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Left Ventricular Assessment in Patients with Significant Mitral Incompetence; a Multi-Modality Imaging Study

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Abstract: *Background:* Mitral valve regurgitation (MR) is a major cause of morbidity and death across the world. It obliges volume overload over left ventricle (LV) leading to LV dysfunction and subsequently heart failure. Detection of deleterious effect on left ventricle is crucial in guiding surgical decision in such cases. *Aim of the study:* Comprehensive assessment of left ventricle in case of significant primary mitral incompetence using multimodality imaging tools, namely 2D echo, 3D echo and cardiac magnetic resonance (CMR). *Methods:* 40 consecutive patients have been recruited from May 2019 to May 2021 in a prospective observational study which has been conducted in Aswan and Tanta heart centers. All patients suffered from significant primary MR. Patients underwent 2D echo where LV volumes, function and global longitudinal strain (GLS) were calculated. The same parameters were calculated by 3D echo. CMR study for all patient was done and post processing was done on appropriate software. LV volumes, function and GLS (feature tracking) were calculated in addition to detection of myocardial fibrosis. *Results:* End diastolic volume (EDV) and end systolic volume (ESV) were significantly larger when measured by CMR (mean EDV = 220.63, mean ESV = 87.6) as compared to 3D echo (mean EDV =180.43, mean ESV =68.13) and 2D echo (mean EDV =166.25, mean ESV=61.58) (all P <0.001). EDV measures were strongly correlated with CMR and 3D echocardiography (r=0.88, p < 0.001).2D echo ESV measures were strongly correlated with CMR and 3D echo (r=0.7 and 0.63 respectively, P<0.001).3D echo ESV measures were moderately correlated with CMR (r=0.5, P<0.001). GLS values measured by 2D and CMR were moderately correlated (r=0.5, p<0.001). *Conclusion:* Left ventricle is playing an important role in the prognosis and intervention decision in mitral regurgitation. It's important to identify early deleterious LV changes so that intervention is recommended prior to the development of irreversible LV damage.

Keywords: Primary Mitral Regurgitation, MR, CMR, 2D Echo, 3D Echo, GLS, Left Ventricle

1. Introduction

Primary mitral regurgitation (MR) includes abnormalities at any level of the mitral valve (MV) apparatus; mitral leaflets, chordae tendineae, papillary muscles and annulus [1]. Myxomatous degeneration, rheumatic disease, connective tissue disease and mitral annular calcification are the commonest causes of primary MR [2]. on the long run, untreated MR will lead to ventricular dilatation, irreversible LV dysfunction and ultimately heart failure [3]. ESC guidelines have identified the presence of symptoms in addition to an EF <60% and left ventricle end systolic dimension (LVESD)>40 mm as a cutoff for MV repair/ replacement. These parameters usually don't determine the actual transition to LV dysfunction. [4]. In addition, unsatisfactory outcomes have been identified upon delaying MV surgery till meeting the cutoff parameters [5]. TTE is the first choice modality for assessment of MR severity. It determines MR etiology, mechanism and quantify its severity as well as the hemodynamic drawbacks on the left ventricle [6]. Assessment of LV systolic function is a corner stone in the evaluation of mitral valve regurgitation guiding surgical intervention decision [7] Many conventional methods are available for assessment of LV Function using 2D echo i.e. linear Dimensions (M-mode) and modified Simpson Biplane Method which is currently recommended method of quantifying LV volume and systolic function [8]. Global longitudinal strain (GLS) measures the function of longitudinally orientated myofibers, which are most vulnerable to myocardial disease. Therefore it can predict early subclinical myocardial dysfunction particularly in patients with normal LVEF [7]. 3D echo has overcome many of 2D echo limitations i.e. image foreshortening. Besides being superior in measuring LV volumes and function, it provide 3D speckle tracking echocardiography which overcomes (out-of plane phenomenon) of 2D echo STE [9] CMR is currently a reference standard for assessment of LV function and mass with excellent temporal and spatial resolution [10] CMR has a unique utility of myocardial tissue characterization, thus help in differentiating various myocardial pathologies [11] Moreover, CMR feature tracking is a rising up technique which detects myocardial deformation and analyzes the global and segmental function. Therefore it can help in early detection of myocardial dysfunction [12]. In our study, we aimed assessment of left ventricle function in patients with significant mitral regurgitation using multi-modality imaging that includes; 2D echo, 3D echo and cardiac magnetic resonance (CMR) for complementary evaluation.

2. Patients and Methods

Study design: A prospective observational study which has been conducted in Aswan and Tanta heart centers. It included 40 consecutive patients who have been recruited from May 2019 to May 2021. Inlusion criteria: we included all patients with significant (graded as moderate to severe or severe) primary mitral regurgitation were included within the study. Exclusion criteria; we excluded patients with mild to moderate MR, patients with other valvular lesions that may affect left ventricle function i.e. severe aortic incompetence, Patients with atrial fibrillation or atrial flutter rhythm or any ventricular arrhythmia and patient with contraindication to CMR i.e. claustrophobic were excluded. For all included patients the following were obtained: Full history taking (age, identification of risk factors i.e. diabetes mellitus, hypertension, obesity, smoking, current clinical complaint and related past history data were included), Full clinical examination (including heart rate, systolic and diastolic blood pressure) and 12 leads ECG were done.

