reversed flow in the descending thoracic aorta, cm/s	≥20	50.0	93.8	0.72
AR volumetric quantitation				
RegV (mL) (LVOT – MA) [method 1]	≥40	90.0	88.0	0.89
RegV (mL) (LVOT – RVOT [method 2]	≥40	92.9	86.4	0.90
RegV (mL) (PISA) [method 3]	≥41	94.4	91.7	0.93
Average echo RegV (mL) [methods 1 + 2]	≥40	96.7	86.3	0.91
(LVEDV – LVESV) – MA SV, mL	≥39	83.3	85.4	0.84
(LVEDV – LVESV) – RVOT SV, mL	≥42	92.0	88.1	0.90

Parameters in *italics* are less accurate (AUC <0.8, low sensitivity at a high specific cutoff).
Abbreviations as in Table 2.

TABLE 7 Diagnostic Performance of Individual Echo/Doppler Parameters and Their Combinations in Predicting AR Severity

	Available Data	Sensitivity, %	Specificity, %	PPV, %	NPV, %	AUC
Cutoff to predict severe AR						
[1] VCW ≥0.64 cm	63	100.0	85.4	68.2	100.0	0.93
[2] Jet width/LVOT ratio ≥40%	63	78.6	87.8	64.7	93.5	0.83
[3] AV pressure half-time <405 ms	77	76.5	86.7	60.0	91.2	0.79
[4] End-diastolic velocity in the descending aorta ≥20 cm/s	78	64.7	88.5	61.1	90.0	0.77
[5] Indexed LVEDV ≥93 mL/m^2	79	82.4	85.5	60.9	94.6	0.84
[1] AND [2]	62	78.6	95.8	84.6	93.9	0.87
[1] AND [3]	61	66.7	95.7	83.3	89.8	0.81
[1] AND [4]	60	60.0	93.3	75.0	87.5	0.77
[1] AND [5]	62	86.7	93.6	81.3	95.7	0.90
[1] AND [2] AND [3]	60	57.1	97.8	88.9	88.2	0.77
[1] AND [2] AND [4]	59	42.9	100.0	100.0	84.9	0.71
[1] AND [2] AND [5]	61	64.3	100.0	100.0	90.4	0.82
[1] AND [2] AND [3] AND [4]	58	42.9	100.0	100.0	84.6	0.71
[1] AND [2] AND [3] AND [5]	59	42.9	100.0	100.0	84.9	0.71
Cutoff to predict moderate to severe or severe AR						
[1] VCW ≥0.5 cm	63	92.3	86.5	82.8	94.1	0.89
[2] Jet width/LVOT ratio ≥30 %	63	84.6	86.5	81.5	88.9	0.86
[3] AV pressure half-time <455 ms	77	66.7	85.1	73.1	78.4	0.74
[4] End-diastolic velocity in descending aorta ≥20 cm/s	78	50.0	93.8	83.3	75.0	0.72
[5] Indexed LVEDV ≥82 mL/m^2	79	86.7	85.7	78.8	91.3	0.86
[1] AND [2]	62	84.0	91.9	87.5	89.5	0.88
[1] AND [3]	61	57.7	97.1	93.8	75.6	0.77
[1] AND [4]	60	46.2	97.1	92.3	70.2	0.72
[1] AND [5]	62	80.8	97.2	95.5	87.5	0.89
[1] AND [2] AND [3]	60	52.0	100.0	100.0	74.5	0.76
[1] AND [2] AND [4]	59	48.0	97.1	92.3	71.7	0.73
[1] AND [2] AND [5]	61	72.0	97.2	94.7	83.3	0.85
[1] AND [2] AND [3] AND [4]	58	36.0	100.0	100.0	67.3	0.68
[1] AND [2] AND [3] AND [5]	59	44.0	100.0	100.0	70.8	0.72

NPV = negative predictive value; PPV = positive predictive value; other abbreviations as in Tables 2 and 4.

