Cardiovascular Magnetic Resonance for Direct Assessment of Anatomic Regurgitant Orifice in Mitral Regurgitation

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Background—In patients with mitral regurgitation (MR), assessment of the severity of valvular dysfunction is crucial. Recently, regurgitant orifice area has been proposed as the most useful indicator of the severity of MR. The purpose of our study was to determine whether planimetry of the anatomic regurgitant orifice (ARO) in patients with MR is feasible by cardiovascular magnetic resonance (CMR) and correlates with invasive catheterization and echocardiography effective regurgitant orifice [ECHO-ERO] by proximal isovelocity surface area.

Methods and Results—Planimetry of ARO was performed with a 1.5-T CMR scanner using a breath-hold balanced gradient echo sequence true fast imaging with steady state precession (TrueFISP). CMR planimetry of ARO was possible in 35 of 38 patients and was closely correlated with angiographic grading (r=0.84, P<0.0001). In patients with MR grade ≥III on catheterization, CMR-ARO (0.60±0.29 cm² versus 0.30±0.19 cm², P<0.0001) as well as ECHO-ERO (0.49±0.17 cm² versus 0.27±0.10 cm²) were significantly elevated in comparison with MR grade <III. Further, CMR-ARO was closely correlated to CMR regurgitant fraction and volume (r=0.90 and r=0.91, P<0.0001, respectively) and catheterization regurgitant fraction and volume (r=0.86 and 0.83, P<0.0001, respectively). The correlation between CMR-ARO and ECHO-ERO was 0.81 (P<0.0001) and CMR slightly overestimated ECHO-ERO by 0.06 cm² (P<0.05). As assessed by receiver operating characteristic analysis, CMR-ARO at a threshold of 0.40 cm² detected MR grade ≥III as defined by catheterization, with a sensitivity and specificity of 94% and 94%, respectively.

Conclusion—CMR planimetry of the anatomic mitral regurgitant lesion in patients with MR is feasible and permits quantification of MR with good agreement with the accepted invasive and noninvasive methods. Direct measurement by CMR is a promising new method for the precise assessment of ARO area and the severity of MR. (Circ Cardiovasc Imaging. 2008;1:148-155.)

Key Words: catheterization ■ echocardiography ■ magnetic resonance imaging ■ mitral valve ■ regurgitation

In patients with valvular heart disease, accurate characterization of the regurgitant lesion is an ongoing challenge. In mitral regurgitation (MR), a wide range of analytic approaches and diagnostic techniques have been proposed to determine disease severity.4–7 The latter technologies also include assessment of regurgitant volume, regurgitant fraction, and regurgitant orifice by catheterization and echocardiography. Although no uniform reference is established,8 the regurgitant orifice area is a fundamental measure of valvular incompetence and has recently been considered the most accurate index to grade the severity of MR.1,7,9 and aid the timing of surgery.10,11

Clinical Perspective see p 155

Cardiovascular magnetic resonance (CMR) allows accurate measurement of cardiac structures and function. In addition, measurement of blood flow volumes through phase velocity mapping and volumetry allows for the obtaining of stroke and regurgitant volumes and information regarding the hemodynamic relevance of valvular dysfunction.5,12,13 New CMR sequences, such as steady-state precession techniques, also allow visualization of the cardiac valves in any chosen plane, with excellent image quality.14 Very recently, we and others have shown that CMR can be used to directly visualize the orifice of stenotic aortic15–17 and mitral valves18,19 as well as the anatomic regurgitant orifice (ARO) in aortic regurgitation.20

Based on these findings, we hypothesized that the regurgitant orifice could also be visualized in MR and provide direct and anatomic quantification of the regurgitant lesion. Thus, the purpose of the current study was to assess for the first time whether planimetry of the ARO by CMR is feasible in MR and how it correlates with measures of regurgitation derived from cardiac catheterization and the effective regur-

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148
mitral orifice (ERO) by the proximal isovelocity surface area (PISA) method derived from echocardiography.