All patients underwent 2D trans-thoracic echocardiography using a commercially available ultrasound machine (iE33, Philips Medical System, Andover, MA, USA). In the 2D study, end diastolic dimension (EDD) and end systolic dimensions (ESD) were measured in M mode. End-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and the LV ejection fraction (EF) were calculated by the biplane Simpson's method. LV endocardium was traced contiguously from one side of the mitral annulus to the other side, including papillary muscles as part of the LV cavity. Apical four, two-chamber and long-axis views during three consecutive cardiac cycles were acquired in the left lateral decubitus position during a breath-hold. 2D speckle-tracking analysis was performed using vendor-independent speckle-tracking software (2D CPA, TomTec Imaging Systems, Unterschleissheim, Germany) and global longitudinal strain (GLS) was calculated. After that, 3D full-volume datasets were acquired using an iE33 scanner (Philips Medical Systems) equipped with a fully sampled matrix-array transducer (X5-1) through an apical approach. Dataset of the entire left ventricle were acquired throughout at least 3 consecutive cardiac cycles with electrocardiographic gating during a single 5–7 s breath-hold. 3D volumetric measures of LV were measured using (4D LV Analysis, version 3.1.2, Tom Tec Imaging Systems, Unterschleissheim, Germany). 3D speckle-tracking was obtained automatically by the use of same software throughout the cardiac cycle. The software provided averaged longitudinal strain time curves from each segmental strain curve, from which peak global strains were determined. Finally, CMR imaging was performed for all patients using a 1.5-T scanner (Siemens, Germany). Breath-hold ECG-gated steady-state free precession sequences in standard long-axis and multiple parallel short-axis slices were used for the assessment of end-systolic and end-diastolic LV volumes. LV stroke volume (end-diastolic LV volume – end-systolic LV volume) and the LVEF ([end-systolic volume/end-diastolic volume] × 100) were calculated from Cine short axis slices. The antegrade LV stroke volume was obtained by phase contrast velocity mapping of the ascending aorta. Mitral RVol was calculated as the difference between the LV stroke volume and the antegrade LV stroke volume. Standard LGE-CMR sequences were used for assessment of myocardial fibrosis using a magnitude and phase-sensitive segmented inversion-recovery sequence approximately 10 min after intravenous gadolinium contrast administration (gadopentetate dimeglumine, 0.15 mmol/kg) LGE-CMR images were obtained in matching short- and long-axis planes. CMR feature tracking (FT) analysis CMR images were done using commercial feature tracking software (Segment software). LV endocardial and epicardial borders at end-diastolic frame were manually drawn on a single frame and global longitudinal strain was determined by averaging the peak strain values.

3. Statistical Analysis of the Data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. The following test were used in the study: Chi-square test, Monte Carlo correction, Spearman coefficient test to correlate between two distributed abnormally quantitative variables and P value which was considered significant if less than 0.05.

4. Results

The mean age of study population was 50.23 ± 14.31 with a range between 20 and 75 years. Out of the study population 17 (43%) patients were females. It was noticed that the mean body mass index was 27.32 ± 5.12 kg/m2 with a range between 17.9 and 42kg/m2. Most of patients didn't have history of diabetes mellitus or hypertension and the majority were non-smoker. The baseline demographic and clinical characteristics of the study population are summarized in Table 1.

Table 1. *The baseline demographic and clinical characteristics of the study population.*

	Primary MR (n = 40)	
	No.	%
Gender		
Male	23	57.5
Female	17	42.5
Age (years)		
Min. – Max.	20.0 – 74.0	
Mean ± SD.	50.23 ± 14.31	
BMI (kg/m^2)		
Min. – Max.	17.90 – 42.0	
Mean ± SD.	27.32 ± 5.12	
DM	2	5.0%
HTN	4	10.0%
Smoker	8	20.0%

BSA: body surface area, BMI: body mass index, DM: diabetes mellitus, HTN: hypertension

The mean heart rate was 79.55 ± 14.32, while mean systolic blood pressure 119.68 ± 16.75 and the mean diastolic blood pressure was 74.25 ± 11.47. The basic clinical examination parameters of study population are summarized in table 2.

Table 2. *The basic clinical examination parameters of the study population.*

Clinical parameters	Primary MR (n = 40)
HR	
Min. – Max.	56.0 – 110.0
Mean ± SD.	79.55 ± 14.32
SBP	
Min. – Max.	77.0 – 150.0
Mean ± SD.	119.68 ± 16.75
DBP	
Min. – Max.	50.0 – 90.0
Mean ± SD.	74.25 ± 11.47

HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure

Among patients of the study, 2 out of 40 cases were presented by typical chest pain and accounted 5 % of cases. Heart failure symptoms i.e. dyspnea were the main presentation in 19/40 and accounted 47.5%, while the rest 19/40 cases (47.5%) were completely asymptomatic. The main presenting symptoms of study population are summarized in table 3.

Table 3. *The main presenting symptoms of the study population.*

Presentation	Primary MR (n = 40)	
	No.	%
HF	19	47.5
T. C. P	2	5.0
Asymptomatic	19	47.5

HF: heart failure, TCP: typical chest pain

Mitral valve prolapse with and without MAD was the commonest cause of MR, it was detected in 20/40 cases and accounted 50 % of the causes. Rheumatic heart disease came in second place and was found in 8/40 cases, representing 20% of primary MR cases. Rest of causes were; flail posterior mitral leaflet 5/40 cases, degenerative mitral valve 5/40, each of them accounted 12.5%, perforation of anterior mitral leaflet by infective endocarditis was detected in one cases and single case showed flail anterior mitral leaflet, each represented 2.5%. Etiology of primary mitral regurgitation is illustrated in table 4.

Table 4. *Etiology of mitral regurgitation of study population.*

Etiology	Primary MR (n = 40)	
	No.	%
Degenerative	5	12.5
Flail AML	1	2.5
Flail PML	5	12.5
MAD, MVP	5	12.5
MVP	15	37.5
MV perforation	1	2.5
RHD	8	20.0

AML: anterior mitral; leaflet, PML: posterior mitral leaflet, MVP: mitral valve prolapse RHD: rheumatic heart disease

Based on 2D echocardiographic findings; it was noticed that the study population had mean end diastolic dimensions 5.55 ± 0.83 while mean end systolic dimensions were 3.60 ± 0.78. Biplane Simpson volumetric method showed mean end diastolic volume and end systolic volume 166.25 ± 33.71 and 61.58 ± 17.09 respectively. Mean stroke volume was 112.40 ± 17.69 and mean ejection fraction was 62.53 ± 7.34. The mean global longitudinal strain was -21.64±4.03.3D volumetric method showed mean EDV and mean ESV 180.48 ± 32.28 and 68.13 ± 26.59 respectively. Mean stroke volume was 112.40 ± 17.69 and mean ejection fraction was 62.52 ± 8.70. The mean global longitudinal strain was -23.50 ± 9.92. The results of 2D and 3D echo volumetric measurements are summarized in table 5.

