Original Article

Mitral leaflet separation index. An easy two dimensional echocardiography technique for assessment of mitral valve area before and after percutaneous balloon mitral valvuloplasty

Sameh S. Raafat [a],*, Ali A. Ramzy [b], Amr F. El-Hadidy [c], Mohamed A. Abd Allah [a], Hany F. Hanna [a]

[a] Cardiology Department, AinShams University, Egypt
[b] Cardiology Department, Al-Azhar University, Egypt
[c] Cardiology Department, Ministry of Health Hospitals, Egypt

ARTICLE INFO

ABSTRACT

Aim: To evaluate the reliability of the mitral leaflet separation (MLS) index against the traditional echocardiographic methods in measuring mitral valve area (MVA) pre and post percutaneous balloon mitral valvuloplasty (PBMV).

Methods: Ninety patients suffering symptomatic moderate to severe MS underwent PBMV at Ain Shams University Hospital in cardiology department. Seventy of the patients were females representing 77.8% and 20 were males representing 22.2%. Their age ranged from 22 to 56 years. All patients were subjected to full transthoracic echocardiography (TTE) examination pre and post PBMV. MLS index was introduced as a comparative parameter with traditional echocardiographic methods for assessment of MVA, measuring average of distance between tips of MV leaflets in parasternal long axis and four chamber two dimensional echocardiographic views.

Results: MVA increased **from 0.95 ± 0.28 to 2.21 ± 0.41 cm^2 (P=0.001)** using 2D planimetry; and increased **from 0.93 ± 0.23 to 2.21 ± 0.46 cm^2 (P= 0.0011)** by pressure half time method (PHT). MLS index was correlated with MVA by 2D planimetry pre and post PBMV (r=0.453) and (r=0.668) respectively (p=0.0001) and strongly correlated with MVA using PHT post PBMV (r=0.768) (p=0.0001). Post PBMV 14 patients suffered significant mitral regurgitation 3 of them were transferred to surgery. MLS index above 11.75 mm and below 9.15 mm had excellent positive predictive value for detecting mild and severe MS respectively.

Conclusion: The MLS index it is a simple and effective method for assessment of the MVA, it has an excellent correlation with MVA with an excellent sensitivity and specificity for the prediction of effective MVA. The MLS index cannot evaluate outcome of PBMV because it is an anatomical parameter and not flow dependent thus does not correlate with grades of mitral regurgitation.

1. Introduction

Rheumatic heart disease remains a major cause of cardiovascular disease in developing nations, although the prevalence of rheumatic heart disease (RHD) has declined sharply in industrialized countries during the last century.[1] RHD is by far the most important form of acquired heart disease in children and young adults living in developing countries which are inhabited by 80 percent of the world's population; RHD accounts for about a quarter of all patients with heart failure in endemic countries.[2,3]

In the great majority of cases, mitral stenosis is caused by rheumatic involvement of the mitral valve,[4,5] although only 50 to 70 percent of patients report a history of rheumatic fever.[6,7]

Mitral stenosis (MS) is a disabling and eventually lethal disease. Untreated progressive disease can lead to significant symptoms (eg, dyspnea and fatigue) and serious complications (eg, pulmonary edema, systemic embolism, and pulmonary hypertension).[8–10]

Although medical therapy can relieve symptoms, it does not affect the obstruction to flow. As a result, surgical commissurotomy and open valvuloplasty were, for many years, the only methods by which MS could be corrected. However, the development of

percutaneous balloon mitral valvuloplasty (PBMV) by Inoue in 1984 and Lock in 1985 for the treatment of selected patients with MS has revolutionized the treatment of this disorder.[8–10] The long-term results, lower costs, and the avoidance of thoracotomy make PBMV the treatment of choice in patients with MS who have the following features:

- Moderate to severe MS
- Pliable, noncalcified mitral valves
- Symptomatic or, if asymptomatic suffering from pulmonary artery hypertension
- The absence of left atrial thrombus or moderate to severe mitral regurgitation

In addition, patients who are too old or frail for surgery or those with severe valve deformities might consider PBMV as a palliative procedure in the absence of left atrial thrombus or moderate to severe mitral regurgitation.[11]

The mitral valve was the first structure to be identified by echocardiography. Technical advances have enabled echocardiography to identify almost any anatomic or functional abnormality of the mitral valve.[12,13]

