

VALVULAR HEART DISEASE

# Severity of Mitral and Aortic Regurgitation as Assessed by Cardiovascular Magnetic Resonance: Optimizing Correlation with Doppler Echocardiography

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## ABSTRACT

**Background:** Cardiovascular magnetic resonance (CMR) is widely recognized as a non-invasive gold standard for quantification of ventricular volumes. In addition, it is an emerging diagnostic modality for clinical evaluation of mitral regurgitation (MR) and aortic regurgitation (AR). CMR facilitates accurate quantitation of regurgitation volumes and regurgitant fraction, but referring physicians are often more comfortable with qualitative measures, and few data exist for correlation of qualitative CMR regurgitation severity with that obtained by more conventional qualitative Doppler echocardiography. Because patients with AR and MR may commonly be assessed by both echocardiography and CMR modalities, consistency between qualitative gradient of regurgitation severity is important for follow-up. Therefore, we sought to define the CMR regurgitant fractions that best correlate with qualitative mild, moderate, and severe regurgitation by color Doppler echocardiography. **Methods and Results:** Data from 141 consecutive patients (age  $53 \pm 15$  yr; 43% female) with contemporary (median, 31 days) CMR and echocardiographic data, including 107 regurgitant valves and 70 normal valves, were compared. Thresholds were developed on an initial cohort of patients with 55 regurgitant valves, and subsequently tested on a later cohort of patients with 52 regurgitant valves. Regurgitation fraction (RF) limits that optimized concordance of CMR and echo severity grades were similar for MR and AR and were: mild  $\leq 15\%$ , moderate 16–25%, moderate-severe 26–48%, severe  $>48\%$ . **Conclusions:** The current study provides simple qualitative threshold grades for MR and AR severity that allows for standardized reporting of regurgitation severity by CMR and excellent correlation with clinical echocardiography.

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## INTRODUCTION

Mitral regurgitation (MR) and aortic regurgitation (AR) are common valvular disorders (1). Doppler echocardiography readily identifies MR and AR and provides the imaging basis for clinical follow-up of patients with these disorders. However, quantitative assessment of regurgitation severity, as well as concomitant assessment of left ventricular (LV) dimensions and LV ejection fraction by echocardiography, has notable limitations. LV dimension data determined by echocardiography, do not account for geometric distortions, while Doppler

echocardiography often relies on the subjective assessment of regurgitant severity. In addition, echocardiographic measurements are sometimes dependent on a "threshold" parameter, e.g., severe mitral regurgitation requires demonstration of flow reversal in the pulmonary veins (2). More recently, effective regurgitant orifice area has been described as a useful prognostic parameter in chronic MR (3). This parameter is derived using the proximal isovelocity surface area (PISA) method, which can be difficult to apply in cases where the regurgitation jet is eccentric or where image quality does not allow for flow convergence to be well seen (4, 5). In contrast, quantitative volumetric CMR measures overcome many of these deficiencies (6).

CMR is widely recognized as the non-invasive gold standard for quantification of LV volumes and ejection fraction, and is considered superior to echocardiography in assessing normal, dilated and hypertrophied hearts (7). Volumetric CMR assessment of MR and AR has been shown to be accurate and reproducible (8). Patients with AR and MR may commonly be assessed by either echocardiography or CMR, and referring physicians are often more comfortable with qualitative interpretations. Therefore, concordance between quantitative CMR and qualitative echocardiographic determinations of regurgitation severity is important for meaningful clinical follow-up. Using Doppler echocardiography as a qualitative reference standard, we sought to create a quantitative CMR-regurgitant fraction (CMR-RF) scale with strong correlation to the qualitative assessment of MR and AR with Doppler echocardiographic measurements.

## METHODS

For this study, approved by the hospital's Committee on Clinical Investigation, data were collected from all subjects who underwent contemporary (within 6 months) clinical CMR and clinical Doppler echocardiography for assessment of MR or AR at our institution from March 2002 to November 2004. Subjects were included if Doppler echocardiography demonstrated at least mild MR or at least mild AR. In order to define CMR-RF limits for no significant regurgitation, data were also collected from 35 consecutive patients with trivial or less MR and no AR who had also undergone contemporary echocardiography and CMR examination during the same time period.

### CMR

CMR was performed using a commercial 1.5 T Philips Gyroscan ACS/NT whole body scanner (Philips Medical Systems, Best, The Netherlands) with a 60 cm diameter bore, Powertrak 6000 gradients (23 mT/m, 219 msec rise time), and a 5-element cardiac synergy coil. Following initial localizing scans, cine left ventricular long-axis, 4-chamber and contiguous short axis images were obtained as previously described (6, 9), using a breath-hold electrocardiogram-triggered steady state free precession (SSFP) sequence. Sequence parameters included TE 1.5 ms, TR 3.0 ms, flip angle 60°, field-of-view 320 mm, matrix 160 × 160, with 10mm slice thickness. Temporal resolution was 30–35 msec, and the breath-hold duration was 10–12 sec.