Table 5. *2D and 3D echocardiographic volumetric measurement of the study population.*

	Echo parameters	Primary MR (n = 40)
EDD	2d	
	Min. – Max.	4.30 – 6.90
	Mean ± SD.	5.55 ± 0.83

	Echo parameters	Primary MR (n = 40)
ESD	2d	
	Min. – Max.	2.30 – 5.80
	Mean ± SD.	3.60 ± 0.78
EDV	2d	
	Min. – Max.	105.0 – 226.0
	Mean ± SD.	166.25 ± 33.71
	3d	
	Min. – Max.	128.0 – 254.0
	Mean ± SD.	180.48 ± 32.28
ESV	2d	
	Min. – Max.	39.0 – 105.0
	Mean ± SD.	61.58 ± 17.09
	3d	
	Min. – Max.	31.0 – 137.0
	Mean ± SD.	68.13 ± 26.59
	2d	
	Min. – Max.	54.0 – 155.0
	Mean ± SD.	104.68 ± 26.14
	3d	
	Min. – Max.	70.0 – 146.0
	Mean ± SD.	112.40 ± 17.69
EF	2d	
	Min. – Max.	46.0 – 77.0
	Mean ± SD.	62.53 ± 7.34
	3d	
	Min. – Max.	45.0 – 78.0
	Mean ± SD.	62.52 ± 8.70
GLS	2d	
	Min. – Max.	-29.20 – -11.10
	Mean ± SD.	-21.64 ± 4.03
	3d	
	Min. – Max.	-32.60 – 30.80
	Mean ± SD.	-23.50 ± 9.92

EDD: end diastolic dimension, ESD: end systolic dimension EDV: end diastolic volume, ESV: end systolic volume, SV: stroke volume, EF: ejection fraction, GLS: global longitudinal strain

By CMR, it was noticed that mean of EDV and ESV were 220.63 ± 53.15 and 87.60 ± 35.04 respectively. Mean stroke volume was 132.33 ± 25.52 and mean ejection fraction was 61.0 ± 7.90. The mean global longitudinal strain mean was 20.47 ± 3.58. Mean mitral regurgitant volume measured by CMR was 58.28 ± 19.87, while mean regurgitation fraction 43.80 ± 8.86. The results of CMR volumetric measurements are summarized in table 6.

Table 6. *MRI volumetric measurements and remolding parameters.*

MRI parameters	Primary MR (n = 40)
EDV	
Min. – Max.	135.0 – 395.0
Mean ± SD.	220.63 ± 53.15
ESV	
Min. – Max.	39.0 – 211.0
Mean ± SD.	87.60 ± 35.04
SV	
Min. – Max.	81.0 – 189.0
Mean ± SD.	132.33 ± 25.52
EF%	
Min. – Max.	41.0 – 78.0
Mean ± SD.	61.0 ± 7.90
AO	
Min. – Max.	43.0 – 104.0
Mean ± SD.	74.0 ± 14.13
RV	
Min. – Max.	29.0 – 113.0
Mean ± SD.	58.28 ± 19.87
RF%	
Min. – Max.	35.0 – 69.0
Mean ± SD.	43.80 ± 8.86
GLS	
Min. – Max.	-27.90 – -12.20
Mean ± SD.	-20.47 ± 3.58

EDV: end diastolic volume, ESV: end systolic volume, SV: stroke volume, EF: ejection fraction, GLS: global longitudinal strain: AO: aortic forward flow, RV: regurgitant volume, RF: regurgitant fraction

Majority of patients 26/40 showed no fibrosis at all, they accounted 65% of cases. While 11/40 cases showed non-specific pattern of fibrosis (i.e. insertion point fibrosis) and they represented 27.5% of cases. Only 3 out of 40 cases showed specific pattern (non-territorial focal sub-endocardial), they accounted 7.5% of the study population. Pattern of myocardial fibrosis detected by CMR is demonstrated in table 7.

Table 7. *Patterns of myocardial fibrosis detected by cardiac MRI.*

Fibrosis	Primary MR (n = 40)	
	No.	%
None	26	65.0
None specific	11	27.5
Specific	3	7.5

In primary mitral regurgitation patients, EDV was significantly larger when measured by CMR (mean EDV = 220.63) as compared to 3D echo (mean EDV =180.43) and 2D echo (mean EDV =166.25) which significantly underestimated EDV (all P <0.001). However, the volumetric measures of 2D end diastolic volume (EDV) were strongly correlated with CMR (gold standard for quantification of left ventricular volumes and function) and 3D echocardiography (r=0.88, p < 0.001). In the same way, ESV was significantly larger when measured by CMR (mean ESV = 87.6) as compared to 3D echo (mean ESV =68.13) and 2D echo (mean ESV =61.58) which significantly underestimated ESV (all P <0.001). However, 2D echo end systolic volume (ESV) measures were strongly correlated with CMR and 3D echo (r=0.7 and 0.63 respectively, P<0.001). 3D echo ESV measures were moderately correlated with CMR (r=0.5, P<0.001). 2D echo significantly underestimated stroke volume (mean SV =104.68) as compared to 3D echo (mean SV = 112.4) and CMR (mean SV =132.33), (all P <0.001). On the other side 2D echo measures of stroke volume were strongly correlated with 3D echo measures (r=0.8, p<0.001), however both echo modalities were moderately correlated with CMR (all r=0.5, P<0.001).

Regarding Ejection fraction, 2D echo measured mean EF =62.52 while 3D echo mean EF was 62.53 and CMR mean EF was 61.0 (p>0.05).2D echo measures of ejection fraction (EF) showed strong correlation with 3D echo measures (r=0.

8, p<0.001), however both modalities were weekly correlated with CMR (all r<0.5, P>0.05).

GLS values measured by 2D echo showed mean GLS =-21.46, while mean GLS measured by 3D echo was -23.5 and by CMR=-20.47. GLS values measured by 2D and CMR were moderately correlated (r=0.5, p<0.001), while 3D echo measure were weakly correlated with 2D echo and CMR measures (all r<0.5, p =0.012 and 0.064 respectively).

The correlation between the three imaging modalities measurements are summarized in table 8.

Table 8. *Correlation between three imaging modalities in measuring different parameters.*

	2d	3d	MRI	Coefficient		
				2d vs 3d	**2d vs MRI**	**3d vs MRI**
EDV	166.25	180.48	220.63	r=0.809 p<0.001*	r=0.717 p<0.001*	r=0.887 p<0.001*
ESV	61.58	68.13	87.60	r_s=0.727 p <0.001*	r_s=0.639 p <0.001*	r_s=0.517 p=0.001*
SV	104.68	112.40	132.33	r_s=0.886 p <0.001*	r_s=0.509 p=0.001*	r_s=0.558 p<0.001*
EF	62.53	62.52	61.0	r_s=0.863 p <0.001*	r_s=0.291 p=0.068	r_s=0.306 p=0.055
GLS	-21.64	-23.50	-20.47	r_s=0.393 p=0.012*	r_s=0.564 p<0.001*	r_s=0.296 p=0.064

EDV: end diastolic volume, ESV: end systolic volume, SV: stroke volume, EF: ejection fraction, GLS: global longitudinal strain, r=correlation coefficient.

