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Research Article

Comparison of Chronic Rheumatic Mitral Regurgitation Severity between Cardiac Magnetic Resonance Imaging and Echocardiography

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Abstract

Background and Purpose

Traditionally, echocardiography has been used for assessing mitral regurgitation (MR) severity. However, existing qualitative, semi-quantitative and quantitative parameters suffer from several limitations. The shortcomings of the current echocardiographic methods for MR severity assessment are especially pronounced in the context of eccentric MR jets. Cardiac magnetic resonance (CMR) imaging is useful for assessing valvular lesions as it is now the gold standard for assessing left ventricular and left atrial volumes. Therefore, we sought to study and compare echocardiography with CMR for assessment of chronic rheumatic MR severity.

Methods

Twenty-two patients with chronic rheumatic MR who underwent both CMR and echocardiography were studied. For the echocardiography part of the study, the MR severity was assessed as per current guidelines. The CMR measurements were performed per standard guidelines by a single operator experienced in this technique.

Results

The mean age of the study population was 36.3±13.9 years and 81% were females. There was overall poor agreement for the assessment of MR severity using the quantitative parameters for MR assessment between echocardiography and CMR. Although the measurements for end diastolic volume index (EDVi), end systolic volume index (ESVi), regurgitant volume (RV) and regurgitant fraction (RF) showed moderate correlation, these parameters displayed poor agreement between the two tests. We noted discrepant findings in terms of classification of valve lesion severity in seven patients. Six patients were reclassified after CMR to severe MR and one to moderate MR based on quantitative parameters of regurgitant volume (RV) and regurgitant fraction (RF).

Conclusion

In patients with severe chronic rheumatic MR with eccentric jets, when MR quantification by echocardiography is inadequate, CMR derived quantitative volumetric parameters may be useful for accurate classification of the severity of mitral regurgitation.

Keywords: Rheumatic mitral regurgitation, echocardiography, Magnetic Resonance Imaging

INTRODUCTION

Quantification of severity of mitral regurgitation (MR) is of utmost importance when considering a patient for surgery, yet the best method for grading MR remains elusive.(1) Chronic rheumatic mitral regurgitation (CRMR) is a disease characterised by mitral leaflet restriction and eccentric MR jets. Echocardiography assessment of MR severity is most widely used and accessible method to quantify MR.(2) However, there are several limitations associated with this technique, especially in the context of eccentric jets. Currently the guidelines recommend use of qualitative, semi-quantitative and quantitative methods to assess MR severity. Each of these techniques has their own set of limitations and thus an integrated approach is advised. The proximal iso-velocity surface area (PISA) method is the recommended quantitative method but cannot be used in eccentric jets, the most common type of jets observed in rheumatic MR. Its role is very limited if applied for eccentric jets because of error-proneness of the PISA radius detection. Thus, high inter-observer variability is described.(3)

In a symptomatic patient with severe MR (meeting the criteria of severity unequivocally) surgery is indicated as per the standard guideline recommendations.(4) In cases where patient is asymptomatic with severe MR and left ventricular ejection fraction (LVEF) and diameter are preserved, other indications for surgery include presence of atrial fibrillation, significant pulmonary hypertension and increased left atrial volume and dimensions.

In cases where patient is symptomatic but MR severity as per the standard echocardiographic criteria is questionable, alternative explanation must be sought. Further quantification of MR severity by CMR is a useful adjunctive tool in these cases.(4) It's role in risk-stratification of patients with MR has been emphasised especially in moderate and severe MR where echocardiographic assessment alone may be insufficient.(5,6) The main advantage of CMR in assessment of MR severity is its ability to quantify left ventricular (LV) volumes, left atrial (LA) volumes and flow much more precisely, using semi-automated methods of volume calculation and phase contrast velocity mapping, respectively.(7) It provides excellent accuracy and reproducibility for the evaluation of atrial and ventricular function which allows for detailed longitudinal and postsurgical assessment of reverse left ventricular remodelling.(8) Cine CMR imaging allows for detailed study of mitral valve anatomy, characterisation of mitral regurgitation and determine aetiology of MR. Mechanism of MR can be evaluated by identification of morphological abnormalities in apparatus of the mitral valve. Similarly in functional MR CMR provides accurate LV function assessment and able to delineate scarring of the myocardium and papillary muscles. Tissue characterisation by CMR with late gadolinium enhancement has revealed myocardial fibrosis in primary MR and this finding has been associated with ventricular arrythmias and sudden cardiac death.