Echocardiography is the most accurate approach for diagnosis and evaluation of MS.[14] Echocardiography is recommended in all patients with MS at initial presentation, for reevaluation of changing symptoms or signs, and at regular intervals for monitoring disease progression.[15]

When transthoracic images are suboptimal, transesophageal echocardiography (TEE) is appropriate.[15] TEE is also necessary to exclude left atrial thrombus and to evaluate mitral regurgitation (MR) severity when PBMV is considered.[15]

In all patients with MS, a detailed echocardiographic examination, including 2D echocardiography (transthoracic or transesophageal), a Doppler study, and color flow Doppler imaging, provides sufficient information to develop a therapeutic plan without the need for cardiac catheterization.[15]

The mitral leaflet separation (MLS) index, measures the distance between the tips of the mitral leaflets in parasternal long-axis and four- chamber views. These two readings are averaged to yield the mitral leaflet separation index. It was recently presented as a reliable measure of MS severity and as a surrogate for mitral valve area (MVA).[16]

2. Objective

To evaluate the accuracy of MLS index in selected patients with MS, before and after PBMV, compared to conventional methods by transthoracic echocardio-graphy [TTE].

3. Methods

This study was approved by our institutional review board and informed consent was obtained from all individuals enrolled in the study.

3.1. Study population

This was a prospective observational study which included all patients referred for elective BMV in the Cardiology Department Ain Shams University hospital. The study included ninety patients.

The inclusion criteria for the study group were as follows: (i) patients' age from 10 to 60 years, (ii) Symptomatic mode rate-to-severe MS. (iii) Asymptomatic moderate-to-severe MS with pulmonary hypertension (PASP more than 50 mmHg at rest) (iv) patients in sinus rhythm or atrial fibrillation.

The exclusion criteria were as follows: (i) patients with mild MS (MVA > 1.5 cm^2), (ii) Patients who are not candidates for BMV (due to either Wilkins score > 10, commissural calcification or left atrial thrombus), (iii) Moderate-to-severe valvular disease other than MS. (iv) Congenital MS. (v) Patients with organic tricuspid valve disease. (vi) Evidence of rheumatic activity during the preceding 6 months.

3.2. Standard trans-thoracic echo- cardiographic study

All patients were studied in the left lateral decubitus position using an ultrasound system (GE vivid 5). Standard 2D and M-mode echocardiograms were obtained according to the American Society of Echocardiography guidelines. The conventional indices for assessment of the severity of MS; MVA by planimetry and pressure half-time and the mean mitral valve pressure gradients and PASP were measured as recommended.

All echocardiographic examinations as well as follow-up measurements were done by a senior echocardiographer with 10 years' experience in performing echocardiograms. To avoid personal bias in assessing the anatomic scores and the mitral valves, these parameters were graded by at least two experienced echocardiologists and in case of disparity, by a third one to ensure correct measurements.

Grading of the severity of the MS and MR was done according to ACC 2006 guidelines for valvular heart disease.[15]

3.3. Severity of MS was determined using the following methods

Severe MS was defined as a MVA of 1 cm^2 or less by planimetry or pressure half-time method and/or a mean transmitral gradient of greater than 10 mm Hg (Figs. 1 and 2). Moderate MS was defined as a MVA between 1 cm^2 and 1.5 cm^2 by planimetry or pressure half-time method, with a mean transmitral gradient of 5 to 10 mm Hg. Mild MS was defined as a MVA of greater than 1.5 cm^2 by planimetry or pressure half-time and/or a transmitral gradient of less than 5 mm Hg.

Mitral valve scoring using Wilkin's scoring system of mitral valve on scale of 1 through 4, with a score of 1 representing normal. The four elements were the mobility of the anterior leaflet, the severity of subvalvular disease, the calcification of the anterior leaflet, and the thickness of the anterior leaflet. The value for each of these four scores was added together for a total "splitability index" of 4 to 16.[17]

3.4. Severity of MR was determined using the following methods

Severe MR was defined as a large central color doppler jet area more than 10 cm^2 or more than 50% of LA area or variable size
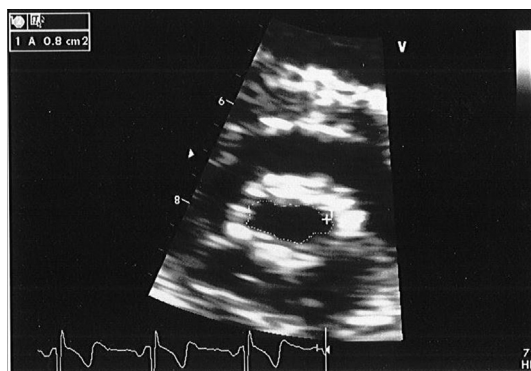