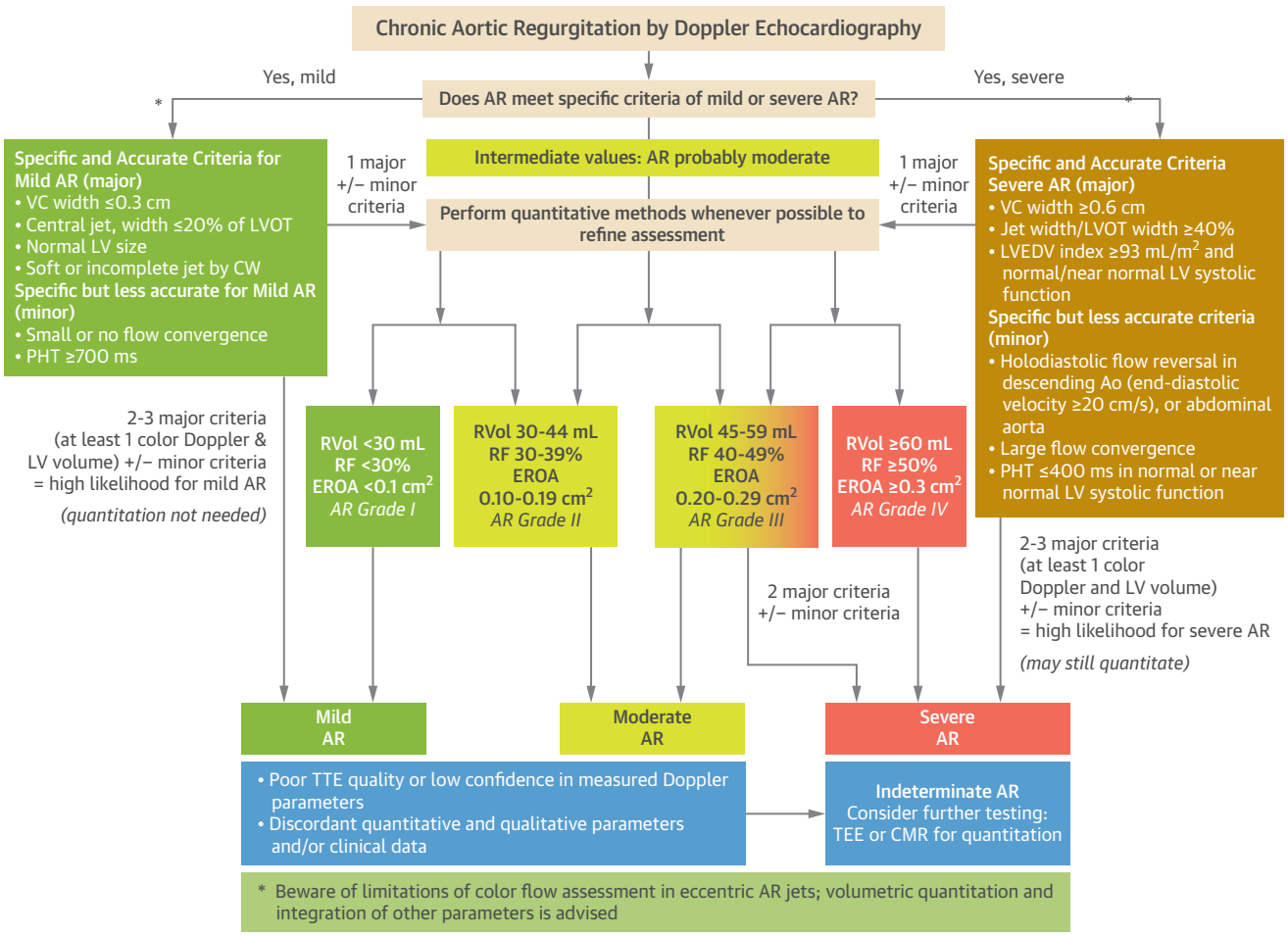
AR using CMR as the reference standard to allow use of these indices in the evolving field of AR assessment and outcomes. Furthermore, we wanted to have a full spectrum of AR severity (mild to severe) to allow evaluation of the accuracy of echocardiographic parameters. Notably, recent studies have only studied patients referred to CMR with severe or moderate to severe AR,[2,13] precluding an overall assessment of accuracy.

Our grading of AR in this study tended to emphasize RegV over RegF, which may be more suitable to reflect the extent of volume loading in patients with preserved systolic function and normal/dilated ventricles (increased total LV stroke volume), as encountered in this population. The RegF is important as well, particularly in patients with reduced or normal total stroke volume (reduced ejection fraction or small LV cavity).

QUANTITATION OF AR SEVERITY. In the current investigation, although there was underestimation of ventricular volumes by echocardiography, Doppler AR quantitation techniques had overall good agreement with CMR without significant bias, whether using the stroke volume at the MA, RVOT site, or the PISA method. However, the limits of agreement were wide, and the interobserver and intraobserver variability was higher than that of CMR. The feasibility was highest for the MA (98.8%), followed by the RVOT, and was poor for PISA (37%). The low feasibility of PISA in AR, as opposed to its use in mitral regurgitation, has been previously reported (32%).[2] The PISA method is particularly challenging in highly eccentric AR jets and/or because of shadowing of PISA from calcification of the aortic valve in the apical window. Integration of volumetric findings and internal checks (eg, comparing stroke volume from biplane LV volumes and LVOT stroke volume) are recommended to increase the reliability and accuracy of echo assessment.

