Commentary

Cardiovascular magnetic resonance, mitral regurgitation and outcomes: the importance of accurate assessment in an era of increasing intervention

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Assessing the severity of mitral regurgitation has been part of clinical practice since the advent of the stethoscope (presence of S3, soft S1, early A2, signs of pulmonary hypertension—loud P2 and parasternal heave, displaced apex beat, signs of left ventricular failure). Nowadays, imaging with echocardiography is the worldwide standard with its ability to give semi-quantitative and quantitative measures, including vena contracta length, effective regurgitant orifice area (EROA) and regurgitant volume (RVol) using the proximal isovelocity surface area (PISA) method, and measures of the haemodynamic consequences of mitral regurgitation (pulmonary vein systolic flow reversal, LV end-systolic diameter, left atrial area or volume, pulmonary systolic arterial pressure at rest). However, in practical terms, many clinicians rely on the simpler, albeit less quantitative, colour flow imaging. Recommendations for evaluation of the severity of regurgitation are old (circa 2003), but remain clinically relevant (1).

Relatively new to the field of non-invasive imaging is cardiovascular magnetic resonance (CMR). It has evolved as the 'gold-standard' of measuring cardiac volumes, mass and systolic function with excellent accuracy and reproducibility (2). CMR provides a great insight into cardiac diseases and has revolutionised imaging in cardiology with expanding applications in both clinical and research domains. The applications of different CMR techniques are still evolving because of complexities in studying a moving organ, the need for specialised hardware and complex software, not to mention cost and limited availability. Despite these challenges CMR is a rapidly growing field and is arguably central to the future of non-invasive Cardiology. The United Kingdom (UK) leads development in this field and Australasia is on the initial steep upslope of adoption. The most common indications for CMR include the assessment of heart failure and cardiomyopathy, ischaemia, and viability (3). However, its clinical scope is wide and includes suspected coronary artery disease (CAD), known CAD—viability, acute coronary syndromes and chest pain differentials, cardiomyopathies, rare diseases, tumours and masses, congenital and structural heart disease, and detailed assessment of flow including valvular heart disease—relevant to this Commentary.

There are many forms of mitral regurgitation—chronic organic, functional, ischaemic, myxomatous, to name a few. Medical or surgical treatment is directed at the specific mechanism of regurgitation in each individual patient and the associated clinical picture. The onset of symptoms can be several years from the time of diagnosis of significant regurgitation, and depends on the aetiology of mitral valve disease (4,5). Furthermore, the two major concerns in patients with asymptomatic mitral regurgitation are the risk of sudden death and the risk of irreversible left ventricular dysfunction (6). Severe chronic organic mitral regurgitation carries significant morbidity and mortality, but can be curbed by timely surgical intervention (7). There is debate that early surgical intervention improves outcomes in asymptomatic patients (8-11), although there are no randomized controlled trials to support this against the more traditional 'watchful waiting' strategy (12).

With increasing access to percutaneous cardiac intervention and surgical advances with mitral valve repair, the importance of correct identification of patients with mitral regurgitation needing intervention is critically important. Guidelines tell us that mitral valve repair or replacement is indicated when there are: (I) symptoms or (II) adverse cardiac features detected using echocardiography—left ventricular dilatation (LVESD ≥45 mm) or dysfunction (LVEF <60%), or new onset atrial fibrillation, or pulmonary artery systolic pressure >50 mmHg, or other risk factors: LVESD >40 mm with flail leaflet, LA volume ≥60 mL/m^2 and sinus rhythm or pulmonary hypertension on exercise (SPAP ≥60 mmHg) (13,14). These guidelines have been derived from studies evaluating the effect of preoperative factors on long-term outcome after surgical intervention in patients with "severe" mitral regurgitation. However, the definition of severity varies from study to study and typically is based on clinical factors, not quantitative criteria.

The authors of the recent *Circulation* paper "Determination of Clinical Outcome in Mitral Regurgitation With Cardiovascular Magnetic Resonance Quantitation" (15) applied one of the key strengths of CMR—its accuracy and precision—to evaluate the association between CMR measurements of the degree of chronic organic mitral regurgitation in asymptomatic individuals and the future need for surgery (the development of symptoms and/or traditional indications for surgery).