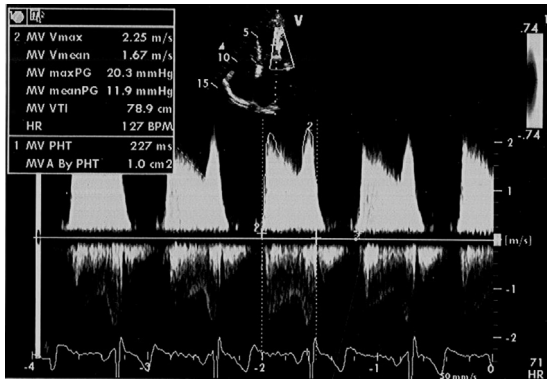Fig. 1. MVA by 2D planimetry echocardiography pre PBMV from a patient included in our study number 79.

Fig. 2. MVA by PHT echocardiography pre PMBV from a patient included in our study number 17.

Fig. 4. MLS measured in parasternal 2D echo pre PBM V from patient number 55.

wall-impinging jet swilling in LA. Moderate to Severe MR was defined as a color doppler jet area greater than mild but no criteria for severe MR or 35–50% of LA. Moderate MR was defined as a color doppler jet area greater than mild but no criteria for severe MR or 15–30% of LA. Mild MR was defined as small, central jet less than 4 cm^2 or less than 15% of LA area.[15,18]

3.5. Mitral Leaflets Separation (MLS) index

The maximal separation of the mitral valve leaflet tips was measured from inner edge to inner edge in diastole in the parasternal long-axis and apical 4-chamber views. These two readings were averaged to yield the MLS index. All measurements were obtained from the mean of 3 beats. All measurements were made blinded to the MVA and transmitral gradient (Figs. 3 and 4).

3.6. Percutaneous Balloon Mitral Valvuloplastv (PBMV)

During cardiac catheterization, a transseptal puncture was used to gain access to the mitral valve from the left atrium. A double balloon technique was used where two balloons were advanced from the venous circulation to the right atrium, across the interatrial septum to the left atrium, and across the stenotic mitral valve. Inflation and rapid deflation of the balloons would open the stenotic valve via separation of the fused commissures. [9,16]

3.7. Follow up echocardiogram

Patients in the study group underwent full echocardiographic study including MLS INDEX within 24 to 48 h post-BMV.(Figs. 5–8).

Fig. 3. MLS measured in apical 4chamber view pre PBMV from patient number 48.
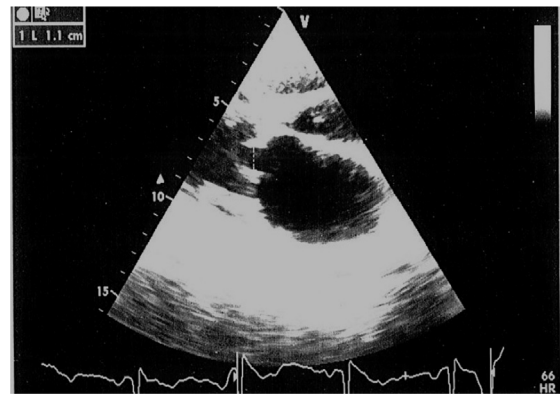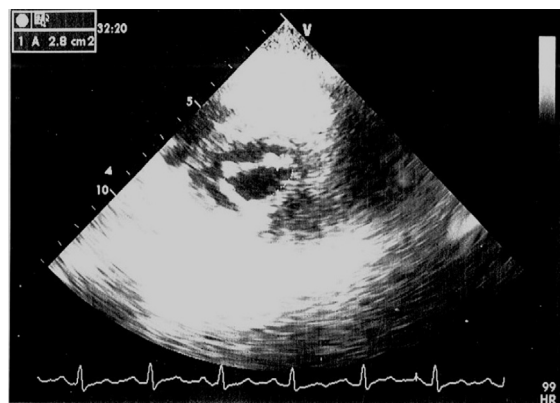

