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Two- and Four-Dimensional Echocardiographic Assessment of Mitral Valve Area in Rheumatic Mitral Stenosis Patients

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ABSTRACT

Background: Mitral stenosis (MS) is one of the most prevalent valvular heart diseases with relevant morbidity and mortality. Echocardiography is the primary imaging modality for assessing the severity of MS. New transthoracic and transesophageal echo-Doppler modalities (TTE and TEE) have been developed to determine MS severity, which is crucial for diagnostic, therapeutic and prognostic purposes.

Objective: Assessment of mitral valve area (MVA) in rheumatic MS patients using different two- and four-dimensional echocardiography studies.

Patients and methods: The study included 50 adult patients with moderate to severe MS, whose mean age was 45.64±10.35 years. All study cases were evaluated by TTE followed by TEE using various echo-Doppler modalities. MVA by 3D-TEE full volume-multiplanar reconstruction (FV-MPR) was used as the reference method.

Results: There was a statistically highly significant positive correlation between MVA by 3D-TEE FV-MPR and mitral leaflet separation index (MLSI), MVA by (2D planimetry, 3D-TTE, 3D-TEE direct planimetry and mitral valve navigation (MVN)), p value= 0.001. It was found that MLSI value < 0.65 cm can detect severe MS with MVA ≤ 1 cm^2, with sensitivity 50% and specificity 85%. MVN could detect the severity of MS with 90% sensitivity and 80% specificity at a cut-off value ≤1.2 cm^2.

Conclusion: MS severity should be assessed by different echo-Doppler modalities, with incorporation of recent 3D echo technologies, especially the novel method (MVN); however, more research is required for further validation.

Keywords: MS, MVA, 3D TEE.

INTRODUCTION

Rheumatic MS is the most prevalent valvular heart disease (VHD) in developing nations and causes death and disability in low-income nations. It is more prevalent in females, usually occurring in the 3rd to 4th decades of life [1,2].

It is distinguished by mechanical blood flow obstruction, marked by distinctive features including thickening and reduced mobility of the chordal and leaflet tissues, which ultimately progress to commissural fusion and calcification [3].

The management of MS patients depends on accurate assessment of MS severity and precise measurement of MVA. Echocardiography is the primary diagnostic modality for assessing the severity of MS [4]. Gorlin's formula is a corner stone method for MVA measurement, but being an invasive method makes it an obsolete method to be used in our routine daily clinical practice. There are now a number of non-invasive methods for evaluating MS, such as planimetry, pressure half-time (PHT), transmitral pressure gradient (PG), continuity equation, proximal isovelocity surface area (PISA) and MLSI. Nonetheless, these methods have their own potential drawbacks [5].

Because it generates high-quality images with a better resolution when it crosses the MV, the real-time 3D-TEE (RT-3D TEE) has proven to be a useful tool in evaluating VHD and may be suitable for planimetric MVA assessment and MVN [4].

Because 3D-TEE FV-MPR planimetry has the best agreement with the Gorlin's formula when compared to other conventional 2D and Doppler methods, it is the gold standard method for assessing MVA in rheumatic MS patients using two- and four-dimensional echocardiography studies [4].

This study aims to assess of mitral valve area (MVA) in rheumatic MS patients using different two- and four-dimensional echocardiography studies.

PATIENTS AND METHODS

This study included 50 adult patients who were recruited from those referred to echocardiography lab of Al-Zahraa University Hospital at the period from September 2023 to October 2024. The study included moderate to severe MS patients.

Exclusion Criteria:

- Patients during rheumatic activity.
- Patients with contraindications for TEE.
- Patients with previous history of balloon or surgical mitral valvuloplasty.
- Patients with severe mitral regurgitation.
- MS of non-rheumatic etiology.

Methodology:

Thorough medical history and physical examination, 12-lead surface ECG, laboratory investigation (e.g., INR) before TEE in patients on warfarin, and TTE followed by TEE studies were performed on each patient.

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Transthoracic echocardiographic examination:

All patients had comprehensive transthoracic echo-Doppler examination (TTE) in the standard views using VIVID-E95 GE ultrasound, Horton, Norway (N95) using (multi frequency M5Sc- XD Clear (Sector) 1.4 - 4.6 MHz for 2D) and (GE 4V-D Probe (Volume) 1.5 - 4.0 MHz) phased-array probes. Examinations were done with activation of tissue Doppler imaging (TDI) function, 4D imaging with simultaneous ECG physio signal displayed with all recorded echo images and loops. All imaging and loops of at least three cardiac cycles were recorded for patients in sinus rhythm and 5 cycles for AF patients. All acquisitions were recorded and digitally stored as echo images and loops for subsequent off-line analysis using EchoPAC, software version (113).