Firstly, the authors established that CMR can accurately quantify mitral regurgitation. They report two significant CMR thresholds—RVol greater than 55 mL or a regurgitant fraction of greater than 40%—that predicted those who progressed to symptoms or other indications for surgery. It is important to note that the absolute thresholds reported may not necessarily represent a true clinically meaningful value because, as the authors also mention, there was no separate validation cohort.

Secondly, the authors also assessed the more traditional measures of physiological consequences (volumetric indices) with outcome. Interestingly, CMR-derived end-diastolic volume index showed only a weak correlation with outcome and added little to the discriminatory power of regurgitant fraction and RVol. Likewise, the longstanding traditional measure of end-systolic volume used in current guidelines did not show a strong association with outcome. This raises the question—are our traditional indicators good enough? Could CMR be a more robust tool to detect early disease and stratify risk? Should severe mitral regurgitation be defined by quantitative techniques instead of by the physiologic consequences of chronic volume overload? This latter approach certainly assumes that patients will rapidly develop irreversible consequences of regurgitation, such as left ventricular dysfunction. Also, it is unclear whether mitral valve surgery alters the risk of sudden death. Until there is prospective data showing early intervention decreases the adverse consequences of chronic mitral regurgitation, mitral valve surgery based on these criteria is not appropriate.

How does this paper differ from others?

This paper by Myerson *et al*. is the first to use CMR-derived measures to predict the future need for surgery in mitral regurgitation. It highlights that CMR may be able to identify appropriate people for early surgery, beyond the information provided by echocardiography. Mitral regurgitation is difficult to assess with echocardiography, especially if the jet is eccentric or multiple and when there are changing degrees of regurgitation during the cardiac cycle. The CMR technique is robust in these settings. CMR also has the power to detect small changes in cardiac structure and function, which could be advantageous in this setting, and also for monitoring and distinguishing between stable and progressive disease.

The authors have also performed similar work examining the predictive value of CMR measures in aortic regurgitation with progress and outcome (16). There were differences between CMR assessment in mitral regurgitation and in aortic regurgitation. Certainly, regurgitant fraction and RVol were predictors of the future need for surgery in both valvular diseases, but the thresholds were higher for mitral regurgitation: mitral regurgitant fraction 40%, RVol 55 mL versus aortic regurgitation: 33%, 42 mL. This is in comparison to echocardiographic guidelines indicating that mitral regurgitation and aortic regurgitation have the same thresholds for severe regurgitation—regurgitant fraction 50%, RVol 60 mL (13). Comparing different imaging modalities such as echocardiography and CMR has its pitfalls but these results suggest that there are different thresholds for each valve lesion and that we should establish CMR specific reference ranges and guidelines.

Future directions

Although these CMR results are associated with a need for surgery, there is still the need for confirmation with a clinical trial that proves early surgery actually conforms benefit.

CMR techniques of measuring mitral regurgitation include analysis of LV volumes and aortic flow quantification using phase contrast velocity mapping. There is no doubt that CMR is considered the 'gold-standard' of measuring cardiac volumes and function. Regurgitatant fractions are not always calculated numerically in CMR reports—these results indicate that perhaps this indirect measure should be reported more routinely. However, the indirect measure of mitral regurgitation using aortic flow quantification has inherent weaknesses (despite documented to have high accuracy and reproducibility) and requires high quality control for accurate application. CMR with 4D-flow could offer potential in this field since a typical 4D-flow acquisition acquires a single coherent volume, permitting a comprehensive "whole heart" audit of flow that should be internally consistent. Previously there were barriers to the application of this technique, however these are now becoming less problematic.

CMR measures could also be used in other settings—to identify patients for percutaneous intervention of mitral regurgitation, monitoring/follow-up of chronic regurgitation from other causes in asymptomatic patients, and other valvular lesions and pathology. We are in an era now of translating CMR research into the clinical arena to advance our knowledge and care of patients.

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Footnote

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