Quantitative measures of aortic flow were assessed using a free-breathing, ECG-triggered phase contrast velocity sequence oriented in the axial plane at the level of the bifurcation of the pulmonary artery. Sequence parameters included FFE sequence: TR 15 ms, TE = 6.5 ms, flip angle = 30°, FOV = 300 × 210, matrix = 128 × 128, slice thickness 6 mm. Respiratory motion compensation was accomplished with the use of multiple signal averages (NSA = 4).

### CMR data analysis

CMR image analyses were performed on a commercial workstation (Easy Vision 5, Philips Medical Systems, Best, The Netherlands) in accordance with previously published methods (6, 10). Endocardial LV borders were manually traced at end-diastole and at end-systole. Papillary muscles were included as part of LV cavity volume. Left ventricular end-diastolic volume (EDV) and end-systolic volume (ESV) were determined using a Simpson's rule method. Stroke volume was calculated as the difference between EDV and ESV. Ejection fraction (EF) was calculated as  $EF = (EDV - ESV)/EDV$ . Aortic regurgitation volume was directly calculated from the aortic flow curve by integrating diastolic reverse flow. Aortic regurgitation fraction ( $AR_{RF}$ ) was taken from the phase contrast data as the ratio of AR volume and LV stroke volume. Mitral regurgitant volume was calculated as the difference between the LV stroke volume and the forward aortic flow volume. Mitral regurgitant fraction ( $MR_{RF}$ ) was then calculated as the ratio of the MR volume and the LV stroke volume. All CMR data were independently generated by experienced and blinded observers.

### Echocardiography

All subjects were evaluated with conventional two-dimensionally-guided color flow and pulsed-wave Doppler mapping using a 3 or 4 MHz transducer and Sonos 5500 system (Philips Medical Systems, Best, The Netherlands). Images were interpreted by Level III trained observers. Severity of MR was assessed by estimating the ratio of the regurgitant jet area to the area of left atrial area, while taking into consideration the turbulence and eccentricity of the regurgitant jet (11, 12). Demonstration of systolic flow reversal in the pulmonary veins was required to make a diagnosis of severe mitral regurgitation (2). Severity of AR was assessed by estimating the area and width of the regurgitant jet in the LV outflow tract and by calculating the pressure half time of the regurgitant jet (13, 14).

### Statistical analysis

Continuous data are reported as mean ± standard deviation. Categorical data are reported as counts and percentages. Analysis of variance (ANOVA) with the Student-Newman-Keuls adjustment for multiple comparisons was used to compare groups with different echocardiographic regurgitation severity. For purposes of ANOVA, groups with moderate-to-severe and severe AR were combined into a single group. CMR-RF thresholds were calculated to identify a qualitative scale with maximal concordance between echo and CMR grading of regurgitant

**Table 1.** Baseline study subject characteristics

	MR	AR	No MR/no AR
N	83	24	35
Age, y*	54.8 ± 14.9	55.6 ± 13.6	45.6 ± 12.7
Women, n (%)	36 (43)	8 (33)	16 (47)
LVEF by CMR (%)*	56.7 ± 15.0	58.9 ± 10.9	60.2 ± 8.5
Median time between echo and CMR (range), D	29 (0–55)	37 (0–168)	24 (0–154)

\*Data are expressed as mean ± standard deviation

severity. For purposes of this analysis, mild-moderate and moderate regurgitation grades by echo were combined into a single “moderate” group. Discordance was then quantified by summing the class discrepancy for each regurgitant valve in the study population. Regurgitation thresholds that minimized this discordance were calculated. To test the validity of these thresholds, the data for both AR and MR were combined and separated into those studies that were performed before September 2003 and those performed after September 2003. Studies prior to September 2003 were used to determine combined thresholds for both AR and MR. These thresholds were then used prospectively to generate qualitative CMR grades from the studies done after September 2003. The agreement between the CMR and echo grades was assessed with Spearman correlation and the  $\kappa$  statistic. Statistical analysis was performed using SAS for Windows (v9.1, SAS Institute, Cary, NC, USA).