5. Examples of the Study Cases

Case 1 (myxomatous mitral valve disease with flail posterior mitral leaflet):

62 years old male, not known to be diabetic or hypertensive or smoker presented with dyspnea on minimal exertion (NYHA class III). 2D echocardiography revealed flail posterior mitral leaflet with severe mitral regurgitation resulting into mild dilatation of LV, mildly impaired systolic function, EF=56% and mildly impaired GLS =-17.2%. 3D echo revealed the same data with EF=55%, GLS=-19.4%. CMR showed mildly dilated LV with mildly impaired LV systolic function, EF=57%, GLS=-17.7%. No fibrosis was detected at LGE.

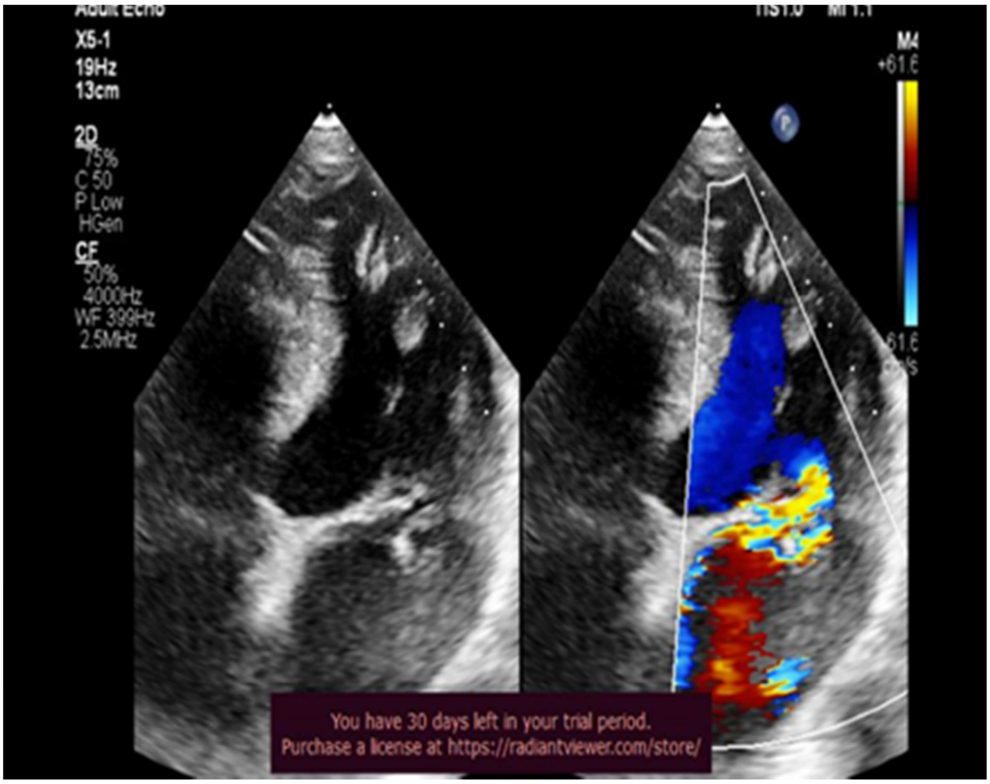

Figure 1. *2DTTE, 4 chamber view revealed myxomatous mitral valve disease with flail posterior mitral leaflet with severe MR, eccentric jet.*

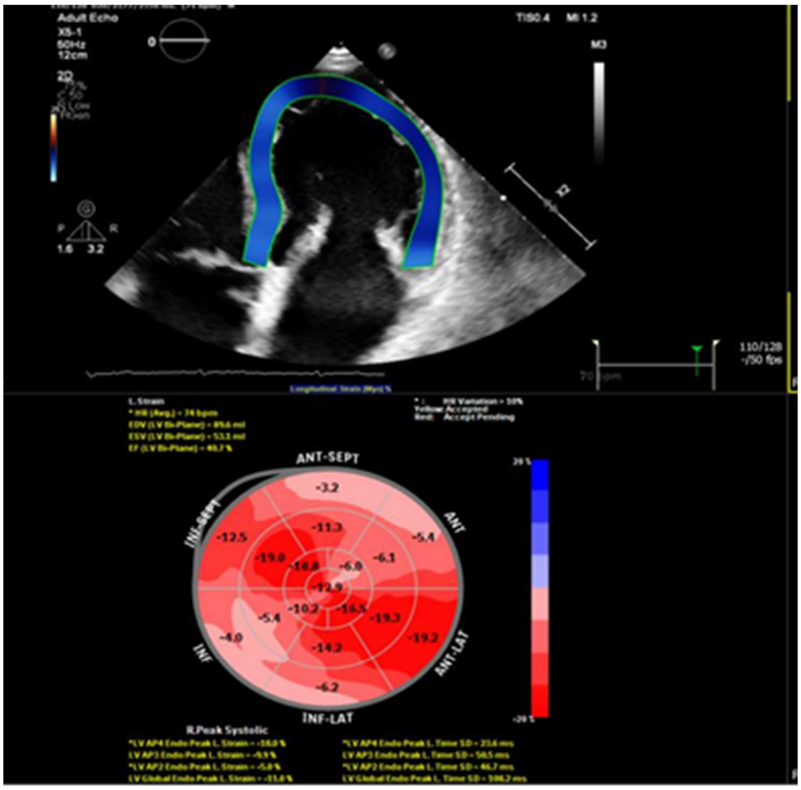

Figure 2. *2D speckle tracking of left ventricle revealed mildly impaired GLS =-17.2%.*

