RESEARCH ARTICLE

Mitral leaflet separation index correlation with mitral stenosis severity, a reliable easy 2-d echocardiography technique

Saba Hussain[1], Fateh Ali Tipoo Sultan[2], Mariam Naz[3], Sumyia Gurmani[4], Shazia Rasheed[5]

Abstract

Objective: To evaluate accuracy of mitral leaflet separation index for the determination of mitral stenosis severity in patients with rheumatic mitral stenosis.

Method: The prospective, cross-sectional study was conducted at the National Institute of Cardiovascular Diseases, Karachi, from March 2021 to February 2022, and comprised patients with rheumatic mitral stenosis detected on echocardiography. The best end-diastole parasternal long axis and apical four-chamber views were acquired and Mitral leaflet separation was measured as the distance between the inner edges of the tip of mitral leaflets. Pearson correlation coefficient was computed for mitral leaflet separation index and mitral valve area. Receiver operating characteristic curve was used to determine the cut-off value of the mitral leaflet separation indexto categorise mitral stenosis. Data was analysed using SPSS 19.

Results: Of the 277 patients, 205(74%) were females and 72(26%) were males. The overall mean age was 39.93±11.22 years. The mean mitral leaflet separation index value was 7.65±2.23. The correlation was significant and strong between mitral leaflet separation index and mitral valve area on planimetry ($p<0.001$), and was significant and moderate when measured by pressure half-time ($p< 0.001$). Mitral leaflet separation index cut-off value <8.625mm and <8.25mmcould predict severe mitral stenosis with 84% and 86.3% sensitivity and 84.6% and 78.3% specificity on planimetry and pressure half-time, respectively.

Conclusion: The mitral leaflet separation index was found to be an independent, reliable and simple measure for assessing mitral stenosis severity.

Key Words: Echocardiography, Mitral stenosis, Mitral leaflet separation index, Pressure half-time, Planimetry.

(JPMA 74: 243; 2024) **DOI: https://doi.org/10.47391/JPMA.8269**

Introduction

Around 33 million individuals suffer from rheumatic heart disease globally, accounting for 275,000 annual fatalities[1] The situation is even worse in underdeveloped countries, like Pakistan.[2] Mitral valve (MV) is the most frequent valve to be affected in rheumatic carditis, with mitral stenosis (MS) being the most frequent presentation.[2,3] Accurate diagnoses of MV stenosis and its severity are essential for treatment and prognosis assessment. The current gold standard for MS diagnosis and severity assessment is two-dimensional (2D) Doppler echocardiography.[4] Standard methods used in echocardiogram to determine MV area (MVA) are planimetry, proximal is velocity surface area, pressure half-time (PHT) and continuity equation.[5] Test complexity, operator, and haemodynamic dependency are, however, the Achilles heel of these parameters that hinder an accurate determination of MVA.[5] To overcome this limitation, a few studies in small groups of patients have been done on a simple novel technique of calculating the mitral leaflet separation index (MLSI) to determine MS severity.[6-10] Severe MS can be predicted with 90-92% sensitivity and 82-92% specificity when the mitral leaflet separation is <7.8mm.[6-10]

The current study was planned to evaluate the accuracy of MLSI in the determination of MS severity in patients with rheumatic MS, and to assess the reliability of MLSI in different concomitant conditions, like atrial fibrillation (AFib) and mitral regurgitation (MR).

Patients and Methods

The prospective, cross-sectional study was conducted at the National Institute of Cardiovascular Diseases, Karachi, from March 2021 to February 2022, and comprised patients with rheumatic mitral stenosis detected on echocardiography. After approval from the institutional ethics review committee, the sample size was calculated using the World Health Organisation (WHO) calculator with expected sensitivity 90%, specificity 82%, and margin of error 5%.[8,11] The sample was raised using consecutive sampling technique. Those included were patients of either gender aged >18 years who were referred for echocardiography because of multiple

[1,3-5]National Institute of Cardiovascular Disease, Karachi, Pakistan, [2]Aga Khan University Hospital, Karachi, Pakistan.