Methods

Patients

We enrolled 38 patients with known or suspected MR in this study. Patients with evidence of severe MR on echocardiography underwent cardiac catheterization in preparation for cardiac surgery and an additional research CMR for evaluation of CMR-ARO and CMR regurgitation fraction. Patients with mild or moderate MR underwent cardiac catheterization for other reasons such as clarification of dyspnea and angina pectoris, but MR was not the primary indication for catheterization. The mean time interval between CMR and catheterization for all patients was 1.24±4.9 days (range, 13 days); 2 patients had an interval of 13 days and 1 patient had an interval of 11 days.

The CMR regurgitant fraction and the CMR regurgitant volume were calculated from the left ventricular stroke volume (LVSV) and phase contrast velocity mapping flow measurements in the ascending aorta by CMR in all patients. Planimetry of the ARO in MR by CMR (CMR-ARO) was possible in 35 of 38 patients (92%). In all patients, ECHO-ERO was assessed by PISA, and an invasive quantification of the severity of MR was performed (left ventricular angiography in all 38 patients and calculation of the regurgitant fraction by additional right heart catheterization in 30 patients). Grading of MR was defined by the current guidelines of the American Heart Association, the American College of Cardiology, and the American Society of Echocardiography.21,22 Specifically, MR grade 1 was defined as regurgitant fraction of <30%; MR grade II was defined as regurgitant fraction of 30% to 39%; MR grade III was defined as regurgitant fraction of 40% to 49%; and MR grade IV was defined as regurgitant fraction of ≥50%. All studies were performed within 2 weeks. All patients gave informed consent to participate.

Cardiac Catheterization

For left ventricular angiograms, a pigtail catheter was positioned in the left ventricle retrograde from the femoral artery. Standard left ventriculograms were performed in the right anterior oblique (RAO) 30° angulation, usually with 30 mL contrast agent delivered at 10 mL/s by automated injector and filmed with a frame rate of 12.5/s. Severity of MR was semiquantitatively estimated by left ventricular angiography according to the classification of Seller et al3 (1, mild MR; 2, moderate MR; 3, moderately severe MR; 4, severe MR). Catheterization regurgitant fraction and regurgitant volume were calculated from left ventricular angiographic stroke volume by left ventriculography and cardiac output by thermodilution (average of ≥3 measurements), as follows:

\[
\text{Catheterization regurgitant fraction} = \frac{\text{stroke volume} - \left(\text{cardiac output/heart rate}\right) \times \text{stroke volume}}{\text{cardiac output/heart rate}}
\]

Echocardiography

Color-coded Doppler echocardiography was performed in a standard fashion using commercially available equipment (Sonos 7500, Philips, Eindhoven, The Netherlands), and the effective regurgitation orifice area was calculated by the PISA method according to the recommendations of the American Society of Echocardiography.21 For the PISA method, the appearance of the proximal convergence field was optimized by shifting the color Doppler aliasing velocity to 23 to 58 cm/s. In addition, the position of the transducer was modified to minimize the angle between the centerline of the flow convergence and the ultrasound beam.

Cardiovascular MRI Studies

CMR studies were performed on a 1.5-T scanner (Sonata, Siemens Medical Solutions, Erlangen, Germany) using a phased array re-
Statistical Analysis

The agreement between the methods of quantification of MR was assessed by univariate regression analysis. Spearman’s rank correlation method was used to assess the association between grading of MR by the left ventricular angiographic degree or by CMR regurgitant fraction and continuous measurements. Differences in mean values between 2 groups were analyzed by t test. \( t \) test was performed to compare frequencies between groups. Intra- and interobserver variability were expressed as the percentage of variability (absolute value of the difference between 2 measurements divided by the mean of 2 measurements). Receiver operating characteristic analysis was performed to determine the predictive values of CMR-ARO to detect MR grade III or IV. A level of significance of below 0.05 was defined as statistically significant. Results are shown as mean±SD for continuous variables and as percentages for categorical variables. SPSS version 12.0 (SPSS Inc, Chicago, Ill) was used for statistical analysis.