MS severity was assessed by 2D-TTE (including MLSI and MVA by planimetry), Doppler echocardiography (including PHT and trans-mitral PG), 3D-TTE, 2D-TEE and 3D-TEE (including assessment of MVA by 3D-TEE FV-MPR, direct planimetry and MVN). Wilkins score was used to assess the patient's suitability for percutaneous mitral commissurotomy (PMC).

Mitral Leaflet Separation Index (MLSI):

The MLSI was calculated by averaging the distance between the inner edges of both mitral leaflet tips in diastole in both apical 4-chamber and parasternal long axis (PLAX) views [6].

MVA by 2D planimetry:

The parasternal short axis view (PSXV) was carefully scanned from base to apex at the level of the MV in order to acquire the frame with the smallest aperture. The zoomed-in image was obtained and the gain optimization was modified. At the start of the p wave ECG gated loop, the inner rim of the orifice, including any opening commissures, was then drawn in mid-diastole [7].

3D-TTE Planimetry:

The MV was focused from the parasternal or apical window using the 3D-TTE zoom mode acquisition after the gain, compression settings, and time-gain compensation were adjusted. The MV orifice's MPR indicated the plane at which it was the smallest. This plane was then carefully moved in three dimensions in minuscule depth and spatial angulation increments [8].

Transesophageal echocardiographic examination:

All patients of the study group were examined by TEE under conscious sedation, using the same machine, with 6 VT-D probe (3-8 MHz) with ECG physio signal recorded. 2D-TEE study was done (for assessment of LAA flow velocities and presence of SEC or thrombi in LA and LAA), followed by 4D-TEE study for assessment of MVA.

Measurement of MVA by MPR:

The maximal diastolic opening of the MV orifice was detected in order to make the MPR measurement of the MVA. A 3rd cropping plane at the level of the MV orifice was then observed after two orthogonal planes were found using MPR to cross the MV's tips [8]. Planimetry was then used to measure MVA **(Fig. 1)**.

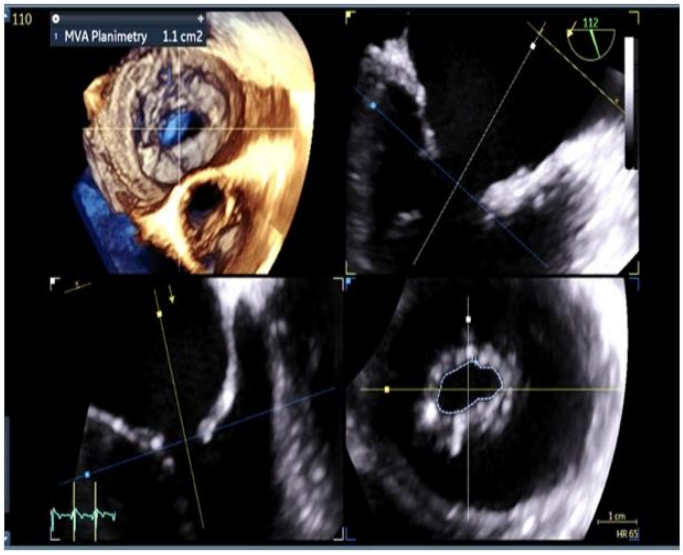

Fig. (1): Measurement of MVA by 3D-TEE MPR method.

Measurement of MVA by 3D direct planimetry:

MVA was ascertained using an en-face image of the MV. Initially, the frame employed for the MPR method—the maximum early diastolic opening of the MV—was chosen. To make sure the MV orifice was parallel to the screen at the highest MVA, the 3D picture was then manually rotated. After that, MVA was manually located [4].