If the patient is asymptomatic, exercise treadmill assessment may assist in eliciting symptoms, as well as changes in regurgitant volume and rise in pulmonary artery systolic pressure.(4) Additionally, biomarkers such as BNP may be useful as a low BNP level has been shown to be associated with a low mortality. If the question of severity is still not answered then CMR gives complimentary information for better decision making as described above.

To the best of our knowledge there has been no study evaluating the severity of CRMR by echocardiography and CMR. Our postulate is that CMR could be valuable in quantification of CRMR where the MR jets are predominantly eccentric. Thus, we sought to compare the assessment of MR severity using CMR quantitative methods (Regurgitant fraction (RF), Regurgitant volume (RV) and LV volumes) and echocardiography based integrated approach (qualitative, semi-quantitative and quantitative methods).

METHODS

This study was part of a prospective cross-sectional study at a large public hospital, Chris Hani Baragwanath Academic Hospital (CHBAH), Johannesburg, South Africa. Patients were enrolled from January 2014 to October 2014. All patients were screened, and those deemed to have moderate or severe CRMR were referred for possible inclusion in the study. A final number of 91 patients with presumed chronic, rheumatic MR underwent clinical evaluation, resting electrocardiogram and detailed echocardiographic assessment according to a pre-determined protocol.

The inclusion criteria were patients aged 18 years or older with echocardiographic features of moderate to severe chronic rheumatic MR.

We sought a pure MR cohort with no confounders to allow study of MR in isolation. Thus, patients were excluded if they had: comorbidities, significant aortic valve disease, concurrent mitral stenosis with a valve area of less than 2.0 cm^2, documented ischaemic heart disease, preexisting non-valvular cardiomyopathy, prior cardiac surgery, congenital or pericardial disease, pregnancy, severe anemia (haemoglobin <10g/dL), presence of a pacemaker or defibrillator, claustrophobia, renal dysfunction eGFR<60mL/min or refusal to undergo CMR.

Anaemia results in overestimating severity of MR due to high flow state, hence resulting in errors in grading.(9) Conditions such as hypertension, diabetes result in diastolic dysfunction and impaired LV relaxation resulting in high afterload which exaggerates MR severity.(10) HIV in-itself has been associated with diastolic and systolic LV function impairment, with resultant errors in MR severity grading.(11,12)

Of the original 91 patients with CRMR, 69 were excluded due to the following: Comorbidities such as HIV (n=22), hypertension (n=44), diabetes mellitus (n=3), atrial fibrillation (AF) (n=4), anaemia (n=3), renal dysfunction (n=3), and inadequate image quality (n=5).

The final sample comprised 22 patients. Fourteen healthy age and gender-matched controls were also enrolled. A tolerance of 5 years was allowed for age matching.

In degenerative MR, varying haemodynamics due to alterations in systolic blood pressure, impact MR assessment.(2) In rheumatic MR where the orifice tends to be fixed rather than dynamic, the impact of change in afterload is minimal.(2,5) Despite this assertion, we performed echocardiography and CMR imaging on the same day to negate the impact of varying afterload. The baseline clinical characteristics of these individuals were recorded and they subsequently underwent comprehensive echocardiography and CMR imaging.

The study was approved by the University of the Witwatersrand ethics committee.

ECHOCARDIOGRAPHIC EVALUATION

Transthoracic echocardiography was performed on all patients in the left lateral position by experienced sonographers using a S5-1 transducer on a Philips iE33 system (Amsterdam, The Netherlands).

