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Mitral Leaflet Separation Index as a Simple Parameter to Ddetermine Mitral Stenosis Severity in Adam Malik Hospital

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Abstract : Background: Occurrence rate of mitral stenosis (MS) in developing countries remain high. Determining the severity of MS is important for both prognostic and therapeutic reasons. Transthoracic echocardiograhy (TTE) is the gold standard method for assessment of MS severity by using planimetry and pressure half time (PHT) methods. Planimetry is accurate but highly operator dependent. PHT is affected by hemodynamic significance, like aortic regurgitation (AR) and bradycardia or tachycardia.

Patients and Methods: This study included 102 patients with MS who had undergone echocardiographic examination from June 2016 to December 2017 at Adam Malik General hospital. The maximal separation of the mitral valve leaflet tips was measured from inner edge to inner edge in end diastole in the parasternal long axis and apical 4-chamber views. These two parameters were averaged to yield the MLSI. The index was compared with mitral valve area determined by planimetry method.

Results: Of the 102 study subjects, 14 patients had mild MS (13,7%), 14 patients had moderate MS (13,7%), and 74 patients had severe MS (72,6%). There was a very strong correlation between MLSI with mitral valve area by planimetry using Pearson correlation (r = 0.888; p<0.001) and there was a very strong correlation between MLSI with mitral valve area by PHT (r = 0,813; p<0.001) . Using receiver operating characteristic (ROC) curve, MLSI less than 0.77 cm can predict severe MS with 93.2% sensitivity, 89.3% specificity, 95.8% of positive predictive value (PPV), 83.3% of negative predtive value (NPV), and positive likehood ratio (LR+) of 8.71. On the other hand, using ROC curve, MLSI 0.91 cm or more can predict mild MS with 100% sensitivity, 97,7% specificity, 91.67% PPV, 96.67% NPV, LR+ of 43.478. MLSI was still have a very strong correlation with mitral valve area, even in the presence of mitral regurgitation, AR, or atrial fibrillation. Intraobserver and interobserver variabilities showed by Kappa value had a high concordant measurement.

Conclusions: The MLSI is an easy, accurate and reliable measure to estimate severity of MS, it provides a quick estimate of MS severity from standard 2D echocardiographic views without having to resort to tedious measurements.

Key Words: Mitral leaflet separation index and MS severity.

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1. Introduction

Occurrence rate of mitral stenosis (MS) in developing countries remain high. Two-thirds of the world's population live in the developing countries with a high prevalence of rheumatic fever or rheumatic heart disease resulting in a large population with mitral stenosis. It is an acquired progressive valvular heart disease characterized by diffuse thickening of the mitral leaflets, fusion of the commissures, and shortening and fusion of the chordae tendineae, which occur as a sequel to acute rheumatic fever.[1,2]

Determining the severity of MS is important for both prognostic and therapeutic reasons. Transthoracic echocardiography (TTE) is the gold standard method for assessment of MS severity by using planimetry and pressure half time (PHT). The mitral valve area (MVA) can be measured by planimetry, PHT, continuity equation, and proximal isovelocity surface area methods.[3]

Direct measurement of MVA by planimetry is considered to be the reference method and correlates closely with anatomical findings. It is accurate but is highly operator dependent. The procedure requires an experienced operator because minor changes to the depth or angle of the ultrasound beam may lead to significant MVA overestimation. To avoid such overestimation, it is important to scan slowly from the apex to the base and to select the narrowest orifice. This must be done carefully to obtain the smallest orifice in space and the largest opening in time. Planimetry may not be feasible in approximately 5% of patients because of a poor echocardiographic window or massive calcifications.[3,4]

The main advantage of PHT is its simplicity ; then, it is used widely in clinical practice in addition to, or even instead of, planimetry. It is also most effective for the native valve before surgical intervention. However, PHT is affected by alteration in preload or left ventricular compliance. The PHT method should be used with caution, especially in older patients or those in atrial fibrillation in whom the PHT may be highly variable from beat to beat. The PHT method is also invalidated by severe aortic regurgitation.[3,5,6]

Mitral Leaflet Separation Index (MLSI)was recently presented as a reliable measureof MS severity and as a surrogate for MVA.[7]In this study, we evaluate Mitral Leaflet MLSI as a new simple parameter for assessment of MS severity by using 2-Dimensional (2D) echocardiography.