Measurement of MVA by MVN method:

The 4D was acquired on MV in the mid-esophageal long axis view at (110–140 degrees), and the zoom box was oriented to include the posterior mitral annulus and the aortic valve. The box was adjusted to fit both the medial and lateral mitral annulus. Both planes' depths were modified to account for the aortic and mitral valves. The MV annulus hinge points were best visualized by adjusting three orthogonal planes using the MVN tool. Anterolateral, posteromedial, anterior, and posterior segmentation points were positioned along the mitral valve annulus. Then, two additional points were positioned over the distal aortic annulus and the tip of the anterior leaflet. The software then automatically traced the mitral leaflets and mitral annulus. The diastolic MVA was then defined by manually tracing the tips of both leaflets [5]. The software reports the MV orifice area as the "orifice area" **(Fig. 2).**

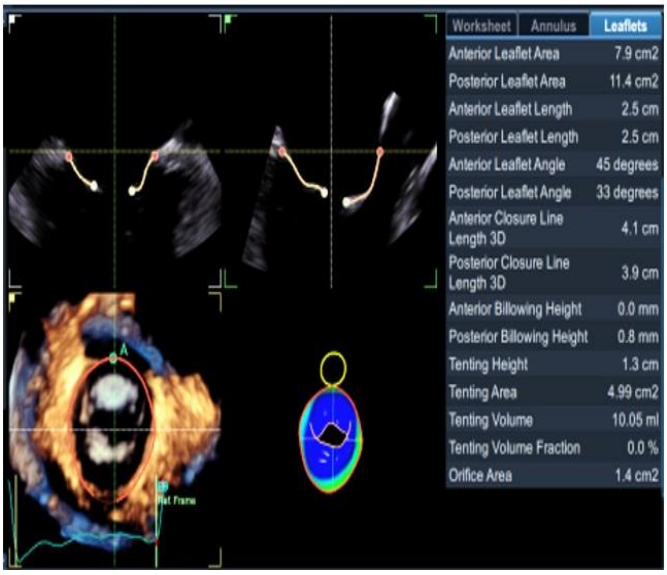

Fig. (2): Measurement of MVA by MVN method.

Ethical Approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Al-Azhar University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical analysis

SPSS statistics for Windows software (version 26) was used to conduct the statistical analysis. Data were gathered, tallied, and subjected to statistical analysis. Numerical data were reported as mean± SD and categorical data as frequency and percentages. Paired t-test was used to compare continuous variables. The Shapiro-Wilk and Kolmogorov-Smirnov tests were employed to evaluate the normality distributions of the variables that were measured. A positive or negative link between two variables was tested using Pearson's correlation test, which produced the correlation coefficient (r). The optimal cut-off value with detection of sensitivity and specificity at this cut-off value, as well as the overall predictivity of the parameter, were established through the use of receiver operating characteristic (ROC) curve analysis. P values below 0.01 were considered very significant, while P values below 0.05 were considered statistically significant.

RESULTS

We divided the patients into 2 groups according to MVA by 3D-TEE FV-MPR: Group 1: those with MVA ≤1 cm^2 and Group II: those with MVA >1 cm^2. Group 1 consisted of 30 patients while Group II consisted of 20 patients. Dyspnea was the major clinical presentation among our study patients, with increased NYHA functional class among severe MS patients. AF was present in 36%, while the remainder had sinus rhythm. Baseline demographic data, anthropometric measurements and symptoms are shown in **(Table 1).**

Table (1): Sociodemographic data

Baseline data	**N=50**
Demographic data	
Age (years)	
Mean±SD	45.64±10.35
Range	26-68
Sex	
Female	41 (82.0%)
Male	9 (18.0%)
Anthropometric measurements	
Weight (kg)	
Mean±SD	78.60±15.40
Range	50-118
Height (cm)	
Mean±SD	162.96±8.00
Range	149-182
BSA (m^2)	
Mean±SD	1.84±0.20
Range	1.4-2.3
BMI (kg/m^2)	
Mean±SD	29.39±5.69
Range	20.8-48.6
Symptoms	
NYHA class	
II	24 (48.0%)
III	26 (52.0%)
Orthopnea	4 (8.0%)
PND	6 (12.0%)
LL edema	20 (40.0%)
History of cerebrovascular stroke	4 (8.0%)
Palpitation	26 (52.0%)

BSA: Body surface area. BMI: Body mass index. NYHA: Newyork Heart Association. PND: Paroxysmal nocturnal dyspnea. LL: Lower limb

Considering assessment of MVA by 3D-TEE FV-MPR as the reference standard, there was a statistically significant positive correlation between MVA by 3D-TEE FV-MPR with MLSI, MVA by 2D planimetry, MVA by PHT, MVA by 3D-TTE, MVA by 3D-TEE direct planimetry and MVA by MVN method, with p and r value as shown in (**Table 2)**. There was a statistically significant negative correlation between MVA with mean PG and Wilkins score.