Correspondence: Saba Hussain. Email: sabahussain23@gmail.com

ORCID ID. 0000-0002-9187-2124

Submission complete: 27-11-2022 **Review began**: 16-01-2023

Acceptance: 14-10-2023 **Review end:** 30-08-2023

reasons, including a wide range of symptoms, murmur, follow-ups, post-percutaneous transvenous mitral commissurotomy (PTMC) check-up, and arrhythmia evaluation. Those identified as having MS of rheumatic aetiology were prospectively included. Those excluded were patients having check-up within 72 hours of PTMC, with suboptimal images or with significant calcium on MV that prevented accurate MS assessment.

After taking informed consent from all the participants, scans were done by echocardiography board-certified level 3-trained consultant cardiologists for the evaluation of MS and its severity, using a 2.5MHz multifrequency phase array transducer and Aplio-i600 Toshiba (made in Japan). The best end-diastole parasternal long axis and apical four-chamber views were acquired and MLS was measured as the distance between the inner edges of the tip of mitral leaflets. The two values were averaged to get the MLSI value.

Concomitant MR and AFib were noted. Five values were taken and averaged in cases of AFib. Echocardiographic findings along with baseline data of the patients, including height, weight and past history of PTMC, were collected on a predesigned proforma. MV areas of <1.5cm2 and >1.6cm2, measured with planimetry or PHT, were categorised as severe and progressive MS, respectively.

Data was analysed using SPSS 19. Frequencies and percentages were used to express qualitative data, while quantitative/continuous variables were expressed using mean ± standard deviation. Pearson correlation coefficient was calculated for MLSI and MVA measured by the two conventional methods. For various MV areas, the MLSI discriminating values were calculated using a receiver operating characteristic (ROC) curve. A subgroup analysis was performed on the basis of rhythm and MR.P<0.05 was taken as significant.

Results

Of the 277 patients, 205(74%) were females and 72(26%) were males. The overall mean age was 39.93±11.22 years. The mean MLSI value was 7.65±2.23 (Table 1).

The correlation was significant and strong between MLSI and MVA on planimetry (p<0.001), and was significant and moderate when measured by PHT (p< 0.001). The relation was seen maintained in the presence AFib and significant moderate to severe MR (Table 2, Figures1-2).

MLSI cut-off value <8.625mm and <8.250mm

Table-1: Baseline and echocardiographic parameters.

Participant Characteristics	Total Number
Total (N)	277
Gender	
Male	26% (72)
Female	74% (205)
Age (years)	39.93 ± 11.22
Height (cm)	157.9 ± 12.75
Weight (kg)	59.72 ± 13.87
BSA (m2)	1.61 ± 0.21
Echo Parameters	
MVA Planimetry (cm2)	1.15 ± 0.42
Progressive (>1.5)	18.1% (50)
Severe (≤1.5)	81.9% (227)
MVA PHT (cm2)	1.17 ± 0.41
Progressive (>1.5)	18.4% (51)
Severe (≤1.5)	81.6% (226)
MLS PLAX (mm)	7.63 ± 2.29
MLS A4C (mm)	7.66 ± 2.46
MLSI (mm)	7.65 ± 2.23
Wilkins Score	7.52 ± 1.02
LA dimension AP (mm)	45.33 ± 8.03
LAVI ml/m2	79.41 ± 39.71
EF (%)	51.8 ± 11.49
Mitral regurgitation	
None	10.8% (30)
Mild	56.3% (156)
Moderate	20.6% (57)
Severe	12.3% (34)
Atrial Fibrillation	
No	51.6% (143)
Yes	48.4% (134)

BSA: Body surface area, MVA: Mitral valve area, PHT: Pressure half time, MLS: Mitral leaflet separation, PLAX: Parasternal long axis, A4C: Apical four chamber, MLSI: Mitral leaflet separation index, LA dimension AP: Left atrium dimension anterio-posterior, LAVI: Left atrial volume index, EF: Ejection fraction.