2. Patients and Methods

This study included 102 patients with MS who had undergone echocardiographic examination from June 1st 2016 to December 31st 2017 at Adam Malik hospital. Patients with heavy mitral valvular calcification and suboptimal images were excluded from the study. Patients with degenerative MS and congenital MS were also excluded.

The mitral valve area was estimated by the standard 2D echo planimetry and PHT methods. The maximal separation of the mitral valve leaflet tips was measured from inner edge to inner edge in end diastole in the parasternal long axis (PLAX) and apical 4-chamber (A4C) views. Three measurements were obtained in PLAX and A4C views each for patients with sinus rhythm, and five measurements were taken in PLAX and A4C views for patients with atrial fibrillation. These two parameters were averaged to yield the MLSI.[2,7] The index correlation with mitral valve area (MVA) determined by planimetry and PHT methods were measured.Cutt off points between MLS index and MVA determined by receiver operating characteristic (ROC) curvewere obtained for each mild and severe MS.

Severe MS was defined as MVA of 1 cm^2 or less by planimetry or PHT. Moderate MS was defined as MVA between 1 cm^2 and 1.5 cm^2 by planimetry or PHT. Mild MS was defined as an MVA of more than 1.5 cm^2 by planimetry or PHT.[3] The parameters of echocardiography taken were mitral valve area from 2D and PHT, left atrial (LA) size, ejection fraction (EF), and cuspal separation in PLAX and A4C view. The correlation between the MLS index with MVA in presence of mitral regurgitation, atrial fibrillation, and aortic regurgitation were also determined. Intraobserver and interobserver variabilities calculated by Kappa value.

2.1. Statistical Analysis

Correlation between the MLS index and the MVA by planimetry method was determined by linear regression analysis. The MLS index for mild, moderate, and severe MS was analysed using analysis of variance

to determine if the index could differentiate categories of MS. The value of MLS index which predicted mild and severe MS with best sensitivity and specificity was determined by receiver operating characteristics curve analysis and tested under this research samples. All statistical analysis was done using SPSS software for windows.

Table 1 : Baseline Characteristics of Patients Diagnosed with Mitral Stenosis (MS)

Parameter	All (n=102)	Mild (n=14)	Moderate (n=14)	Severe (n=74)	Significance p<0,05
Age					
(year ± SD)	40.26 ± 11.31	35.36±12.23	42.43±13.16	40.78±10.66	0.08
Sex (%)					0.375
Male	33.3	21.4	50	32.4	
Female	66.7	78.6	50	32.4	
LA diameter					
(mm ± SD)	52.5±11.67	50.35±8.68	51.50±7.35	53.10±12.80	0.46
EF					
(% ± SD)	59.99±7.85	61.21 ± 9.62	57.28±8.28	60.27±7.40	0.533
MS severity (%)					0.000*
Mild	13.7	100	0	0	
Moderate	13.7	0	100	0	
Severe	72.5	0	0	100	
MR severity (%)					0.000
Normal	29.4	14.3	14.3	35.1	
Mild	30.4	14.3	21.4	335.1	
Moderate	24.5	0	42.9	25.7	
Severe	15.7	71.4	21.4	4.1	
AR severity (%)					0,286
Normal	71,9	64,3	64,3	71,6	
Mild	11,8	7,1	21,4	10,8	
Moderate	53,1	21,4	14,3	16,2	
Severe	6,3	7,1	0	1,4	
MVAby planimetry					0,00*
(cm^2 ± SD)	0,88±0,42	1,78±0,21	1,13±0,12	0,66±0,167	
MVA by PHT					0,00*
(msec ± SD)	0,92±0,45	1,836±0,41	1,21±0,15	0,69±0,136	
MVAbymean *PG*					0,09
(mmHg)	11,02±6,49	8,29±4,766	9,34±4,79	11,85±6,89	
MR (%)	70,6	85,7	95,7	64,9	0,000
AR (%)	31,4	35,7	35,7	28,4	0,2
MLSI (i ± SD)	0,69±0,20	1,05±0,121	0,83±0,11	0,59±0,12	0,000*
Rhythm (%±SD)					
Sinus rhythm	20,6	35,7	14,3	18,9	
Atrial fibrillation	79,4	64,3	85,7	81,1	
LVEDD (mm ± SD)	45,8±8,79	51,71±8,00	49,57±8,28	43,97±7,89	0,006*