Table (2): Correlation between different methods for assessment of MS with MVA by 3D-TEE FV-MPR.

Different methods for assessment of MS N=50	MVA by 3D-TEE FV-MPR	
	r-value	p-value
By 2D-TTE		
MLSI	0.715	0.001
MVA by 2D planimetry	0.957	0.001
Wilkins score	-0.581	0.001
By colored Doppler		
Mean PG	-0.415	0.003
PHT	0.740	0.001
MVA by 3D-TTE	0.956	0.001
By 3D-TEE		
MVA by direct planimetry	0.957	0.001
MVA by MVN	0.962	0.001

We found that there was over estimation of MVA when assessed by 2D planimetry and MVN with mean difference 0.17±0.07 and 0.18±0.07 cm^2 respectively, while there was no statistically significant difference in measurement of MVA by PHT, MVA by 3D-TTE and MVA by 3D-TEE direct planimetry **(Table 3).**

Table (3): Comparison between MVA by 3D-TEE FV-MPR and MVA obtained by different TTE and TEE methods.

MVA by 3D-TEE FV-MPR as a gold standard (1.01±0.25 cm^2)	Mean± SD	Paired Sample t-test		
		Mean of overestimation	t-test	p-value
MVA by 2D planimetry (cm^2)	1.18±0.25	0.17±0.07	2.749	0.014
MVA by PHT (cm^2)	1.07±0.23	0.06±0.02	1.575	0.294
MVA by 3D-TTE (cm^2)	1.01±0.24	0.002±0.0001	0.198	0.844
MVA by 3D-TEE direct planimetry (cm^2)	1.03±0.26	0.02±0.01	1.871	0.067
MVA by MVN (cm^2)	1.19±0.25	0.18±0.07	2.938	0.003

ROC curve showed a cut-off point of ≤1.2 cm^2 could differentiate severity of MS with sensitivity of 90% and specificity of 80% **(table 4).**

Also; MLSI with a cut-off value <0.65 for detection of severe MS had a specificity of 85% and sensitivity 50% **(Table 4).**

Table (4): Sensitivity, specificity and predictive values of MLSI and MVN.

	Cut-off	Sensitivity	Specificity	PPV	NPV	AUC (C.I.95%	Agreement	p-value
MLSI	**<0.65**	50%	85%	78.6%	47.2%	0.702 (0.56-0.82)	0.675	0.008
MVN	**≤1.2**	90.0%	80.0%	87.1%	84.2%	0.948	0.850	0.001

DISCUSSION

In developing nations with greater rates of morbidity and mortality, rheumatic MS is thought to be the most common VHD [4]. The first-line imaging technique for assessing the severity of MS is echocardiography [9]. A number of echocardiographic techniques have been developed for evaluating MVAs. When compared to other traditional 2D and Doppler approaches, planimetry employing 3D-TEE FV-MPR has the best agreement with the Gorlin's formula [10]. In order to compare MVA obtained by several echo-Doppler modalities—including 2D planimetry, PHT, and 3D direct planimetry by TTE and TEE and MVN—with 3D-TEE FV-MPR planimetry as the gold standard, this study was conducted.

The most popular technique in our regular clinical practice is the 2D planimetric measurement of the MVA by TTE. Therefore, using the 3D-TEE FV-MPR approach to examine the degree of agreement between it and MVA was crucial. In the current investigation, we discovered that, in comparison to a more precise 3D-TEE FV-MPR planimetric approach, the conventional 2D planimetric assessment of the MVA by TTE overestimated the size of the valve orifice by 0.17±0.07 cm^2. These findings are consistent with those of **Fard *et al.*** [8], who discovered that the 2D-TTE planimetry significantly overestimated MVA by 0.2 cm^2 when compared to the 3D-TEE FV-MPR approach.

Another study by **Min *et al.*** [11] compared the MVA produced by 2D TTE planimetry with 3D TEE FV-MPR and found that, although there was great agreement between the two approaches, the MVA obtained by 2D TTE planimetry was overestimated by 0.19 ± 0.02 cm^2. This could be explained by the fact that MS patients often have significant calcifications and undergo changes in MV geometry and remodeling, which makes it challenging to determine the exact size of the MVA using 2D echocardiography.