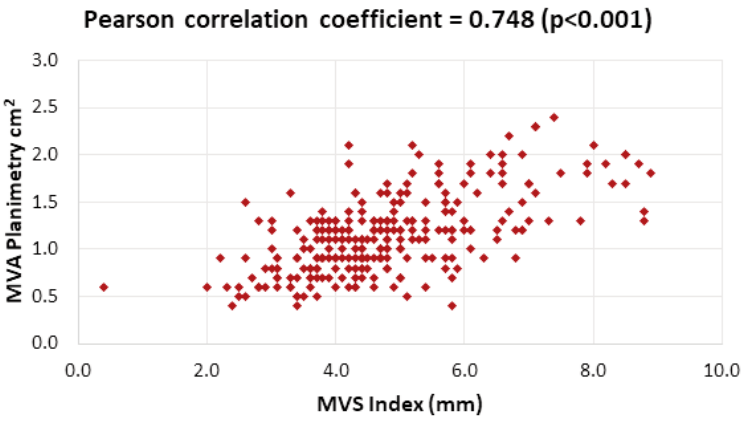

Figure-1: Scatter plot showing significant strong correlation between mitral valve area (MVA) and mitral leaflet separation index (MLS)) measured with planimetry.

Table-2: Pearson correlation between mitral leaflet separation index (MLSI) and mitral valve area (MVA) measured with conventional methods.

	Total Number	MVA Planimetry	MVA PHT
Overall	277	0.748(p<0.001)	0.656(p<0.001)
In the presence of atrial fibrillation	134	0.750 (p<0.001)	0.614(p<0.001)
In the presence of significant mitral regurgitation	91	0.787 (p<0.001)	0.706 (p<0.001)

PHT: Pressure half time.

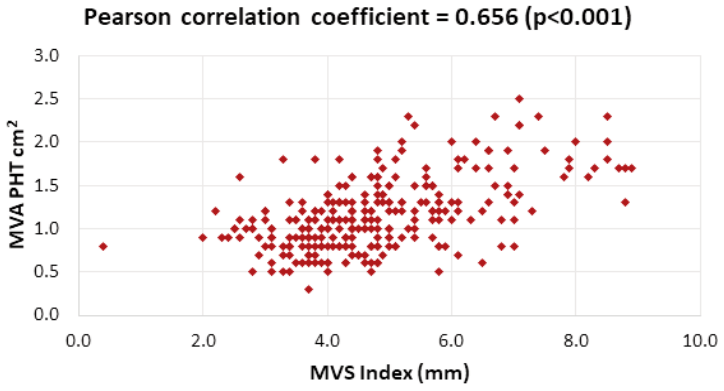

Figure-2: Scatter plot showing significant moderate correlation between mitral valve area (MVA) and mitral leaflet separation index (MLSI) measured with pressure half time (PHT).

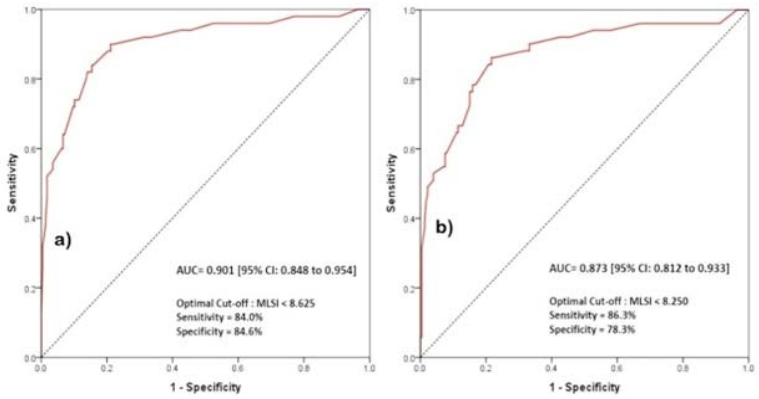

Figure-3: Receiver operating characteristic (ROC) analysis of mitral leaflet separation index (MLSI) for severe mitral stenosis (MS) measured with (a) planimetry and (b) pressure half time (PHT).

could predict severe MS with 84% and 86.3% sensitivity and 84.6% and 78.3% specificity on planimetry and PHT, respectively (Figure 3).