All linear chamber measurements were performed according to the American Society of Echocardiography (ASE) guidelines.(13) Measurements relating to LV diastolic function were performed in accordance with the ASE guidelines on diastolic function, and included pulse wave Doppler at the mitral tips and tissue Doppler of both medial and lateral mitral annuli.(14) Mitral regurgitation was considered rheumatic in aetiology when the morphology of the valve satisfied the World Heart Federation criteria for the diagnosis of chronic rheumatic heart disease.(15) MR severity was assessed using qualitative, semi-quantitative and quantitative methods as the ASE and European Society of Cardiology valvular regurgitation guidelines.(2,16) MR jet was classified as eccentric if there was contact with the leaflet of the mitral valve posterior to the regurgitant orifice and impingement to the lateral or medial wall of the left atrium (LA) was present. It was deemed central if the MR jet was directed into the centre of the LA.(3) In equivocal cases the echocardiographic data was integrated with the clinical evaluation by an experienced cardiologist to distinguish moderate from severe MR. All echocardiographic data was transferred and analysed off-line using the Xcelera workstation (Philips).

CARDIOVASCULAR MAGNETIC RESONANCE ACQUISITION AND ANALYSIS

CMR studies were performed on a 1.5-Tesla whole body scanner, using a six-channel phased-array body coil. The images were obtained during patient breath-hold for approximately 8 seconds and were ECG gated.(17) Left and right ventricular volumes and mass and LA volumes were acquired in line with standard cardiovascular MRI (Siemens Healthcare, Germany) protocols. Using standardised protocols, long axis cines and a contiguous stack of short-axis cines for assessment of LV dimensions, mass and ejection fraction (EF) were obtained.(18) Images were analysed by an independent experienced reader blinded to the echocardiographic results with Argus software version 2002B (Siemens Medical Solutions) as previously described.(19)

LV volumes and EF were obtained by semi-automatic tracing of contours on the short-axis images in end-diastole and end-systole, with manual corrections when required.(20) The anatomy of the MV was assessed in both the basal short axis and long axis steady-state free-precession cines of the MV, using a standardised approach.(21) The severity of MR was based on RV and RF. RV was calculated as the difference between the LV stroke volume and the aortic forward stroke volume. RF was calculated with the aid of the following formula: *Regurgitant fraction (%) = [mitral regurgitant volume ÷ LV stroke volume] ×100)*. Mitral regurgitation was considered severe when RF≥42%.(22)

STATISTICAL ANALYSIS

Statistical analysis was performed with Statistica (version 12.5, series 0414 for Windows). Continuous variables are expressed as means ± SDs or medians (IQRs). Categorical data was expressed as percentages. The differences for continuous variables were calculated using Student's t- test or Mann-Whitney U test when the distribution was non-normal. Wilcoxon's matched pairs test was used to compare two dependent samples when distribution was not normal. Chi-square and Fisher's exact test were used to calculate the difference for categorical data for independent samples. McNemar's test was used to compare two dependent samples. Pearson's and Spearman's correlation coefficient were used to calculate correlations depending on whether data was normally or non-normally distributed. Bland-Altman plots were used to assess agreement between CMR imaging and echocardiographic variables used for assessment of MR severity. A p value<0.05 was considered statistically significant.

RESULTS

Baseline characteristics

Of the 22 patients included, the mean age was 36.3±13.9 years and 81% were females (Table 1). All the patients

Table 1: Baseline characteristics of the study patients and controls

Variable	Study group n = 22	Control n = 14	p value
Age (years)	36.3 ± 13.9	40.3 ± 14.2	0.40
Gender (F:M)	18:4	10:4	0.36
Systolic blood pressure (mmHg)	123.2 ± 9.5	122.9 ± 5.1	0.91
Diastolic blood pressure (mmHg)	77.2 ± 6.4	74.6 ± 12.3	0.34
Pulse (beats/min)	74.6 ± 13.1	75.5 ± 13.3	0.55
Body mass index (kg/m^2)	24.8 ± 4.7	28 ± 5.7	0.06
Body surface area (m^2)	1.6 ± 0.2	1.7 ± 0.2	0.24

Data presented as mean± SD.