Abbreviation:
% : percent; AR : aortic regurgitation; cm: centimeter;LVEDD : left ventricular end diastolic diameter;MLSI : mitral leaflet separation index; mm: millimeter; mmHg: milimeterHg; MR : mitral regurgitation; MS: mitral stenosis;msec: millisecond; MVA : mitral valve area;PG : pressure gradient; PHT : pressure half time; SD : standard deviation

1. Results

Of 102 study subjects, 68 were males and 34 were females. Age of patients ranged from 14 to 63 years. LA size ranged from 3.4 to 14 cm. LV size ranged from 2.5 to 7.4 cm. EF ranged from 44% to 79%. Of the 102 study subjects, 14 patients had mild MS (13.75%), 14 patients had moderate MS (13.75%) and 74 patients had severe MS (72.5%). There was a difference between severe MS and non severe MS (measured by planimetry or PHT) and statistically significant. There was a difference between MLS index in severe MS and MLS index in non severe MS that statistically significant. Also, there was a difference between severe mitral regurgitation (MR) that accompanies MS with non severe MR and statistically significant (table 1).

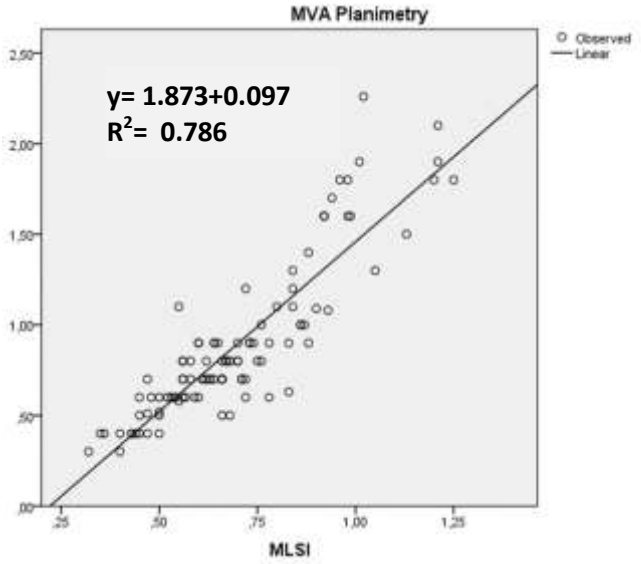

Figure 1. Linear regression graphic showing correlation between MLSI and MVA by planimetry

There was a very strong correlation between MLS index and mitral valve area(MVA) by planimetry using Pearson correlation (r = 0.888, p<0.001) (figure 1; table 2). Also, there was a very strong correlation between MLS index and MVA by PHT (r = 0.813, p<0.001) (figure 2; table 2).

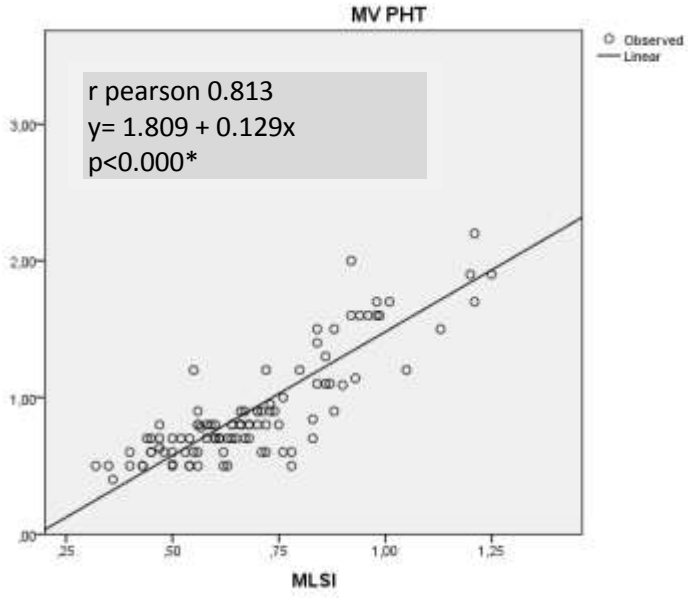

Figure 2. Linear regression graphic showing correlation between MLSI and MVA by PHT.