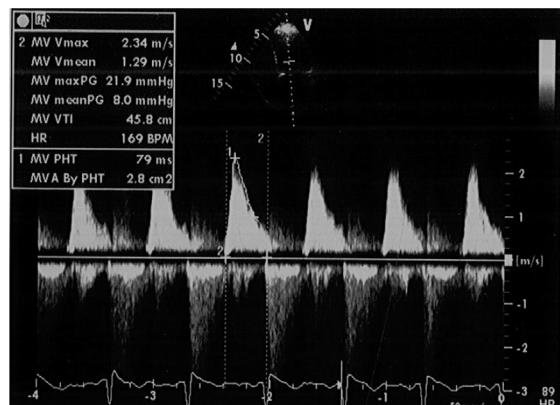**Fig. 5.** MVA by 2D planimetry post PBMV from patient number 83.

Fig. 6. MVA measured by PHT post PBMV from patient number 68.

3.8. Statistical analysis

All data were gathered, tabulated, and statistically analyzed on a PC using a commercially available statistical software package MedCalc version 11.6.1.0 (MedCalc Software, Mariakerke, Belgium). Qualitative variables were expressed as frequency and percentage. Quantitative variables were expressed as mean + SD. Qualitative variables were compared using Chi-squared test. Quantitative variables were assessed using paired t-test. Correlations were performed with linear regression and Pearson's coefficient. Correlation coefficient and intra-class correlation were applied for the substudy to assess inter- and intra-observer variability.
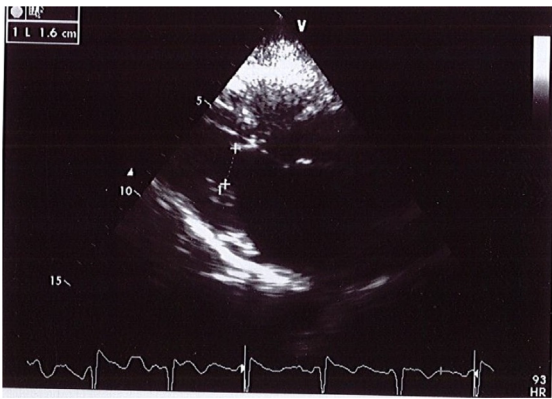
Fig. 7. MLS measured in parasternal view post PBMV from patient number 38.
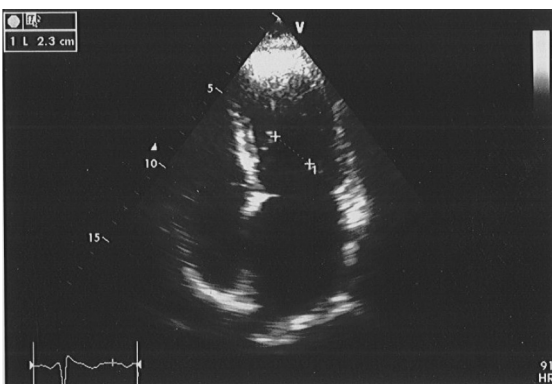

Fig. 8. MLS measured in 4chamber view post PBMV from patient number 19.

ROC Curve was generated to identify the cut off value of MLS index to determine the grade of MS using 2D plannimetry and PHT. P < 0.05 was considered significant, and P < 0.01 was considered highly significant.

4. Results

Out of 115 patients referred to our hospital in the specified period of time for elective BMV, 90 patients were enrolled in this study. Twenty-five patients were not fit for BMV due to presence of LA thrombus by transoesophageal echo.

The age ranged from 22 to 56 years with mean age of 28.3 ± 10 years. Seventy of them were females representing 77.78% of the population while 20 were males representing 22.22% of the population. The echocardiographic score ranged from 5 to 12 (8.50 ± 1. 26). The mean duration of symptoms was 3.1 + 4.2 years; all patients were in NYHA class II-III.

Fig. 9. MVA pre PBMV using 2D planimetry.

Half of the patients (50%) suffered severe MS and the rest suffered moderately severe MS as assessed by 2D planimetry echocardiography (Fig. 9).

Successful BMV was achieved with significant increase in planimetry and pressure half time (PHT) measured MVA as well as significant drop in mean PG across the mitral valve and pulmonary artery systolic pressure (Table 1) where 94% of the study population improved to mild MS while 6% improved to moderate MS (Fig. 10).