Table 2: Echocardiographic characteristics of the study patients compared to controls

Variable	Study group n=22	Control n=14	p value
Echocardiographic parameters			
LV EDD (mm)	56.2 ± 7.4	42.2 ± 6.1	<0.001
LVESD (mm)	41.5 ± 8.6	26.7 ± 4.0	<0.001
LV EDVi (mL/m^2)†	90.4 (71.5–103.8)	43.2(35.2–43.2)	<0.001
LV ESVi (mL/m^2)†	39.6 ± 19.6	15.3 ± 4.6	0.001
EF (%)	59.8 ± 10.6	60.6 ± 17.1	0.5
LV mass index (g/m^2)†	100.1 ± 33.8	61.4 ± 18.7	0.004
E wave (cm/s)	147 (95.3–197)	81.2(66.6–95.0)	<0.001
E/A ratio	1.7 ± 0.68	1.4 ± 0.38	0.1
Lateral E' (cm/s)	12.8 ± 4.6	13.8 ± 3.9	0.5
Lateral E/E' (cm/s)	13.6 ± 7.5	6.0 ± 1.6	<0.001
Lateral S' (cm/s)	7.6 ± 2.1	7.2 ± 2.2	0.11
PASP (mmHg)	35.0 ± 17.0	20.7 ± 3.8	0.08
LAVi (mL/m^2)†	44.8(39–62.7)	23.2(17.7–25.4)	<0.001

Data are presented as median (interquartile range), mean± SD or %. † Values are indexed to BSA. EDVi - *End-diastolic volume indexed*; ESVi - *End-systolic volume indexed*; LAVi - *Left atrial volume indexed*; LV - *Left ventricle*; EDD - *End- diastolic diameter*; EF - *Ejection fraction*; ESD - *End- systolic diameter*; PASP - *Pulmonary artery systolic pressure*.

had isolated moderate, or severe chronic rheumatic MR and no comorbidities. Of the 22 patients 10 were in New York Heart Association (NYHA) functional class I, the remainder were NYHA functional class II. Four patients were on medical treatment with diuretics (furosemide) and anti-remodelling therapy (spironolactone, carvedilol, enalapril) for previous heart failure (HF) secondary to MR. Eight patients were on diuretics alone.

CMR AND ECHOCARDIOGRAPHIC CHARACTERISTICS

The end diastolic volume indexed to body surface area (EDVi) and end systolic volume indexed (ESVi) were increased on both echocardiography and CMR but when the two modalities were compared with student's t- test there was no difference in ESVi between the two techniques (39.6±19.6 mL/m^2 vs 49.1±36.7 mL/m^2, p=0.1) (Tables 2 and 3). However, there was a difference in EDVi [EDVi-90.4 (71.5–103.8) mL/m^2 vs 98.5(81–111.1) mL/m^2, p=0.03)] on Mann-Whitney U test. On echocardiography, nine patients had LV end diastolic diameter (EDD) <55 mm and 13 patients had LV EDD >55 mm. There was no statistically significant difference between EDVi and ESVi between echocardiography and CMR in those with LV EDD<55 mm (EDVi: 84.2±18.4 mL/m^2 vs 91.0±15.7 mL/m^2, p=0.21; ESVi: 32.8±11.7 mL/m^2 vs 31.2±10.3 mL/m^2, p=0.5). In those with LV EDD >55mm (EDVi: 106.8±35.5 mL/m^2 vs 130.5± 49.2 mL/m^2, p=0.08, ESVi: 49.1±24.9 mL/m^2 vs 75.1±45.9 mL/m^2, p=0.050) there was a tendency of volumes to be greater on MRI compared to echocardiography but was not statistically significant. The mitral RV was higher on CMR than on echocardiography (34.3 ±15.1 mL vs 47.0±19.9 mL, p=0.003). There was no difference in regurgitant fraction (RF) between the two modalities (MRI vs echo: 49.2% (31.7–56.2) vs 33.3% (27.4–47.6), p=0.1) using the Chi-squared test. The LV EF measurements were similar on both MRI (58.8%±15.1%) and echocardiography (59.8%±10.6%). Using the Bland-Altman plots, there was poor agreement between EDVi and ESVi measurements between the two imaging modalities (Figure 1 and Figure 2). Similarly, little agreement was noted for RV and RF measurements between the imaging modalities (Figures 3 and 4).