Among the TTE parameters of AR severity that do not involve volumetric quantitation, the VCW, jet

FIGURE 6 Suggested Revision of the ASE Guideline Algorithm for Evaluation of Aortic Regurgitation Severity



Suggested revision of the American Society of Echocardiography guideline algorithm for the evaluation of patients with chronic AR with modifications to highlight the study findings of specific and accurate criteria (major criteria) and specific but less accurate parameters (minor criteria) for mild and severe AR. CW = continuous wave; PHT = pressure half-time; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram; RF = regurgitant fraction; other abbreviations as in Figures 1, 2, 3, and 5.

width ratio in LVOT, and indexed LVEDV had the highest overall accuracy. Measures of diastolic flow reversal were highly specific for significant AR but much less sensitive. Using thresholds of LVEDV in AR quantitation is advantageous because LV dilatation is a principal feature of chronic AR and was shown to have a strong and linear correlation against RegV by CMR,[14,15] and related to severe AR with a similar threshold (87 mL/m²).[13] On the other hand, the use of pressure half-time was the least accurate in assessing AR severity due to confounding factors such as LV diastolic function, variable size and recoil of the aorta, or differential flow in vascular beds. End-diastolic velocity of flow reversal in the descending thoracic aorta was specific but less sensitive for significant AR, similar to earlier observations. A combination of VCW and indexed LVEDV was the best for differentiating significant AR by CMR from mild AR and vice versa. In cases in which LV volume quantitation is not feasible, the combination of VCW and jet width/LVOT diameter can be used along with RegV quantitation and diastolic flow reversal in the aorta.

CURRENT GUIDELINES. At the time of the publication of the ASE guidelines, there were no comparative data to provide a recommendation for a hierarchical accuracy of the echo parameters when assessing AR severity. A more recent study of 45 patients with significant AR (22 with severe AR; 51% with bicuspid aortic valve) compared echo vs CMR by using the ASE

guidelines.[2] Volumetric quantitation was not performed by Doppler. The best linear relations with CMR were found with the LVEDV index, RegV by PISA (although feasibility was low), and VCW (r range: 0.78-0.60); the worst relation was with pressure half-time. The current study showed that color Doppler parameters (VCW, jet width/LVOT width) and indexed LVEDV are the most accurate parameters to assess the significance of chronic AR. Diastolic flow reversal in the aorta is not sensitive enough to be used without further corroboration with other data. The least accurate parameter is pressure half-time, and its cutoff value for high specificity in chronic severe AR is close to 400 milliseconds (**Tables 5 and 6**) and 700 milliseconds for mild AR in this population with predominantly normal LV systolic function. It is important to emphasize that in acute AR (not addressed here nor in the guideline algorithm), pressure half-time is short and helpful in alerting the clinician to the significance of AR.

Based on the findings, we hereby propose a slight modification to the ASE algorithm (**Figure 6**). The changes are mostly in the "box" detailing the specific signs for chronic severe and mild AR, arranging them hierarchically based on both specificity and accuracy. The most reliable are based on color Doppler parameters of the jet and LVEDV index; the other parameters are supportive.

STUDY LIMITATIONS. This study was performed in a select cohort of patients referred for CMR, with a high prevalence of patients with eccentric AR jets, which may limit the feasibility of color Doppler methods and may not apply to the general AR population. Nonetheless, we found that integration of quantitative AR parameters and LV volumes in these challenging cases can yield good overall assessment compared with CMR. The cohort studied was relatively younger and predominantly male, in keeping with the epidemiology of bicuspid aortic valve and AR, and thus applicability of our findings to older patients, women, and the spectrum of etiologies of AR should be further studied. Although our patient cohort included the full spectrum of AR severity, the number of patients with ≥moderate to severe AR is relatively lower. Future larger studies that include more patients with ≥moderate to severe AR are needed.

We did not perform 3-dimensional echocardiograms in this study, nor did we use contrast-enhancing agents. We did not evaluate the association of echocardiographic parameters against symptoms or clinical outcomes; larger studies are needed to address these associations.

CONCLUSIONS

AR assessment by echocardiography using the ASE guidelines has good feasibility and concordance against the reference quantitative standard of CMR when performed near simultaneously. We evaluated the relative accuracy of Doppler echocardiographic variables used in assessing AR severity that can be used hierarchically and in combination. The most accurate non-volumetric AR parameters were color Doppler characteristics of the AR jet and LVEDV index.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In a prospective study of same-day echo and CMR, quantitation of AR severity on echo has overall good concordance against a CMR reference standard. We evaluated the hierarchical strength of echo-Doppler parameters used in AR assessment and developed simplified echo algorithms to evaluate significant and mild AR.

TRANSLATIONAL OUTLOOK: Studies are needed to evaluate the refined criteria of AR severity in larger and diverse populations and to explore the association of quantitative echo parameters with clinical variables and outcomes.

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KEY WORDS aortic regurgitation, aortic valve, cardiac magnetic resonance, Doppler echocardiography

APPENDIX For an expanded Methods section as well as supplemental tables, please see the online version of this paper.