Discussion

Despite significant reduction in the developed world, rheumatic MS is still responsible for significant morbidity as well as premature mortality in the developing countries.[12] A meta-analysis from South Asia showed that Pakistan had the highest prevalence (8 per 1000) of rheumatic heart disease (RHS) with predominant MS.[2,3] Ascertaining MS severity is crucial for disease management and to determine prognosis. Echocardiography is the gold standard for MS evaluation.[4] The customary echochardiography parameter for measuring MVA are planimetry, PHT, proximal isovolumetric surface area(PISA) and continuity equation, with the first two being the more standardised and commonly used techniques.[4,13] The advantages of the validity of these tests are overweighed by the limitation of their difficulty, time consumption, requirement of experienced operators and reproducibility issues.[13] To overcome the flaws of traditional methods for MVA estimation, a novel method of MLSI was introduced in 1979.[9]

MLS is measured as the maximum distance between the tips of anterior and posterior mitral leaflets in parasternal long axis and apical four-chamber view in end-diastole. Both values are averaged to get the index value. Compared to the traditional methods, MLSI is easier, less time-consuming and requires less expertise.[7] Studies have been carried out to determine the validity of MLSI for the estimation of MVA and has shown reliable sensitivity and specificity, but data is generally scarce and the studies done have been performed on a small number of patients[8-10]. The current study was planned to find out the effectiveness of MLSI in determining MV stenosis severity among comparatively larger group of patients coming to the tertiary care hospital.

Similar to the trend seen globally, the current study had female predominance, probably secondary to higher prevalence of the diseases in the female gender.[8,10] Also, most current patients were middle-aged and were having severe disease, which was in line with past studies.[14] This can be explained by the symptomatic state of severe MS leading to hospital visit.

In the current study, a significant strong and significant moderate association of MLSI with MVA, measured with planimetry (R=0.748) and PHT (R=0.656), was found, which is in line with earlier studies.[7-10] It was observed that MLSI had a higher discriminatory ability for different grades of MS. Contrary to previous studies, the recent guidelines for the cut-off value of severe MS area (<1.5cm^2)was followed, and it was found that MLSI of <8.625mm and <8.250mm could anticipate severe MS when measured with planimetry and PHT, respectively,

with high sensitivity and specificity.[4] Measuring MLSI took only a few additional seconds and was conveniently performed in all patients in the current study.

A few studies showed good predictivity of MLSI for MVA even in the presence of AFib, MR and in post-PTMC state.[8,15,16] In the current study's subgroup analysis, the relation was significant between MLSI and MVA in the presence of AFib. It is much quicker, feasible and reliable to take multiple readings of the distance, MLSI, rather than multiple planimetric areas and multiple readings of PHT which is usually significantly affected by the varying haemodynamics of AFib. Similarly, the MLSI was found to correlate equally well even in the presence of MR.

The current study has limitations. Although identifying the tips of mitral leaflet and measuring theirdistance is much easier than planimetry even in suboptimal images and in the presence of significant calcification, MLSI reliability in such scenarios could not be discussed because such cases were excluded from the study sample. Also, there were cases with very poor images where mitral leaflet separation could not be measured and their findings may not be applicable. Patients with non-rheumatic MS and post-PTMC patients for 72 hours were also excluded, so MLSI practicability could not be established in such cases.

Conclusion

MLSI was found to be a simpler and quicker technique for reliably estimating MVA. It could efficiently supplement traditional methods of MVA measurement even in the presence of AFib and MR, and showed the potential to be used as a surrogate of conventional methods for MVA measurement.