Table 2. Correlation Between MLSI with Planimetry and PHT

	MLSI	PHT	p value
2D	0,888	0,931	<0.001*
PHT	0,813	-	<0.001*

2D : two dimensional echocardiography (planimetry); MLSI : mitral leaflet separation index ; PHT : pressure half time

Using receiver operating characteristic (ROC) curve, MLS index less than 0.77 cm can predict severe MS with 93.2% sensitivity, 89.3% specificity, 95.8% PPV, 83.3% NPV, and LR+ 8.71 (figure 3; table 3,4, and 5).

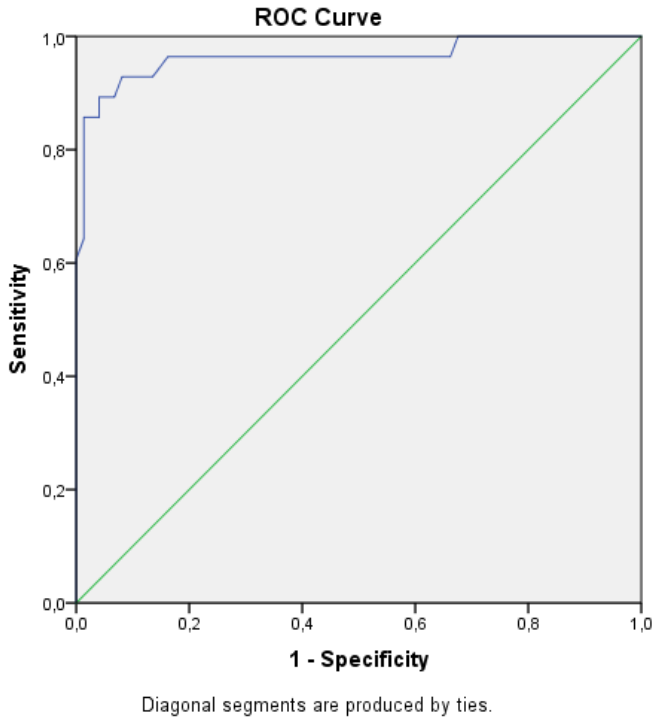

Figure 3.Receiver operating characteristic curve for severe MS

Table 3. Area Under the Curve (AUC) of Mitral Leaflet Separation Index in Severe MS

Parameter	Area Under the Curve (AUC)
Mitral leaflet separation index	0.964

Table 4. Table 2x2 Result of Cutting Point of Mitral Leaflet Separation Index with the Mitral Valve Area by Planimetry (Severe MS)

		Mitral Stenosis Severity Based on Planimetry				P
		Severe MS		Non Severe MS		
		n	%	n	%	
Mitral Leaflet	<0.77	69	93.2	3	10.7	0.00*
Separation Index	≥0.77	5	6.8	25	89.3	

Table 5. Sensitivity, Spesificity, Positve Predictive Value, Negative Predictive Value of Mitral Leaflet Separation Index of Severe MS

Parameter	Sens (CI 95%)	Spes (CI 95%)	PPV (CI 95%)	NPV (CI 95%)	Significance
Mitral Leaflet Separation Index	93.2	89.3	95.8	83.3	0.00*

Sens : sensitivity; Spes : spesificity; PPV : positive predictive value; NPV : negative predictive value; CI 95% : confidence interval 95%

On the other hand, using ROC curve, MLS index 0.91 cm or more can predict mild MS with 100% sensitivity, 97.7% specificity, 91.67% PPV, 96.67% NPV, and LR+ 43.478 (figure 4; table 6,7, and 8).