4.1. MR pre and post PBMV

Before BMV 69 patients (76.7%) had no MR and 21 patients (23.3%) had mild MR (Fig. 13). Post PBMV 25 patients (27.8%) had no MR, 23 patients (25.6%) had mild MR, 28 patients (31.1%) had moderate MR, 8 patients (8.9%) had moderate to severe MR and 6 patients (6.7%) had severe MR 3 of them (3.3%) transferred to surgery (Figs. 11, 12).

Table 1
Comparison between 2D planimetry, PHT and MVG pre and post PBMV.

	Pre	Post	T,p
2D [cm^2]			5.41
Range	0.45–1.44	1.5–3.6	0.001[*]
Mean S.D.	0.95 ± 0.28	2.21 0.41	
PHT [cm^2]			3.22
Range	0.5–1.5	1.5–3.7	0.001[*]
Mean S.D.	0.93 ± 0.23	2.21 ± 0.46	
MVG[mmHg]			5.18
Range	5.5–30	2.4–13	0.001*
MeanS.D.	14.5 ± 6.03	5.17 ± 2.06	

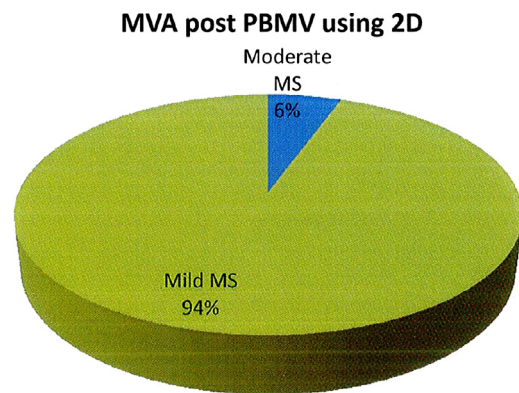[*] Correlation is significant at the 0.05 level.

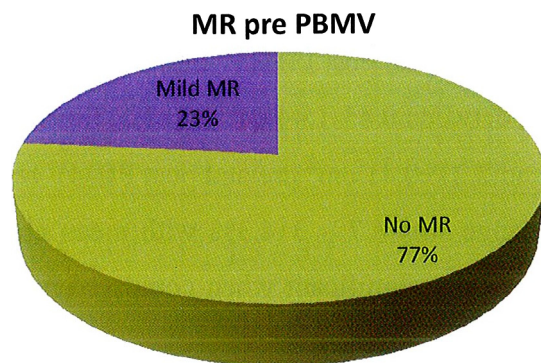**Fig. 10.** MVA post PBMV using 2D planimetry.

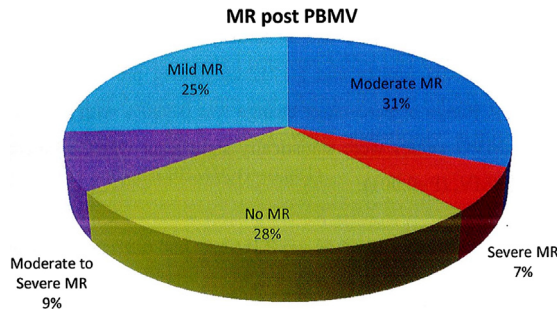**Fig. 11.** Mitral regurgitation pre PBMV.

Fig. 12. Mitral regurgitation post PBMV.

4.2. MLS index pre and post PBMV

Pre BMV, MLS ranged between 3.55 and 11.55 mm with mean of 7.61 ± 2.47 mm, while Post BMV it ranged between 10–19.0 mm with mean of 13.36 ± 2.25 mm these values were statistically significant when compared pre and post PBMV. (P = 0.001) (Table 2) as well as significantly positively correlated with MVA when measured by 2D planimetry both before (r = 0.453) and after the procedure (r = 0.668) and positively correlated with MVA measured by PHT planimetry after the procedure (r = 0.768) as shown in Table 3.

4.3. The cut off value of MLS index in determination the grade of MS

All patients' data were gathered and classified according MVA using: both 2D planimetry and PHT methods and ROC curves were generated to determine the cut off values of MLS index for both methods of MVA measurements.

4.4. ROC Curve to determine the cut off value of MLS index in determination the grade of MS using 2D planimetry

Those patients whose MVA using 2D were less than 1.0 cm^2 (severe MS) were corresponding to cutoff value of MLS index equal to 9.05 mm with sensitivity and specificity 62.2% and 53.9% respectively. And the patients with a MVA using 2D between 1.1 and 1.5 cm^2 (moderate MS) were corresponding to cutoff value of MLS

Table 2
Comparison between MLS pre and post PBMV.