## RESULTS

The study population included 141 consecutive patients with a slight male predominance (57%). Baseline subject characteristics are summarized in Table 1. The median interval between CMR and echocardiographic studies was 31 days. For subjects who had multiple CMR examinations, data from the most contemporary CMR were used. Fifteen patients had both MR and AR. This yielded 107 regurgitant valves (83 mitral, 24 aortic) and 70 normal valves (35 each mitral and aortic) available for analysis.

### Mitral regurgitation

Data from 83 regurgitant mitral valves were evaluated with CMR regurgitant volume varying up to 136 mL. The median interval between echo and CMR studies was 29 days. The mean

**Table 2.** Distribution of mitral (MR<sub>RF</sub>) and aortic (AR<sub>RF</sub>) regurgitant fractions across each echocardiographic regurgitation severity grade. Data are expressed as mean ± standard deviation

Echo	ECHO			
	Mild	Moderate	Mod-sev	Severe
MR <sub>rf</sub> , ml	7 ± 8	20 ± 15	29 ± 10	41 ± 14
AR <sub>rf</sub> , ml	5 ± 3	15 ± 11	33 ± 9	*

\*Severe aortic regurgitation was pooled with moderate-severe

**Table 3.** Agreement between CMR and Doppler echocardiography in severity of mitral regurgitation

Echo	CMR				Total
	Mild	Moderate	Mod-sev	Severe	
Mild	26	2	1	0	29
Moderate	10	5	7	1	23
Mod-sev	1	5	7	3	16
Severe	0	0	7	8	15
Total	37	12	22	12	83

CMR MR<sub>RF</sub> for each echocardiographic grade was significantly different ( $p < 0.001$  for trend,  $p < 0.05$  for each pairwise comparison, Table 2). The CMR-RF thresholds with maximal agreement were: mild ≤15%, moderate 16–24%, moderate-severe 25–42%, severe >42%. These thresholds yielded >95% concordance within 1 regurgitation grade (Table 3). Additionally, data from 35 mitral valves with trivial or less regurgitation were analyzed. For the group without echo evidence for significant MR, the MR<sub>RF</sub> was 10 ± 9%.

### Aortic regurgitation

Data representing 24 subjects with AR, with regurgitant volumes ranging up to 57 mL were compared with echo data. The median interval between echo and CMR studies was 37 days. The mean CMR AR<sub>RF</sub> for each echocardiographic grade was significantly different ( $p < 0.001$  for trend,  $p < 0.05$  for each pairwise comparison, Table 2). The CMR-RF thresholds with maximal agreement: mild ≤15%, moderate 16–27%, moderate-severe or severe >27%. These thresholds yielded 100% concordance within 1 regurgitation grade (Table 4). Additionally, data from 35 aortic valves without AR on echo were analyzed. For the group without echo evidence for AR, the AR<sub>RF</sub> was 2 ± 2%.

### Combined AR and MR thresholds

Because of the similarity of the MR and AR thresholds and potential clinical preference for consistency, we pooled the AR<sub>RF</sub> and MR<sub>RF</sub> data to determine combined thresholds for both regurgitant lesions. Data for 55 regurgitant valves (45 MR, 10 AR) that were evaluated prior to September 2003 were used to determine the CMR-RF thresholds. The CMR-RF thresholds with maximal agreement with echo for MR were: mild ≤15%, moderate 16–25%, moderate-severe 26–48%, severe

**Table 4.** Agreement between CMR and Doppler echocardiography in severity of aortic regurgitation

Echo	CMR			Total
	Mild	Moderate	Mod-sev	
Mild	11	0	0	11
Moderate	6	3	1	10
Mod-severe or severe	0	1	2	3
Total	17	4	3	24

**Table 5.** Agreement between CMR and Doppler echocardiography in severity of regurgitation in a combined cohort of MR and AR

Echo	Mild	Moderate	CMR		Total
			Mod-severe	Severe	
Mild	16	1	0	0	17
Moderate	11	5	2	0	18
Mod-severe	1	2	7	0	10
Severe	0	0	7	3	10
Total	28	8	0	3	55

>48% (Table 5). These thresholds were then used to prospectively determine the CMR-RF grade. Data for 52 regurgitant valves (38 MR, 14 AR) were included in this analysis. The correlation (Spearman's  $\rho$  between the echo and CMR grades was 0.78 ( $p < 0.001$ ) (Table 6). The  $\kappa$  statistic was 0.58 (95% confidence interval, 0.44 to 0.72), indicating good agreement between the echo and MR assessments.

## DISCUSSION

In this consecutive cohort of patients with MR or AR undergoing contemporary clinical echocardiography and CMR, we have established qualitative CMR severity grades that best correlate with Doppler echocardiography. The regurgitant fraction thresholds were similar for MR and AR and demonstrated strong concordance with the commonly used qualitative echocardiographic regurgitation severity grades.