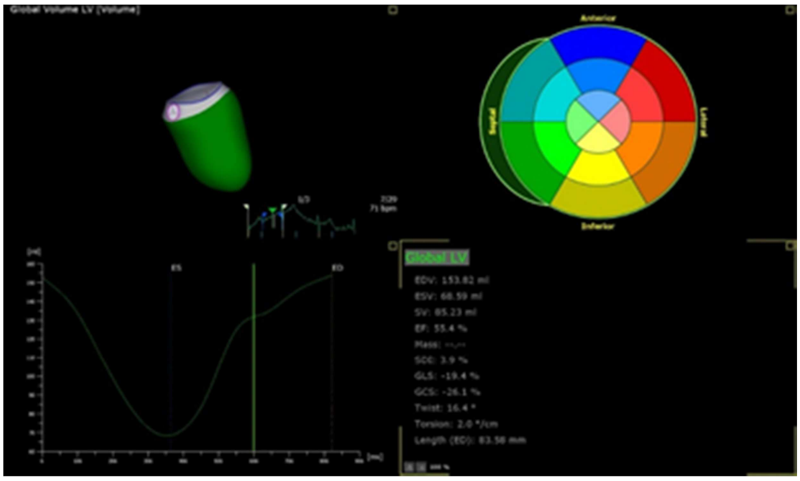

Figure 3. *3D TEE revealed mildly dilated LV volumes with GLS =-19.4%.*

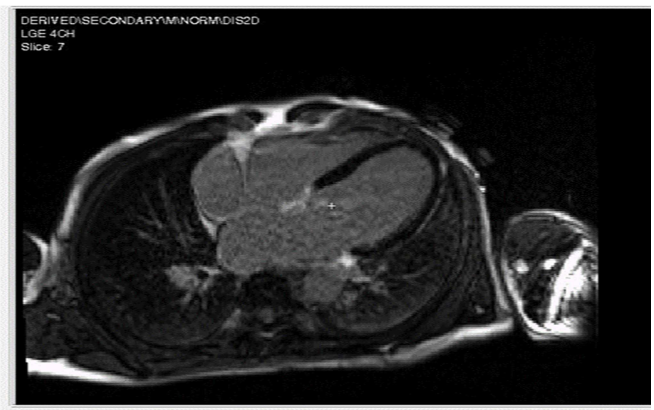

Figure 4. *CMR-LGE 4 chamber view revealed no fibrosis.*

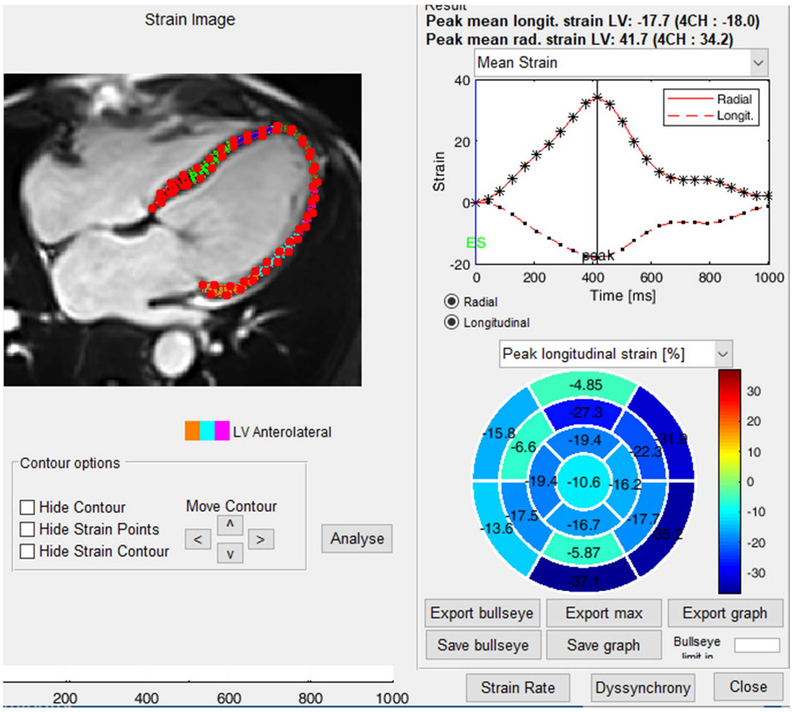

Figure 5. *Feature tracking of LV revealed mildly impaired GLS =-17.7% Primary mitral regurgitation.*

Case 2: mitral annulus disjunction (MAD) with mitral valve prolapse:

25 years old male, presented by palpation. 2D echocardiography revealed MAD with mitral valve prolapse causing moderate to severe mitral regurgitation. Average LV volume were noted with preserved systolic function, EF=62 % and GLS =-19.7%. 3D echo revealed average LV volumes with mildly impaired, EF=52% and mildly impaired GLS=-17.2%. CMR showed average LV with preserved LV systolic function, EF=64 % and impaired GLS=-13.4%. Non territorial subendocardial fibrosis was noted affecting mid segment of inferolateral and anterolateral walls.