MLS index	Pre PBMV	Post PBMV
Range	3.55–11.55	10–19.0
Mean	7.61	13.29
S.D.	2.47	2.25
T	5.21	
P	0.001[*]	

Table 3
Correlations between MLS and MVA by 2D and PHT pre and post PBMV.

		MLS index Pre	MLS index post
2D Pre	Pearson Correlation	.453([**])	.366
	Sig. (2-tailed)	.001	.017
2D Post	Pearson Correlation	−.291	.668([**])
	Sig. (2-tailed)	.0419	.0001
PHT Pre	Pearson Correlation	−.201	.357
	Sig. (2-tailed)	.168	.021
PHT Post	Pearson Correlation	−.207	.768([**])
	Sig. (2-tailed)	.151	.0001

[*] Correlation is significant at the 0.05 level.
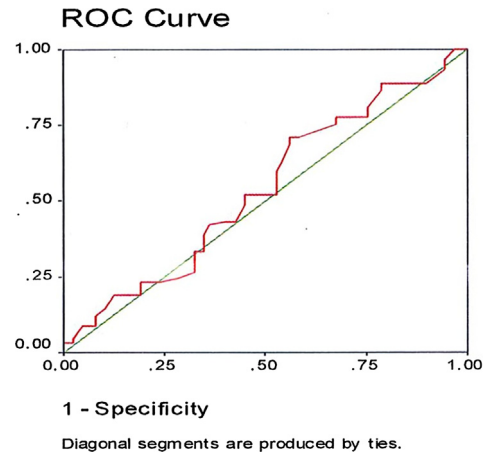[**] Correlation is significant at the 0.001 level.

Fig. 13. cutoff values of MLS index using 2d planimetry method.

index equal to or greater than 10.1 mm with sensitivity and specificity 60.4% and 54.1% respectively (Fig. 13) and (Tables 4 and 5).

4.5. ROC Curve to determine the cut off value of MLS index in determination the grade of MS using PHT

Those patients whose MVA using PHT were less than 1.0 cm^2 (severe MS) were corresponding to cutoff value of MLS index equal to 9.150 mm with sensitivity and specificity 93.9% and 91% respectively. And the patients MVA using PHT between 1.1 and 1.5 cm^2 (moderate MS) were corresponding to cutoff value of MLS index equal to or greater than 10.15 mm with sensitivity and specificity 87.9% and 92% respectively. And the patients MVA using PHT more than 1.5 cm^2 (mild MS) were corresponding to cutoff value of MLS index equal to or greater than 11.75 mm with sensitivity and specificity 77.9% and 95% respectively (Fig. 14) and (Tables 6 and 7).

5. Discussion

Mitral stenosis (MS) comprises a main portion of valvular heart disease and in the great majority of cases mitral stenosis is caused by rheumatic involvement of the mitral valve.[4,5] Rheumatic mitral stenosis (MS) is a frequent cause of valve disease in developing countries.[19]

The safety and efficacy of PBMV have been clearly shown over the last 20 years,[20] and PBMV is the treatment of choice[15,21] patients with favorable anatomy.[22]

Echocardiography is the most accurate approach for diagnosis and evaluation of MS.[14,15] Echocardiography is recommended in

Table 4
Area Under the Curve using 2D planimetry method.

Area	Asymptotic 95% Confidence Interval	
	Lower Bound	Upper Bound
0.539	0.455	0.624

Table 5
Coordinates of the Curve using 2D planimetry method.

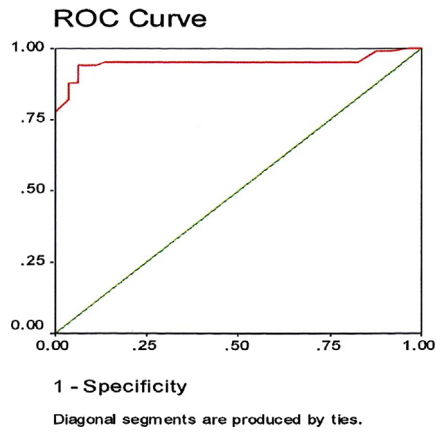|	Greater Than or Equal To (a)	Sensitivity	Specificity
Moderate	10.1	0.604	0.541
Severe	9.0500	0.622	0.539

Fig. 14. cutoff values of MLS index using PHT.