All the MR jets were eccentric (Figure 5). Echocardiography classified 14 patients as moderate MR and eight as severe MR based on quantitative and qualitative parameters. The EROA and RV derived using the PISA method were 0.2±0.12 cm^2 and 34.3 ±15.1 mL, respectively. We noted discrepant findings in terms of classification of valve lesion severity in seven patients, based on current cut- offs for RV and fraction, between CMR imaging and echocardiography. Based on RV and RF, six patients previously classified as moderate MR on echocardiogram were reclassified as severe MR on CMR, and one patient with severe MR on echocardiography was re-categorised as moderate.

Table 3: Comparison between Echocardiographic and CMR characteristics of study patients

Variable	Echocardiographic characteristics n = 22	CMR characteristics n = 22	p value	Correlation coefficient and p value
Regurgitant volume (mL)	34.3 ± 15.1	47.0 ± 19.9	0.003	r = 0.48, p = 0.02
Regurgitant fraction (%)	33.3 (27.4–60.1)	49.2 (31.7–56.2)	0.1	r = 0.26, p = 0.2
Vena contracta (cm)	0.6 ± 0.2	-	-	-
Moderate MR	14 (63.6%)	9 (41%)	0.14	-
Severe MR	8 (36.3%)	13 (55%)	0.3	-
Eccentric jet	22 (100%)	22(100%)	-	-
LV EDVi (mL/m²)	90.4 (71.5–103.8)	98.5 (81–111.1)	0.03	r = 0.69, p < 0.001
LV ESVi (mL/m²)	39.6 ± 19.6	49.1 ± 36.7	0.1	r = 0.7, p < 0.001
Ejection fraction (%)	59.8 ± 10.6	58.8 ± 15.1	0.7	r = 0.3, p = 0.08

* Data are presented as median (interquartile range), mean± SD or %. † Values are indexed to BSA. EDVi - *End-diastolic volume indexed*; ESVi - *End-systolic volume indexed*; LV - *Left ventricle*; MR - *Mitral regurgitation*.

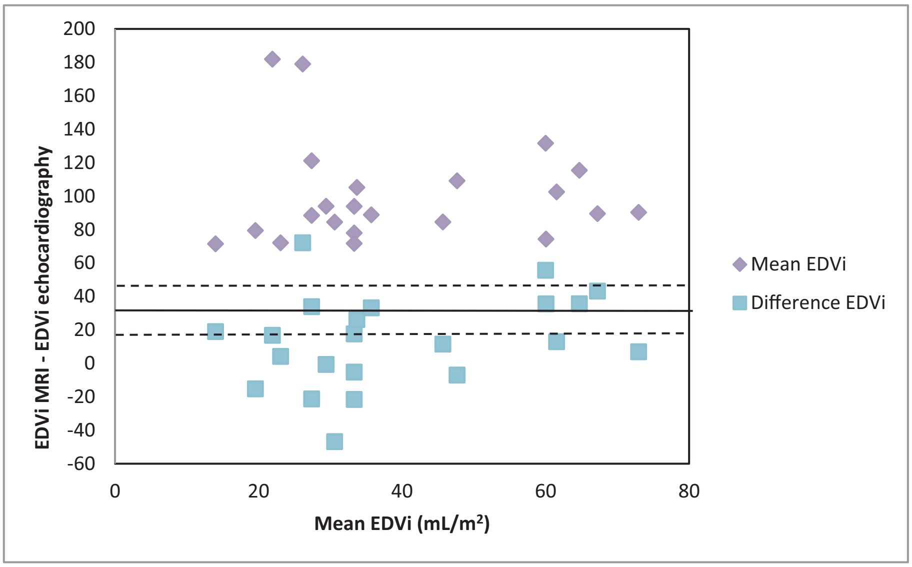

Figure 1: Bland-Altman plot for measuring end-diastolic volume indexed (EDVi)