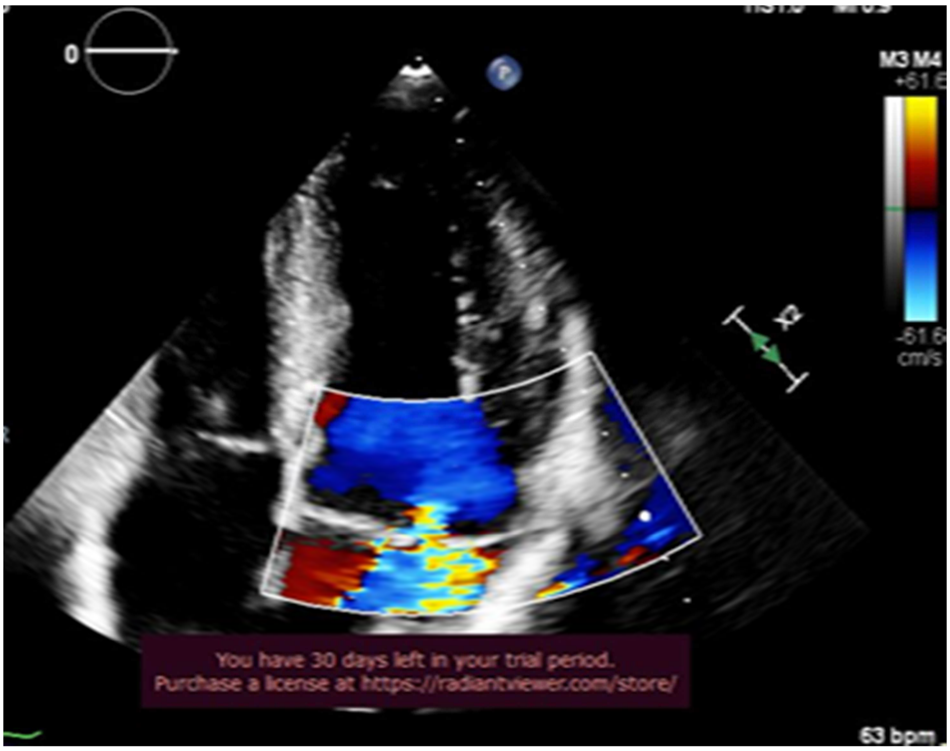

Figure 6. *2D TTE revealed bi-leaflet MVP causing moderate to severe MR.*

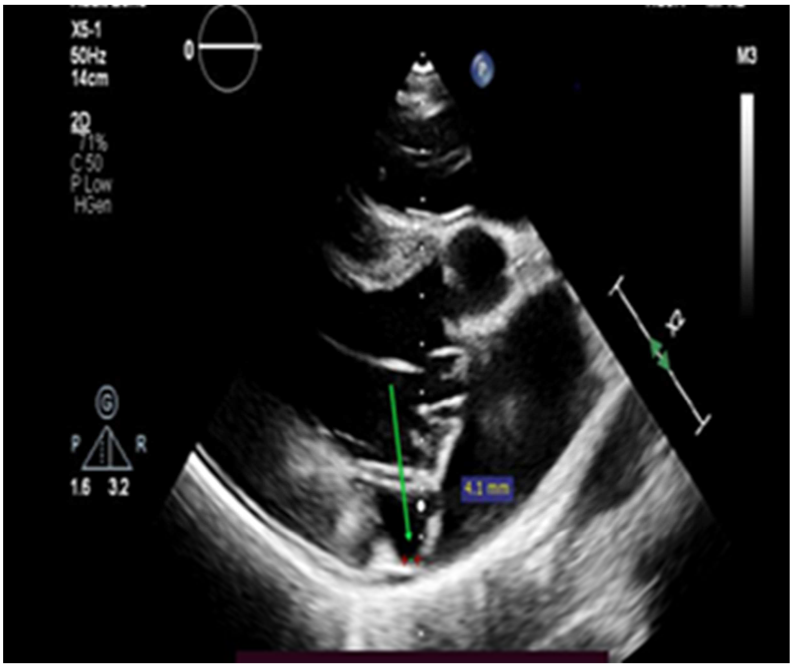

Figure 7. *2D TTE revealed MAD (systolic displacement distance =4.1 mm, arrow).*

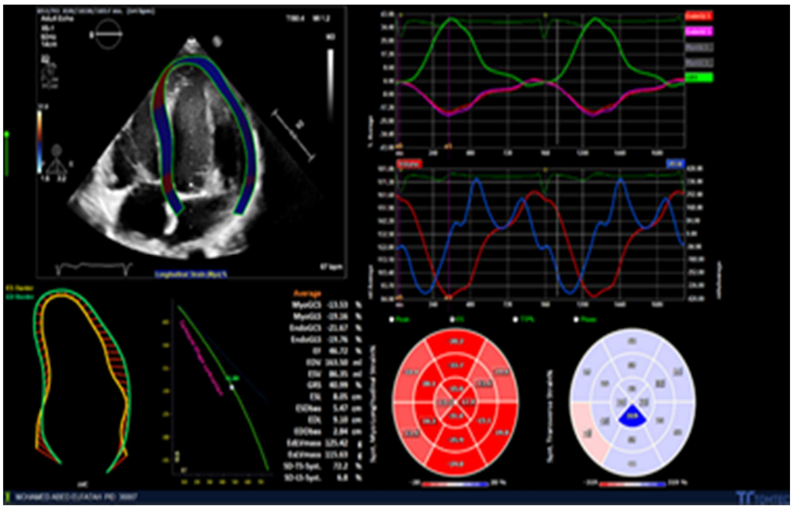

Figure 8. *2D speckle tracking of LV revealed GLS =-19.7%.*

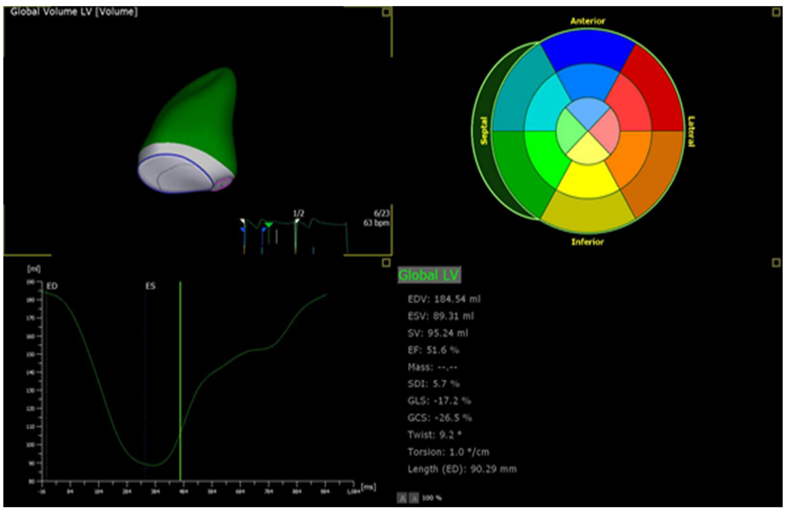

Figure 9. *3D TTE revealed average LV volumes with GLS =-17.2%.*

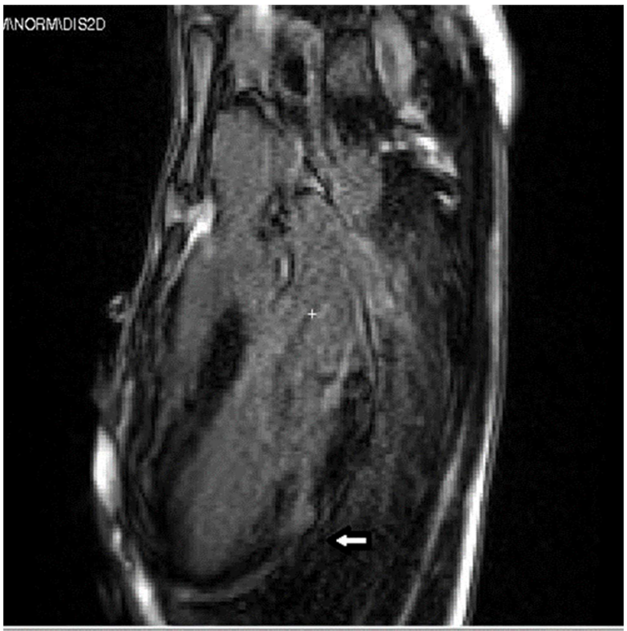

Figure 10. *CMR -LGE, 3 chamber view revealed non territorial sub-endocardial fibrosis of lateral wall (arrows).*