Chronic MR and AR lead to progressive LV cavity dilation, systolic dysfunction and clinical heart failure. Timing of surgical repair of these regurgitant lesions is currently based on the echocardiographic severity of the lesion, LV dimensions and global systolic function, as well as presence of congestive heart failure and secondary cardiopulmonary disease, such as pulmonary arterial hypertension and atrial arrhythmias (15, 16). Traditionally, the clinical severity of MR and AR is qualitatively graded either on the basis of echocardiography or invasive cardiac catheterization (left ventriculography and ascending aortography) data. Serial echocardiography has been an integral part of follow-up of such patients (17, 18). Common clinical grading of MR by echocardiography generally relies on the degree to which the visible regurgitant jet fills the left atrium, and on whether systolic flow reversal in the pulmonary veins is present (2, 11, 12).

**Table 6.** Agreement between CMR and Doppler echocardiography in severity of regurgitation in a combined validation cohort of 52 patients with MR and AR

Echo	Mild	Moderate	CMR		Total
			Mod-severe	Severe	
Mild	22	0	1	0	23
Moderate	5	2	7	1	15
Mod-severe	0	4	4	0	8
Severe	0	0	4	2	6
Total	27	6	16	3	52

During grading of AR, width of the regurgitant jet at the base, the rate of decay of diastolic pressure gradient across the valve (pressure half-time index) and presence of diastolic flow reversal in the descending thoracic aorta are also considered (6, 13). Additional methods, such as calculating the proximal isovelocity surface area (PISA) and regurgitant orifice area may also be helpful but are less commonly used for clinical purposes and often difficult to implement with eccentric regurgitant jets. In addition, accurate assessment of regurgitant jet geometry depends on the imaging plane, gain settings and acoustic windows and thus is subject to bias.

Cardiac catheterization can provide valuable hemodynamic information on the degree to which MR and AR affect the cardiac chambers, but assessment of regurgitation may be limited when based on a single projection and requires assumptions regarding jet geometry. Determination of MR is particularly subjective if there is prominent ectopy during left ventriculography. Similarly, the severity of AR may be greatly overestimated if during ascending aortography, the pigtail catheter descends toward the aortic valve, thereby altering its function.

CMR is ideally suited for serial evaluation of valvular regurgitation and provides an assessment of the effects of regurgitant lesions on the cardiac chambers. Owing to the the associated turbulent flow and its resultant spin dephasing, valvular regurgitation appears as a signal void in the receiving chamber. This phenomenon has been exploited as a qualitative means for assessment. Using cineangiography as a gold standard, early CMR reports with relatively long echo time ( $TE > 10$  ms) gradient echo sequences demonstrated excellent sensitivity and specificity of cine-CMR for detection of MR and AR (19) and showed that regurgitant jet (local dephasing/signal void) planimetry had a good correlation with Doppler echocardiography (20, 21). However, the widespread adoption of recent, more rapid imaging methods using very short echo times has led to a reduction in CMR sensitivity for regurgitant lesions (22). Moreover, quantification of MR and AR regurgitant volumes and regurgitant fractions are now readily performed with CMR (23, 24). Despite such capability, there are no currently accepted standard thresholds for the qualitative assignment of regurgitation severity. Previously, correlation was sought with angiographic severity grades (27, 28), but most patients do not routinely undergo such invasive assessment. Our threshold data provide clinically meaningful criteria for patients being considered for follow-up by both methods.

## LIMITATIONS

Our study has recognized limitations. The assessments by echocardiography and CMR were driven by clinical indications, and though contemporary (median 31 days), were not simultaneous and thus potentially under different loading conditions. Intercurrent initiation of hemodynamically-significant medications by the treating physicians could also have affected the degree of regurgitation between the studies. The finding of 10%  $MR_{RF}$  among subjects without any echo evidence of MR is likely related to right coronary artery systolic flow and our choice to include the papillary muscle as ventricular volume. Though

consecutive, our cohort contained few patients with moderate-severe or severe AR; therefore, the determination of the threshold for severe AR was based on a relatively small data set. Finally, the prognostic relevance of the proposed regurgitation fraction thresholds is unknown and requires further study.

## CONCLUSIONS

In this consecutive series of patients with AR and MR, we have identified quantitative threshold CMR data for qualitative grades of MR<sub>RFr</sub> and AR<sub>RFr</sub> that closely correlate with analogous measures by Doppler echocardiography. These data provide the basis for standardized qualitative reporting of regurgitation severity by CMR and echocardiography, thereby facilitating consistency in longitudinal follow-up of patients undergoing both imaging procedures.

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