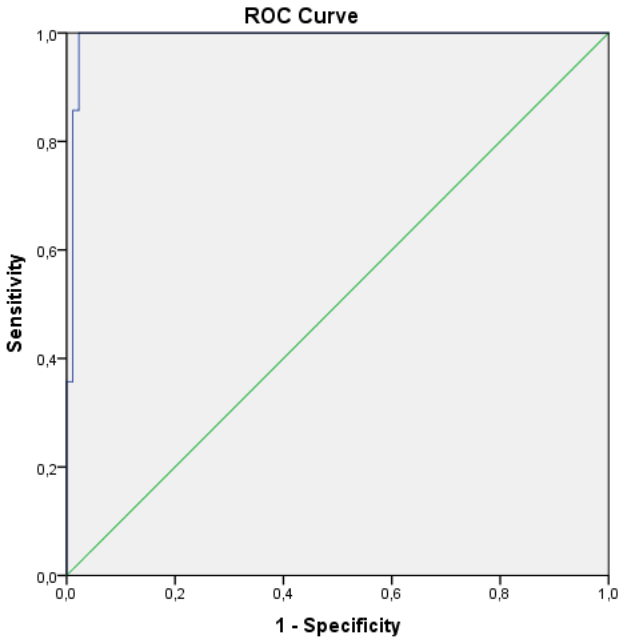

Figure 4. Receiver operating characteristic curve for mild MS

Table 6.Area Under the Curve (AUC) of Mitral Leaflet Separation Index in Mild MS

Parameter	Area Under the Curve (AUC)
Mitral leaflet separation index	0,991

Table 7. Table 2x2 Result of Cutting Point of Mitral Leaflet Separation Index with the Mitral Valve Area by Planimetry (Mild MS)

		Mitral Stenosis Severity Based on Planimetry				P
		Mild MS		Non Mild MS		
		n	%	n	%	
Mitral Leaflet	≥0.91	14	100	2	2.3	0.00*
Separation Idex	<0.91	0	0	86	97.7	
Total		14	100	88	100	

Table 8. Sensitivity, Spesificity, Positve Predictive Value, Negative Predictive Value of Mitral Leaflet Separation Index of Mild MS

Parameter	Sens (CI 95%)	Spes (CI 95%)	PPV (CI 95%)	NPV (CI 95%)	Significance
Mitral Leaflet Separation Index	100	97.7	91.67	96.67	0.00*

Sens : sensitivity; Spes : spesificity; PPV : positive predictive value; NPV : negative predictive value; CI 95% : confidence interval 95%

3.1. Correlation between MVA and MLS Index in Presence of Mitral Regurgitation (MR)

The total number ofMS patientsaccompanied by MR was 72 patients. By using Pearson test, there is a very strong correlation between the MLS index with the MVA in the presence of MR (r 0.884; p value 0.000) (table 9).

Table 9. Correlation Between MVA and MLSI in the Presence of Mitral Regurgitation

N= 72	MLSI	p value
2D	0.884	<0.05*

MLSI : mitral leaflet separation index

3.2. Correlation between MVA and MLS Index in Presence of Atrial Fibrillation

There were 81 patients with atrial fibrillation and 21 patients with sinus rhythm. The coefficient of correlation between the MLS index with the MVA in patients with atrial fibrillation was 0.884 (p value 0.000). There is a very strong correlation between the MLS index with the MVA in presence of atrial fibrillation (table 10).

Table 10. Correlation Between MVA and MLSI in the Presence of Atrial Fibrillation

N= 81	MLSI	Nilai p
2D	0.884	<0.05*

MLSI : mitral leaflet separation index

3.3. Correlation between MVA and MLS Index in Presence of Aortic Regurgitation

There were 31 patients of MS accompanied by aortic regurgitation. The coefficient of correlation between the MLS index with the MVA in patients with aortic regurgitation was 0.942 (p value 0.000). There is a very strong correlation between the MLS index with the MVA in presence of aortic regurgitation (table 11).

Table 11. Correlation Between MVA and MLSI in the Presence of Aortic Regurgitation

N= 31	IPDKM	Nilai p
2D	0.942	<0.05*

MLSI : mitral leaflet separation index

Intraobserver and interobservervariabilities showed a good concordance measurements (table 12 and 13).

Table 12.Intraobserver Variability of MLSI

	Kappa	p value
Mitral Leaflet Separation Index	0.928	<0.01

Table 13.Interobserver Variability of MLSI

	Kappa	Nilai p
Mitral leaflet separation index	0.784	<0.01

2. Discussion

MLS index that measuring the distance between the tips of the mitral leaflets in parasternal long-axis and four-chamber views was presented as a reliable measure of MS severity and as a surrogate for MVA. It is technically easy to obtain. It is a modification of mitral separation that was used by Fisher et al (1979) according to Gorlin's Formula. The formula says that valve area (cm^2) is proporsional to transvalvular blood flow (ml/sec) and inversely related to heart rate (beat/ min) multiplied by diastolic filling time.[7,8,9]

MLS index is simpler and easier than planimetry and PHT in measurement of MS severity. It provides a quick estimation of MS severity from standard 2D echocardiographic views. This method perhaps useful where there is disagreement between existing methods to determine the severity of MS. Thus, MLS index can be an alternative method and beneficial supplement to the existing echo methods.[2,7]