MLS was first proposed by **Fisher *et al.*** [12] in 1979. It is easy and reliable specially in controverse between existing about severity of MS [8]. Using the 3D-TEE FV-MPR planimetric approach, our study showed a substantial positive association between MLSI and MVA. It was discovered that severe MS with MVA ≤ 1 cm^2 can be estimated with a sensitivity of 50% and specificity of 85% using an MLSI value of less than 0.65 cm. This result is consistent with the study of **Artha *et al.*** [13], which demonstrated that severe MS with MVA ≤ 1 cm^2 can be estimated with a sensitivity of 85% and specificity of 82.4% using an MLSI value less than 0.69 cm. Moreover, another study done by **Bigdelu *et al.*** [10] who reported that MLSI value ≤ 8.6 mm can detect severe MS with 100% sensitivity and 76% specificity. The discrepancies between our results and the previously mentioned studies may be explained by relatively small number of patients and the study design where we included patients with severe calcification who have been excluded from the other studies.

Excellent visualization of the MV orifice and leaflets in rheumatic MS is made possible by 3D echocardiography, which also offers crucial supplementary data to 2D technology, particularly now that it is available in TTE. The degree of agreement between the MVA produced by the 3D-TTE reconstruction method and that produced by the 3D-TEE FV-MPR was therefore examined in our work. MVA by 3D-TTE and 3D-TEE FV-MPR showed a statistically significant positive connection in our investigation. Although there weren't many researches comparing MVA measurements made using the two approaches, **Fard *et al.*** [8] obtained similar results, demonstrating a good agreement between 3D-TTE and 3D-TEE in planimetric measurement of MVA.

In our investigation, there was a high degree of agreement between the MVA determined by 3D-TEE direct planimetry and that determined by 3D-TEE FV-MPR. This is in line with research by **Zhong *et al.*** [4], who discovered that the MVA values acquired using the MPR approach and 3D direct planimetry had great agreement. Another study by **Tabrizi *et al.*** [14] found that while 3D-direct planimetry and 3D-MPR planimetry have a good agreement for MVA less than 1.5 cm^2, 3D-direct planimetry tends to underestimate the area more than 3D-MPR, particularly at MVA greater than 1.5 cm^2. It appears that 3D-direct measurement of MVA is hampered by the saddle form of MV.

Because the commissures are not taken into account by the two- or 3D planimetry of the MV orifice, if they are not totally fused, the MVA will be underestimated. It has not been thoroughly researched up to this point. So, we aimed by our study to validate the MVN method as a reliable method for measurement of MVA in MS patients. In the current study, we found that there was a statistically significant positive correlation between MVA by MVN method and 3D-TEE FV-MPR with overestimation of the area by MVN method. This supports the findings of **Elsayed *et al.*** [5], who concluded that the MVN approach is the most accurate way to measure MVA that accounts for MV commissions. Following the validation of MVN against the Gorlin method for measuring MVA, these results demonstrated that there was no discernible difference between the two approaches and that there was a significant linear correlation between MVN-derived MVA and Gorlin-derived MVA.

Moreover, when we use ROC curve, it was found that MVN could detect the severity of MS at a cut-off value ≤1.2 cm^2 with 90% sensitivity and 80% specificity. On the other hand, we found that there was an overestimation of MVA by MVN in comparison to MVA by 3D-TEE FV-MPR by 0.18±0.07cm^2. These results are concordant with **Gök *et al.*** [15] reported a significant correlation by 3D-TEE FV-MPR. This may be explained by taking MV commissures into account during measurement of MVA by the navigation method.

CONCLUSION

Echocardiography with its different modalities, especially recent 3D echo-Doppler modalities, is the primary diagnostic tool for the assessment of MS and excellent visualization of the MV orifice. MLSI can be used as a surrogate measurement, with a remarkable ability to discriminate severity of MS, to be confirmed by other echo-Doppler modalities. 3D-TEE should be considered when the determination of the MVA with 2D echocardiography is difficult, especially the novel method (MVN); however, more research is required for further validation.

LIMITATION

There was no gold standard to compare the accuracy of MVA measurements against. Gorlin's formula was considered the gold standard method of measuring MVA but it is invasive procedure and has several drawbacks and technical restrictions. So we considered 3D-TEE FV-MPR planimetric method the gold standard method as it is widely used as the replacement for the gold standard method for measuring MVA. Small sample size is considered also one of the drawbacks of this study.

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