Results

Patients

Characteristics of the 35 patients are depicted in Table 1. Patients with MR III or IV are younger. Most patients were symptomatic with dyspnea. Seven patients had coronary artery disease (lumen reduction >50%) and 15 had impaired left ventricular function (ejection fraction <50%). Patients with MR grade III or IV had increased left ventricular volume. The mechanism of MR was prolapse or flail in 23 patients and functional in 12 patients. The jet was central in 10 patients and eccentric in 25 patients. There was no significant difference in heart rate between patients with rate-controlled atrial fibrillation and sinus rhythm (76±13 per minute versus 72±14 per minute, \( P=0.34 \)), and the proportion of studies with adequate or acceptable image quality was only slightly higher in sinus rhythm than in atrial fibrillation (n=16 [84%] versus n=12 [75%], \( P=0.398 \)). The correlation between CMR-ARO and ECHO-ERO was \( r=0.81 \) (\( P<0.0001 \)) in patients with sinus rhythm and \( r=0.86 \) (\( P<0.0001 \)) in patients with atrial fibrillation.

Assessment of ARO by CMR

Figure 3 shows CMR images of 3 patients. CMR planimetry of ARO could be performed in 35 of 38 patients (92%). Image quality was of overall good quality in 28 patients, moderate in 7 patients, and not sufficient in 3 patients (tachyarrhythmia in 1 patient and artifacts in 2 patients). The mean CMR-ARO was 0.44±0.29 cm² (range, 0.12 to 1.58 cm²). Interobserver and intraobserver variabilities were 8±7% and 7±6%, respectively.

Comparison of CMR-ARO and MR grading by CMR regurgitant fraction revealed a correlation of \( r=0.95 \) (\( P<0.0001 \)). Mean CMR-ARO increased statistically significant (\( P \) for trend \( <0.0001 \)), with increasing severity of CMR regurgitant fraction grade. The CMR-ARO was closely correlated with CMR regurgitant fraction (\( r=0.91 \), \( P<0.0001 \); Figure 4A) and CMR regurgitant volume (\( r=0.90 \), \( P<0.0001 \)).
Comparison of CMR-ARO With Cardiac Catheterization

A close correlation was present between planimetry of CMR-ARO and angiographic grading of MR on cardiac catheterization (r=0.84, P<0.0001). CMR-ARO was further closely correlated both with catheterization regurgitant fraction (n=28; r=0.86, P<0.0001) as well as with catheterization regurgitant volume (n=28; r=0.83, P<0.0001; Figure 4B). A close correlation was also present between CMR regurgitant fraction and catheterization regurgitant fraction (r=0.89, P<0.0001) as well as CMR regurgitant volume and catheterization regurgitant volume (r=0.84, P<0.0001).

Comparison of CMR-ARO and ECHO-ERO by PISA

On echocardiography, the mean ECHO-ERO determined by PISA was 0.38±0.18 cm² (range, 0.14 to 1.0 cm²). The mean absolute difference between CMR-ARO and ECHO-ERO was 0.06 cm² (range, −0.30 to 0.65 cm²; P<0.05), resulting in an overestimation of CMR-ARO as compared with ECHO-ERO by 16%. There was an excellent correlation between planimetry of the CMR-ARO and ECHO-ERO (r=0.81, P<0.0001; Figure 4C).

Comparison of Cardiac Catheterization and ECHO-ERO by PISA

A close correlation was present between ECHO-ERO and angiographic grading of MR on cardiac catheterization (r=0.73, P<0.0001). ECHO-ERO was further closely correlated both with catheterization regurgitant fraction (n=28; r=0.62, P<0.0001) as well as with catheterization regurgitant volume (n=28; r=0.71, P<0.0001).

Predictive Values of CMR-ARO for MR

As assessed by receiver operating characteristic analysis, the area under the curve for diagnosis of grade III or IV MR by CMR-regurgitant fraction was 0.99 for CMR-ARO, the area under the curve for diagnosis of grade III or IV MR by
CATH-regurgitant fraction was 0.95 for CME-ARO, the area under curve for diagnosis of grade III or IV MR by left ventricular angiography was 0.94 for CMR-ARO and the area under the curve for ECHO-ERO was 0.84. The respective cut points for CMR-ARO and corresponding predictive values are depicted in Table 2.