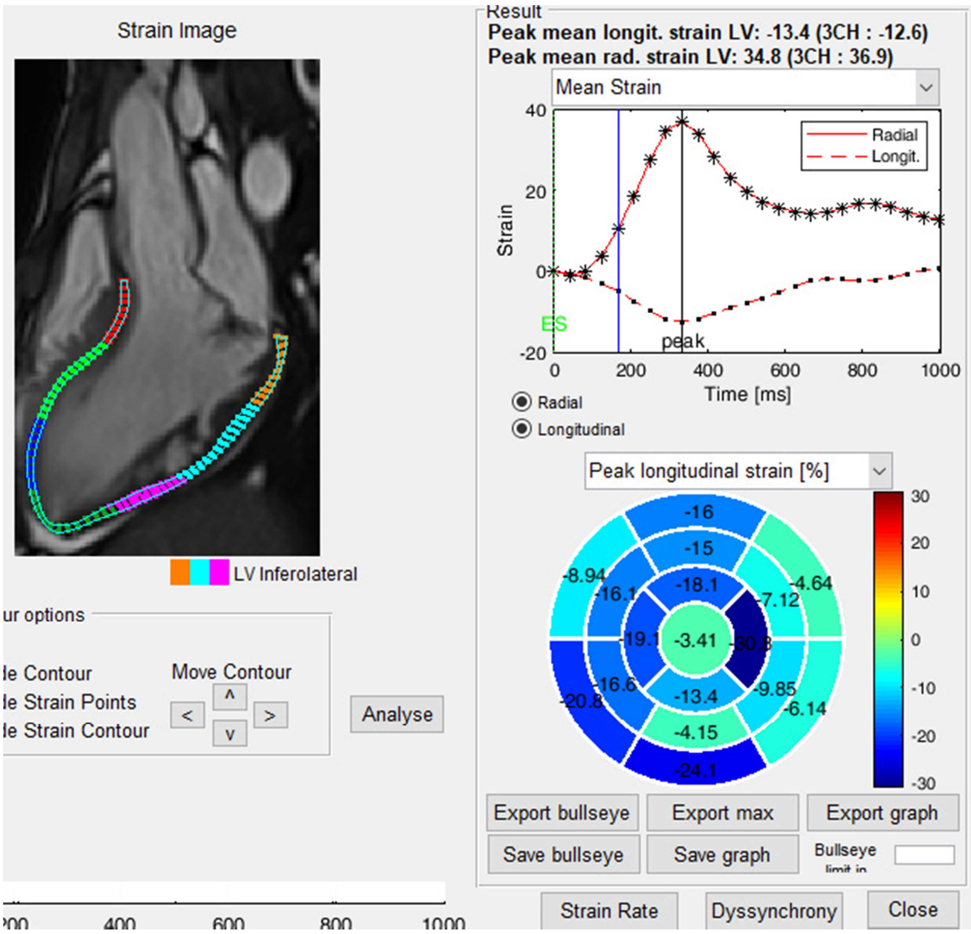

Figure 11. *Feature tracking revealed impaired GLS =-13.4%.*

6. Discussion

Mitral valve regurgitation is a major cause of morbidity and mortality across the world [13]. From a pathophysiology prospective, MR implicates a pure volume overload on the LV and subsequently decreases forward stroke volume. In early stages, eccentric LV hypertrophy compensate low forward stroke volume. However, eventually volume overload causes LV dysfunction [14]. The main issue in MR that the favorable loading conditions made by less resistant pathway (left atrium) often mask LV dysfunction. The second pathway aids in reducing the afterload, while the volume overload itself increases preload leading to supernormal ejection fraction [14]. Currently, the best markers of functional deterioration are the development of symptoms in addition to echocardiographic parameters of systolic failure (EF<60% and LVESD =4.5) [15]. Since comprehensive evaluation of LV is crucial in surgical management of MR, we used multimodality imaging tools in order to fully evaluate LV volumes and function, in addition to detection of early subclinical dysfunction and remolding using GLS.

Our study revealed that in primary mitral regurgitation, EDV was significantly larger when measured by CMR (mean EDV = 220.63) compared to 3D echo (mean EDV =180.43) and 2D echo (mean EDV =166.25) which significantly underestimated EDV (all P <0.001). In the same way, ESV was significantly larger when measured by CMR (mean ESV = 87.6) as compared to 3D echo (mean ESV =68.13) and 2D echo (mean ESV =61.58) which significantly underestimated ESV (all P <0.001). However, 2D echo end systolic volume (ESV) measures were strongly correlated with CMR and 3D echo (r=0.7 and 0.63 respectively, P<0.001).3D echo ESV measures were moderately correlated with CMR (r=0.5, P<0.001).

2D echo significantly underestimated stroke volume (mean SV =104.68) as compared to 3D echo (mean SV = 112.4) and CMR (mean SV =132.33), (all P <0.001). On the other side 2D echo measures of stroke volume were strongly correlated with 3D echo measures (r=0.8, P<0.001), however both echo modalities were moderately correlated with CMR (all r=0.5, P<0.001). Regarding Ejection fraction, 2D echo measured mean EF =62.52 while 3D echo mean EF was 62.53 and CMR mean EF was 61.0 (p>0.05).2D echo measures of ejection fraction (EF) showed strong correlation with 3D echo measures (r=0. 8, p<0.001), however both modalities were weekly correlated with CMR (all r<0.5, P>0.05). GLS values measured by 2D echo showed mean GLS =-21.46, while mean GLS measured by 3D echo was -23.5 and by CMR=-20.47. GLS values measured by 2D and CMR were moderately correlated (r=0.5, p<0.001), while 3D echo measure were weakly correlated with 2D echo and CMR measures (all r<0.5, p =0.012) and 0.064 respectively.

This results helped us in figuring out the utility of different used imaging modalities in assessment of MR impact on LV. The results came in concordance with many previous researches that were dedicated for assessment of LV volumes and function in primary MR.