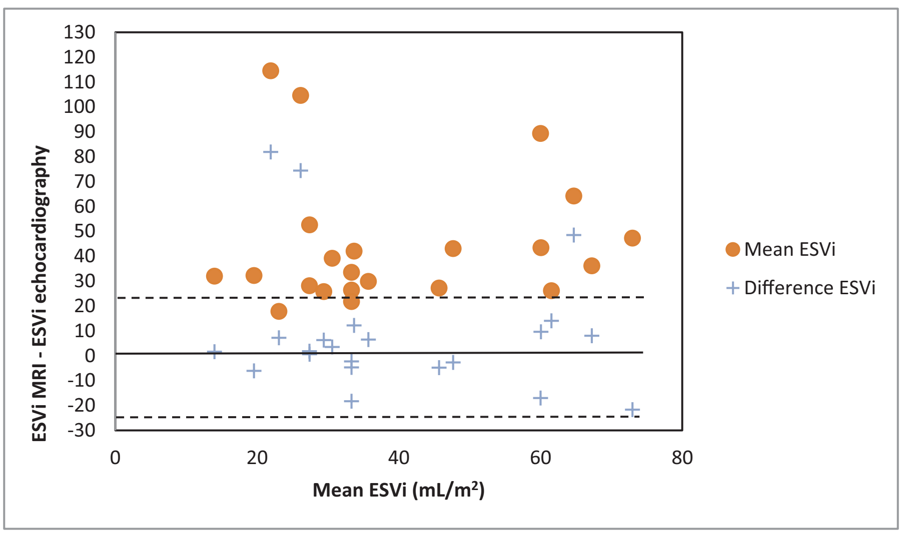

Figure 2: Bland-Altman plot for measuring end-systolic volume indexed (ESVi)

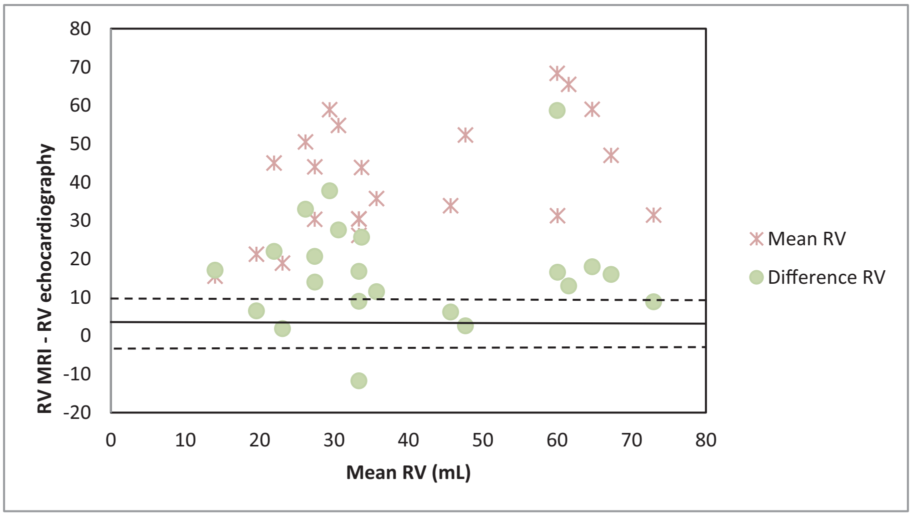

Figure 3: Bland-Altman plot for measuring regurgitant volume (RV)

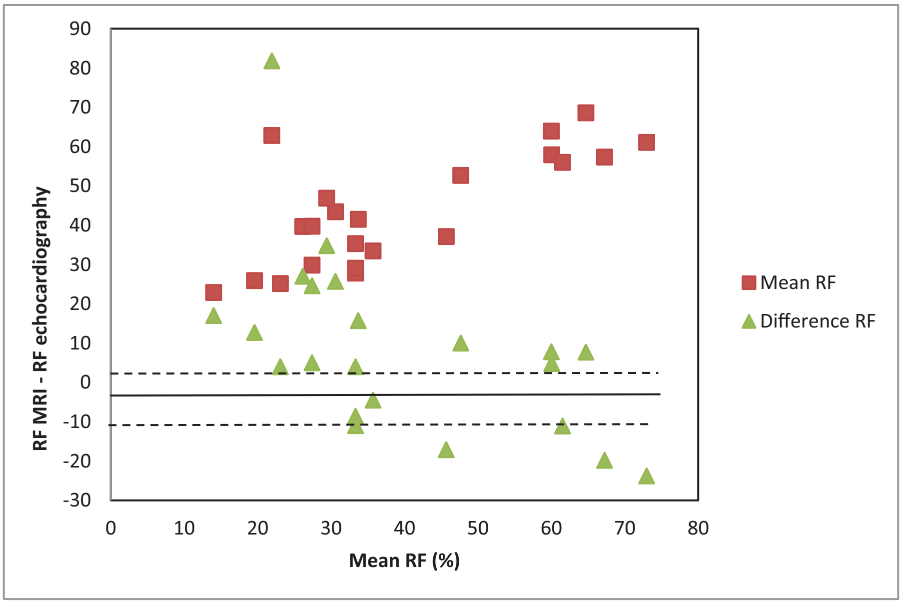

Figure 4: Bland-Altman plot for measuring regurgitant fraction (RF)