Acknowledgement: We are grateful to Musa Karim statistical assistance, and to the institutional echocardiographers.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Nulu S, Bukhman G, Kwan GF. Rheumatic Heart Disease: The Unfinished Global Agenda. Cardiol Clin. 2017; 35:165-80. doi: 10.1016/j.ccl.2016.08.006.
2. Lamichhane P, Pokhrel KM, Pokharel P, Bhandari B, Lamichhane P, Regmi PR. Prevalence of rheumatic heart disease in South Asia: A systematic review and meta-analysis. Int J Cardiol. 2022; 358:110-9. doi: 10.1016/j.ijcard.2022.04.010.
3. Manjunath CN, Srinivas P, Ravindranath KS, Dhanalakshmi C. Incidence and patterns of valvular heart disease in a tertiary care high-volume cardiac center: a single center experience. Indian Heart J. 2014; 66:320-6. doi:10.1016/j.ihj.2014.03.010
4. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021; 143:e35-e71. doi: 10.1161/CIR.0000000000000932.
5. Zeng X, Tan TC, Dudzinski DM, Hung J. Echocardiography of the mitral valve. Prog Cardiovasc Dis. 2014; 57:55-73. doi: 10.1016/j.pcad.2014.05.010.
6. Holmin C, Messika-Zeitoun D, Mezalek AT, Brochet E, Himbert D, Iung B, et al. Mitral leaflet separation index: a new method for the evaluation of the severity of mitral stenosis? Usefulness before and after percutaneous mitral commissurotomy. J Am Soc Echocardiogr. 2007; 20:1119-24. doi: 10.1016/j.echo.2007.02.024.
7. Seow SC, Koh LP, Yeo TC. Haemodynamic significance of mitral stenosis: use of a simple, novel index by 2-dimensional echocardiography. J Am Soc Echocardiogr. 2006; 19:102-6.
8. Thomas JK, Anoop TM, Sebastian GB, George K, George R. Mitral leaflet separation index in assessing the severity of mitral stenosis. ISRN Cardiol. 2011; 2011:768097. doi: 10.5402/2011/768097.
9. Fisher ML, Parisi AF, Plotnick GD, DeFelice CE, Carliner NH, Fortuin NJ. Assessment of severity of mitral stenosis by echocardiographic leaflet separation. Arch Intern Med. 1979; 139:402-6.
10. Raafat SS, Ramzy AA, El-Hadidy AF, Abd Allah MA, Hanna HF. Mitral leaflet separation index. An easy two dimensional echocardiography technique for assessment of mitral valve area before and after percutaneous balloon mitral valvuloplasty. Egypt Heart J. 2018; 70:195-201. doi: 10.1016/j.ehj.2018.04.006.
11. Lemeshow S, Hosmer DW, Klar J, WangeSKL. Adequacy of sample size in health studies: J. Wiley for the World Health Organization; 1990.
12. Coffey S, Thomson RR, Brown A, Carapetis J, Chen M, Sarano ME, et al. Global epidemiology of valvular heart disease. Nat Rev Cardiol. 2021; 18:853-64. doi: 10.1038/s41569-021-00570-z.
13. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. J Am Soc Echocardiogr. 2009; 22:1-23. doi: 10.1016/j.echo.2008.11.029.
14. Bigdelu L, Poorzand H, Azari A, Jarahi L, Ghaderi F, Fazlinejad A, et al. Mitral leaflet separation to evaluate the severity of mitral stenosis: Validation of the index by transesophageal three-dimensional echocardiography. Echocardiography. 2018; 35:361-7. doi: 10.1111/echo.13805.
15. Vimal Raj BS, George P, Jose VJ. Mitral leaflet separation index-a simple novel index to assess the severity of mitral stenosis. Indian Heart J. 2008; 60:563-6.
16. Kinsara AJ, Awadallah AM, Alzaki M, Goda H, Nanda NC. Mitral leaflet separation index for mitral valve assessment during balloon mitral valvuloplasty. Echocardiography. 2020; 37:1159-63. doi: 10.1111/echo.14754.

Author's Contributions

SH: Study design, drafting, data collection, interpretation and manuscript writing.

FATS: Study design, drafting, interpretation, manuscript writing and reviewing.

MN, SG, SR: Contributed in study design, data collection and interpretation.