Firstly, the underestimation of 2D volumetric measurements in comparison with 3D echo and gold standard CMR was expected and have been explained by poor image quality, apical foreshortening and geometrical assumptions [16]. This came in concordance to Levy. F et. al who described that 53 patients with at least mild primary isolated MR, who underwent comprehensive 3D transthoracic echo and CMR studies within 24 h. Compared with CMR, which is the gold standard for cardiac chamber quantification, LV volumes calculated from 3D TTE showed significantly smaller bias and lower intra- and interobserver variability than 2D TTE, EDV obtained by the different methods (CMR and 3D echo) bias = −12 ± 22 mL, with a significant correlation (r = 0.93; P < 0.0001). ESV obtained by the different methods showed the same pattern of underestimation by 3D echo with also small bias (bias = −6 ± 20 mL). LV ejection fraction was similar between CMR and 3D echo with significant correlation between the two measurements (r = 0.81; P < 0.0001). Despite the bias in the present study was larger than of Levy et. al (bias for EDV=40.15 ml and ESV =19.32 ml), a very strong correlation, (r=0.8) between 3D echocardiography and CMR was found in our study as he found out [17].

Also, Van De Heyning CM et. al who prospectively included 38 patients with at least moderate primary mitral regurgitation, a left ventricular ejection fraction ≥60% and a left ventricular end-systolic diameter ≤45 mm. All patients were scheduled for 2D TTE and CMR. LV dimensions and volumes. They found out that LV volumes were significantly underestimated by 2D TTE in patients with moderate to severe primary MR in comparison with CMR. It showed a mean difference of 28 ml regarding the LV EDV and 20 ml for LV-ESV. As regard LV EF in his study both Teichholz formula and modified Simpson’s method by 2D TTE seemed to overestimate LVEF in comparison to CMR [18].

Secondly, 20 % of our patients with severe MR and preserved LV function (LVEF ≥60%) by 2D TTE Simpson’s method had a mild decreased LVEF (50-59%) by CMR. These observations are in line with Van De Heyning CM et. al study in which 33% of his patients with severe MR and preserved LV function (LVEF ≥60%) by 2D TTE Simpson’s method had a mild decreased LVEF (50-59%) by CMR and suggested that more accurate assessment of LVEF by CMR might be indicated in asymptomatic severe MR to determine optimal timing for surgery [18] In patients who do not meet Class I recommendation for surgery, it remains questionable, whether an early surgery versus watchful waiting approach is superior. Recognizing that delaying surgery until the onset of ventricular dysfunction with left ventricular ejection fraction (LVEF) <60% or LVESD >40 mm, may be associated with an outcome penalty [5]. Hence, more sensitive and accurate imaging may provide more data on the optimum timing of surgery. In our study GLS has been used for detection of LV subclinical dysfunction.2021 ESC guidelines declared that despite GLS showing promise as a reliable marker for detection of subclinical LV dysfunction in Primary MR, further investigation is required to determine a predictive GLS cut-off that demonstrates both reproducibility and efficacy [15].

Another literature agrees there is a significant correlation between GLS and LVEF presented by Mascle S, et. al who illustrated that impaired preoperative GLS was negatively correlated with postoperative LVEF. She recruited 88 patients with severe degenerative MR who underwent rest echocardiography before and 6 ± 1 months after mitral valve surgery. This study demonstrated the additive and independent predictive value of preoperative GLS for predicting postoperative LV dysfunction [19]. Alashi A. Also confirmed the same results in his study 2016 that included 48 asymptomatic patients with ≥3+ mitral regurgitation and preserved LV EF who underwent mitral valve surgery [20]. A remaining question, which modality would be better for measurement of GLS in primary MR. Hans-Joachim Nesser, et. al, had nearly the same results of our study by obtaining GLS using 2D TTE, 3D TTE and CMR in 43 patients with a wide range of LV size and function. 2D-STE strongly correlated with CMR (r: 0.72–0.88), however, it underestimated LV volumes with relatively large biases (10–30 mL). The 3D-STE measurements showed higher correlation with CMR (0.87–0.92), and importantly smaller biases (1–16 mL) [21]. This showed a strong agreement with our study.

At last, our study revealed 35% of the patients had different pattern of patchy fibrosis. although the study didn't focus on the prognostic value of the fibrosis, it remains one of the most important factors in arrhythmic events sudden cardiac death [15]. Danai Kitkungvan, et. al enrolled 356 with primary MR patients (177 MVP and 179 non-MVP). LV fibrosis was more prevalent in the MVP group than the non-MVP group (36.7% vs. 6.7%). During follow-up, MVP patients with LV fibrosis had the highest event rate for arrhythmic event [22]. Another two previous studies with smaller sample sizes of patients with chronic, asymptomatic moderate, or severe primary MR have also illustrated high prevalence of LV fibrosis. The first one was made by Edwards NC, et. al who recruited 35 patients with asymptomatic moderate or severe primary degenerative MR. His patients were compared with age and sex controls and underwent cardiopulmonary exercise testing, echocardiography, and cardiac MRI. Longitudinal and circumferential myocardial deformation was reduced with MR in patients with EF (67% ± 10%). Myocardial extracellular volume was increased (0.32 ± 0.07 versus 0.25 ± 0.02, $P<0.01$) and was associated with increased indexed ESV ($r=0.62$, $P<0.01$), indexed left atrial volume ($r=0.41$, $P<0.05$). He concluded that LV indexed ESV and left atrial volume were independent predictors of extracellular volume ($r(2)=0.42$, $P<0.01$) [23]. The second study made by Van De Heyning CM, et al, who showed that out of his 39, 12 (31%) had late contrast uptake of the LV wall. LGE CMR showed an infarct pattern in three patients, a pattern of mid-wall fibrosis in seven patients and two patients had a combined pattern. Patients with fibrosis on CMR had significant higher LV diameters (LV end-systolic diameter 39 ± 4 vs. 34 ± 5 mm, P = 0·002; LV end-diastolic diameter 57 ± 5 vs. 50 ± 5 mm, P = 0·001) [24].

7. Summery and Conclusion

Mitral valve regurgitation (MR) is a major source of morbidity and death worldwide. Left ventricle is playing an important role in the prognosis and intervention decision in MR, therefor comprehensive evaluation of LV using different imaging modalities is recommended. We concluded that CMR followed by 3D echo were more sensitive in assessment of LV EDV and ESV and were strongly correlated, while 2D echo end systolic volume (ESV) measures were strongly correlated with CMR and 3D echo. we also illustrated the parameters for detection of myocardial fibrosis as GLS may be helpful in detection of sub-clinical LV dysfunction particularly in those with apparently normal LV ejection fraction.

8. Limitations of the Study

Small sample size may affect the results, lack of postoperative follow up, no definite cutoff for GLS value in primary MR and lack of quantitative measures of fibrosis detected by LGE –CMR.

Ethical Consideration

Informed consents were obtained from the study population with consideration of their privacy and confidentiality. The research was approved by Tanta university research ethical committee at 5/2019.

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