DISCUSSION

Mitral regurgitation remains an important disease entity.(23) Its accurate quantification, differentiation between moderate and severe MR has important implications in terms of medical management versus surgical intervention. Currently, echocardiography and CMR play an important role in assessing MR severity. The role of CMR in the context of RHD has recently been reviewed by Ntusi.(24) Echocardiography remains the first line tool for assessment of MR but it has its limitations. CMR has emerged as an important additional modality to comprehensively assess MR due to its accuracy and reproducibility in the assessment of ventricular volumes and function.(8) Current guidelines emphasise the role of CMR and acknowledge its strength in assessment of chronic primary MR to assess ventricular volumes, function, severity especially when echocardiography is inadequate.(4) In the absence of absolute contraindications,(25) CMR would be a particularly useful non-invasive modality, when an integrated approach by echocardiography results in inconsistent results.

In this study we found that echocardiographic and CMR techniques differ with regards to assessment of MR severity based on quantitative parameters in almost a third of patients with rheumatic MR. However, some of echocardiography- based integrated approaches of severity of MR assessment was concordant with that of CMR quantitative assessment. Various studies have shown superiority

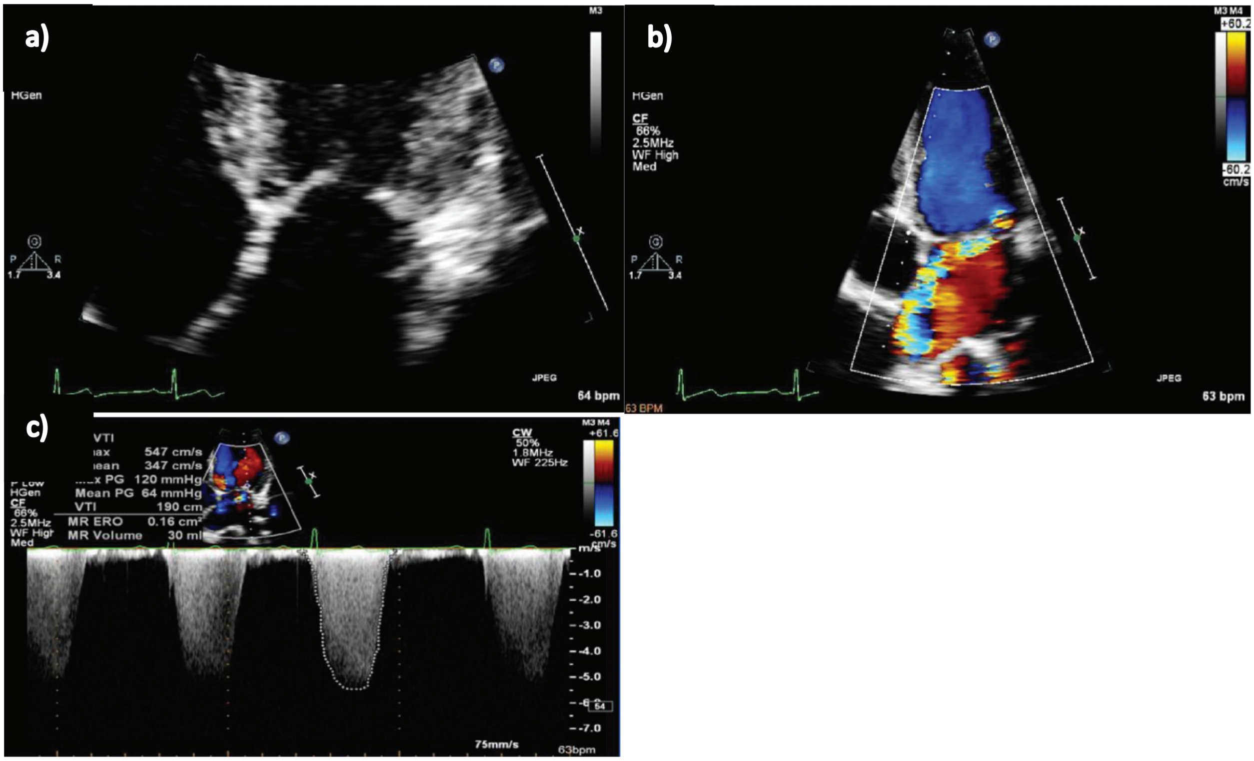

Figure 5: Two dimensional echocardiographic views depicting: a) Restricted leaflet motion of anterior and posterior mitral leaflet secondary to rheumatic heart disease b) Eccentric mitral regurgitation jet c) Incomplete continuous wave Doppler envelope generated by poor continuous wave Doppler alignment of the jet.

or equivalence of MRI over echocardiography when assessing severity of mitral regurgitation, mostly in the context of degenerative MR.(5,6,26–30) Our findings concur with a recent study by Uretsky et al. where similar discrepancies in MR quantification, between the two imaging modalities was noted.(5)

The discordance in MR severity assessment between MRI and echocardiography in this study, we believe is a result of eccentric jets in rheumatic MR due to distorted leaflet morphology. In this group of patients, errors in quantification of MR severity on echocardiography may be due to: a) assumption of a sphere when calculating radius when using the PISA assessment, b) generation of an incomplete continuous wave Doppler envelope and c) inaccurate radius measurement and imprecise identification of regurgitant orifice rendering the PISA method suboptimal for MR quantification.(3,28)