Our findings are similar are similar with the previous studies. MLS index demonstrates a very well correlation with MVA by planimetry and the PHT methods. It is also significantly different for different grades of MS severity, demonstrating high discriminatory ability. It thus reliably differentiated patients with hemodynamically significant MS from those without. The MLS index can differentiate MS severity even in the presence of mitral regurgitation.[2,7]

The MLS index also showed there is a verystrong correlation between the MLS index with the MVA in presence of AF, where at least five MLS measurements in each view were taken and averaged. Thus, it is an acurate measure of MS severity even in the presence of AF.[2,7]

MLS index can be used to assess the severity of MS in the presence of MR where mean gradient could overestimate the severity of MS. It showed very strong correlation with the MVA in the presence of MR. Thus, it is a good predictor to assess MS severity in the presence of MR. MLS index can also be used in the presence of aortic regurgitation. As we know, severe aortic regurgitation can make an overestimation measurement by PHT method.This index measures the MVA anatomically, so it is not influenced by hemodynamic changes caused by mitral regurgitation, atrial fibrillation, or aortic regurgitation. [1,2,3,7]

Although, this method has some limitations. Heavily calcified valves and suboptimalimages may preclude accurate measurement of MLSin some patients. This method is also operator dependantto a certain extent.We cannot use this method for degenerative MS because there is not commissure fusion in it. This index also cannot be used for congenital MS because the complexity of the anomaly that need segmental and systemic analysis.[2,7,10,11]

3. Conclusions

The MLS index is an easy, accurate and reliable measure to estimate severity of MS, it provides a quick estimate of MS severity from standard 2D echocardiographic views without having to resort to tedious measurements. This index is also helpful when there is disagreement between severities of MS estimated by

existing methods, in the presence of mitral regurgitation, atrial fibrillation and in the presence of aortic regurgitation.

References

1. Chandrashekhar Y, Westaby S, Narula J. Mitral Stenosis. Lancet. 2009Sept 10;374(9697):1271-83.
2. Thomas JK, Anoop TM, Sebastian GB, George K, George R. Mitral Leaflet Separation Index in Assessing the Severity of Mitral Stenosis. ISRN Cardiology. 2011; 2011 : 1-4. doi: 10.5402/2011/768097.
3. Messika-Zeitoun D, Lung B, Brochet E, Himbert D, Serfaty JM, Laissy JP, Vahanian A. Evaluation of mitral stenosis in 2008. Archives of Cardiovascular Disease. 2008 Oct 28;101:653-663.
4. Faletra F, Pezzano Jr A, Fusco R, et al. Measurement of mitral valve area in mitral stenosis: four echocardiographic methods compared with direct measurement of anatomic orifices. J Am Coll Cardiol 1996;28(5):1190—7.
5. House CM, Nelson WB, Nickele GA, Ahmed I, Dahiya R. Mitral valve area by the pressure half-time method does not correlate with mean gradient in mitral valve repair patients. European Journal of Echocardiography. 2010 Nov 1; 2011 (12): 124-130.
6. Kim HK, Kim YJ, Chang S, Kim DH, Sohn DW, Oh BH, Park YB. Impact of Cardiac Rhythm on Mitral Valve Area Calculated by the Pressre Half Time Method in Patients With Moderate or Severe Mitral Stenosis. J Am Soc Echocardiograpr. 2009; 22: 42-47.
7. Seow SC, Koh LP, Yeo TC. Hemodynamic significance of mitral stenosis: use of a simple, novel index by 2-dimensional echocardiography. J Am Soc Echocardiogr 2006;19:102-6.
8. Fisher Ml, Parisi AF, Plotnick GD, et al. Assessment of Severity of Mitral Stenosis by Echocardiographic Leaflet Separation. Intern Med 1979; 139: 402-6.
9. Hakki A-H, Iskandrian AS, Bemis CE, et al. 1981. A Simplified Valve Formula for the Calculation of Stenotic Cardiac Valve Areas. Circulation. 1981 May;63(5) : 1050-5.
10. Krapf L, Dreyfus J, Cueff C, et al. Anatomical features of rheumatic and non-rheumatic mitral stenosis: potential additional value of three-dimensional echocardiography. Arch Cardiovasc Dis. 2013;106:111–115. doi: 10.1016/j.acvd.2012.11.004.
11. Remenyi B, Gentles T. 2012. Congenital mitral valve lesions: Correlation between morphology and imaging. Annals of Pediatric Cardiology 2012 Vol 5 Issue 1.

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