Discussion

The current study is the first to apply CMR for direct planimetry of the ARO in patients with MR. It demonstrates that CMR planimetry is feasible in MR and correlates very well with several noninvasive and invasive measures of disease severity, including the PISA method by echocardiography.

CMR for Quantification of MR

Characterization of the severity of regurgitant lesions is among the most difficult problems in valvular heart disease. Such a determination is important because mild regurgitation does not lead to remodeling of cardiac chambers and has a benign clinical course, whereas severe regurgitation is associated with significant remodeling, morbidity, and mortality. In evaluating the severity of the MR, it is ideally desirable to determine regurgitant orifice area as well as regurgitant volume and fraction. In addition, it is important to assess the size and function of the left ventricle to aid the decision toward repair or watchful waiting.

Previously, CMR has been shown as an accurate method to determine regurgitant fraction and regurgitant volume in MR. More recently, CMR has also been shown to allow direct planimetry of stenotic aortic and mitral valves and the ARO in aortic regurgitation. The current study extends these findings as it demonstrates that CMR also allows to accurately visualize of the anatomic regurgitant area in MR. Therefore, CMR seems to be a powerful and comprehensive new method for the accurate quantification of disease severity in MR.

Comparison of Methods for Grading of MR

Regarding the comparison with cardiac catheterization, a strong correlation of ARO by CMR with invasively graded MR was present. Although angiography is dependent on several technical factors and hemodynamics as well as subjective factors, it is a unique method to calibrate newer quantitative methods. In this respect, the close correlation between anatomic regurgitant area by CMR with regurgitant volume and fraction by catheterization supports CMR planimetry for MR as promising new method.
Regarding the evaluation of MR by echocardiography, calculation of the ECHO-ERO by application of the PISA method has been suggested. This measurement provides a quantitative (although indirect) measure of lesion severity reflecting the “hole” in the mitral orifice. The weakness of the PISA method was exposed in both clinical and in vitro studies that showed both under- and overestimation of ECHO-ERO.

Interestingly, CMR provides an opportunity to directly visualize the regurgitant orifice and may overcome the limitations of indirect regurgitant orifice area measurement by the PISA method. Indeed, in the current study, the ARO was oval shaped in many cases with moderate or severe regurgitation (Figure 3B and 3C), which might lead to over- or underestimation of ECHO-ERO. Planimetry of CMR-ARO using steady-state free-precession sequences was possible in 35 patients (although with good image quality in only 28) and correlated well with ECHO-ERO area calculated by PISA. Our current finding of a slightly higher mean CMR-ARO by CMR in comparison with ECHO-ERO by PISA demonstrates a slight overestimation by CMR-ARO of 16%. Regarding this difference between the imaging modalities, it has to be noted that CMR planimetry defines the anatomic regurgitant lesion, whereas the areas of ERO by PISA should yield the narrowest flow stream, which may tend to be smaller than the anatomic orifice area and is sited slightly distal to the anatomic orifice because of flow convergence. Also, potential differences of ECHO-ERO by PISA and CMR-ARO by CMR may be related to valve motion and slice orientation. Specifically, transplanar valve motion during systole might lead to over- or underestimation of valve area when the imaging plane misses the smallest maximal regurgitant orifice. CMR allows for addressing this problem by acquiring the smallest maximal ARO in midsystole of several phases at different levels of the mitral valve, and we highly recommend this approach to minimize the potential of an under- or overestimation of the mitral regurgitant orifice because of imprecise localization.