The volumes obtained on echocardiography by the biplane Simpson's method tend to be underestimated, especially in large ventricles due to foreshortening of the apex.(5,6,29) This results in underestimation of the volumes and thus regurgitant fraction. We tried to minimise the error by selecting only patients with the best imaging quality for this sub-study and, even then we found overall LV EDVi to be higher on CMR imaging compared to echocardiography. The volumes obtained on CMR may be more reliable, as most post-processing software uses semi-automated algorithms to trace the endocardial border.(7,29)

Regurgitant volume measurement was larger on CMR compared to PISA-derived RV in this study. Studies comparing RV measurements on MRI and echocardiography in MR have shown variable results with some overestimating RV on echocardiography, and others underestimating RV.(6) In all studies, these two imaging modalities could not be used interchangeably for measurement of the severity of MR. Cardiac magnetic resonance, probably allows more accurate quantification of MR based on calculation of RV using the formulae stated previously than the PISA method, especially in eccentric jets secondary to rheumatic MR. Additionally, the current cut-offs for RF pertaining to classification of MR severity differ between echocardiography and CMR, with the threshold for severity being lower on CMR compared to echocardiography.(2,31) Thus, more patients were classified as severe MR on CMR than echocardiography. In this study, CMR added incremental value in accurate quantification of MR, in the moderate and severe MR categories.

LIMITATIONS

The main limitation of this study was the small sample size. None of the controls underwent CMR due to logistical reasons. The second limitation of the study is that we did not measure the influence of interobserver variability. For the echocardiography part of the study, the first author assessed the MR severity as per guidelines recommendations. The second author, an expert in echocardiography then cross-checked all MR severity parameters prior to confirming the severity of MR. We did not quantitatively measure the inter-observer variability due to the difference in experience between the two operators at the time of the study. Previous studies have shown that there is poor agreement regarding PISA measurement even amongst experienced operators.(3) The MRI measurements were performed by a single operator who at the time was most experienced in this technique. Thus, we could not perform inter-observer variability. Prior studies have detailed the interobserver variability in CMR measurements between operators.(8)

CONCLUSION

Cardiac magnetic resonance derived quantitative parameters may be a useful adjunct for accurate classification of moderate or severe rheumatic MR characterised by eccentric jets, especially in equivocal cases, where integrated MR quantification by echocardiographic alone is insufficient. A larger study is needed to clarify the importance of CMR in the quantification of rheumatic mitral regurgitation.

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CONFLICTS OF INTEREST

None.

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