**Limitation**

As a limitation, our cohort was derived from patients who were specifically admitted for evaluation of MR and patients in whom presence of MR was only a second finding. Although this allowed us to study a full spectrum of disease severity, it might also introduce selection bias in comparison with patients who are exclusively evaluated for surgical intervention. Furthermore, the regurgitant orifice is not necessarily constant throughout systole, and this can potentially affect the estimation of regurgitant severity, particularly if ARO grading is based on a single systolic still frame showing maximum systolic regurgitant orifice. Therefore, the anatomic measurement (ARO) should be complemented by a functional measurement (regurgitant fraction and volume). Lastly, when compared with the planimetry of stenotic or regurgitant aortic valves and stenotic mitral valves, direct planimetry of ARO in MR seems more difficult and time consuming because angulation may be more difficult because of the longitudinal movement of the mitral annulus and because irregular shapes of regurgitant orifices may be present.
Clinical Relevance
In routine clinical practice, echocardiography is most often adequate to determine the severity of the disease by semi-quantitative and quantitative modalities.1 Quantification of MR may be occasionally difficult, especially if impaired image quality or eccentric regurgitant jets are present.29 In patients with indistinct echocardiographic findings, CMR presents as a promising new tool for assessment of the severity of MR through calculation of regurgitant fraction and volume by phase-contrast velocity mapping6,12 and direct planimetry of the anatomic regurgitant lesion, as presented here. Therefore, we suggest that CMR-ARO measurements are performed in addition to traditional regurgitant fraction and volume measurements.

Conclusion
In this study, we have demonstrated the feasibility of CMR for direct planimetry of the ARO in MR. Further, CMR-ARO agrees closely with regurgitant volume and fraction from CMR and catheterization as well as ECHO-ERO by PISA. This new method complements established methods for the assessment of MR and could be used as new noninvasive anatomic measure for the severity of MR.

Acknowledgments
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Disclosures
None.

Table 2. Predictive Values for CMR-ARO

<table>
<thead>
<tr>
<th>Cases</th>
<th>ROC-AUC (95%CI)</th>
<th>CMR-ARO Cutoff, cm²</th>
<th>Sensitivity/Specificity, %</th>
<th>PPV/NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR-RF ≥III</td>
<td>14/35</td>
<td>0.99 (0.87–0.99)</td>
<td>&gt;0.41</td>
<td>100/91</td>
</tr>
<tr>
<td>CATH-MR ≥III</td>
<td>17/35</td>
<td>0.94 (0.80–0.99)</td>
<td>&gt;0.40</td>
<td>94/94</td>
</tr>
<tr>
<td>CATH-RF ≥III</td>
<td>16/28</td>
<td>0.95 (0.79–0.99)</td>
<td>&gt;0.40</td>
<td>94/92</td>
</tr>
<tr>
<td>ECHO-ERO ≥0.40 cm²</td>
<td>15/35</td>
<td>0.84 (0.68–0.94)</td>
<td>&gt;0.38</td>
<td>93/75</td>
</tr>
</tbody>
</table>

CATH-MR indicates left ventricular angiographic MR grade by cardiac catheterization; CATH-RF, regurgitation fraction by cardiac catheterization; CMR-ARO, anatomic regurgitant orifice as determined by cardiovascular magnetic resonance; CMR-RF, regurgitation fraction by cardiovascular magnetic resonance; ECHO-ERO, effective regurgitant orifice as determined by echocardiography; ROC-AUC, receiver operating characteristic area under the curve; PPV, positive predictive value; NPV, negative predictive value.

References


**CLINICAL PERSPECTIVE**

Accurate quantification of the severity of the regurgitant lesion is an ongoing challenge in patients with mitral regurgitation (MR). The current study was performed to assess whether visualization of the anatomic regurgitant orifice lesion in patients with MR by cardiac magnetic resonance (CMR) is feasible and accurate. We observed that CMR allows visualization and planimetry of the mitral anatomic regurgitant orifice in the majority of patients (92%) and over a wide range of MR severity. Furthermore, CMR often allows visualization of oval-shaped and curved regurgitant orifice areas and contributes to our understanding of the regurgitant mechanism. Finally, anatomic regurgitant orifice correlates closely with measures of MR severity such as regurgitant volume, regurgitant fraction, MR grade by CMR and catheterization, and effective regurgitant orifice by echocardiography (proximal isovelocity surface area method). Determination of anatomic regurgitant orifice by CMR is an accurate and quantitative direct measure of MR. This new method complements established methods and could be used as new noninvasive measure for assessing the severity and mechanism of MR.
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