Table 6
Area Under the Curve using PHT.

Area	Asymptotic 95% Confidence Interval	
	Lower Bound	Upper Bound
0.948	0.910	0.986

Table 7
Coordinates of the Curve using PHT.

	Positive if Greater Than or Equal To (a)	Sensitivity	Specificity
Mild	11.7500	0.779	0.95
Moderate	10.1500	0.879	0.92
Severe	9.1500	0.939	0.91

all patients with MS at initial presentation and for monitoring disease progression.[21]

The mitral valve area (MVA) can be measured by planimetry, pressure half-time, continuity equation, and proximal isovelocity surface area methods.[23]

MVA measured by 2D Planimetry is considered as the reference method but must be precisely performed at the tips of the leaflets. Difficulty in acquiring this plane is one major limitation of the method.[15,21]

Transmitral gradient and the continuity equation depend quadratically on transvalvular flow and are, hence, affected by cardiac output and presence of mitral regurgitation.[24]

The idea of using mitral leaflet separation (MLS) index as a measure of MS severity was first proposed by **Fisher et al.** in **1979.**[17,25] They measured the maximum diastolic separation of the mitral valve leaflets by M-mode echocardiography and found a good correlation with MVA obtained invasively using Gorlin formula.

Unlike planimetry, measuring the MLS on 2D imaging is technically easier and more accurate as the narrowest part of the mitral funnel can be easily identified.[24]

The mitral leaflet separation (MLS) index, measuring the distance between the tips of the mitral leaflets in parasternal long-axis and four- chamber views, these two readings were averaged to yield the mitral leaflet separation index.[24,26]

The MLS demonstrated a very good correlation with MVA measured with 2D planimetry and PHT methods and is very easy to obtain in the hands of the inexperienced and in special setting like Cath lab.[24,26,27]

Also the MLS was reported as a simple and effective method for assessment of the MVA and had an excellent sensitivity and specificity for the prediction of an effective MVA.[27]

In our study 90 patients with wide range of mitral stenosis severity were evaluated before and after PBMV using 2D planimetry and PHT for obtaining MVA to assess our new parameter MLS index.

70 patients were females (77.78%) and 20 of them were males (22.22%).

The current study results demonstrated that percutaneous balloon mitral valvuloplasty (PBMV) is a successful method to improve the mitral valve area and mean pressure gradient across the valve.

The mitral valve area increased **from 0.95 ± 0.28 to 2.21 ± 0.41 cm^2 (P = 0.001)** using 2D planimetry; and increased **from 0.93 ± 0.23 to 2.21 ± 0.46 cm^2 (P = 0.0011)** by pressure half time method (PHT).

Those outcomes from our study are comparable with the results from other studies (Tables 8, 9).

5.1. Standard parameters

In our study Mean pressure gradient across the mitral valve (MYG) decreased **from 14.5 ± 6.03 to 5.17 ± 2.06 mmHg (P = 0.001)** .

Table 8
Results of different studies comparable to this study using 2D and PHT for measuringMVA.

Study	Number of patients	Method	Pre balloon MVA (cm^2)	Post balloon MVA (cm^2)
Drighil' et al. 2008[28]	12	PHT	0.91 ± 0.29	1.86 ± 0.43
Bitigen et al. 2006[29]	20	PHT	0.7 ± 0.2	1.9 ± 0.27
		Planimetry	1 ± 0.2	2.2 ± 0.2
Vahanian et al. 2001[30]	464	PHT	l.l ± 0–3	l-l ± 0–3
		Planimetry	l.l ± 0–3	2 ± 0–4
Fawzy et al. 2007[31]	531	PHT	0.92 ± 0.17	1.95 ± 0.29
Boscarini et al. 1991[32]	31	PHT	0.94 ± 0.17	1.96 ± 0.33

Table 9
Results of different studies comparable to this study using MVG.

Study	Number of patients	Parameter	Pre balloon MVG (mmHg)	Post balloon MVG (mmHg)
Drighil et al. 2008[28]	12	MVG	16.4 ± 8.8	5 ± 1.5
Bitigen et al. 2006[29]	20	MVG	8 ± 5	3 ± 1.3
Fawzy et al. 2007[31]	531	MVG	14.4 ± 2.0	5.4 ± 2.0
Boscarini et al. 1991[32]	31	MVG	8.9 ± 3.1	3.9 ± 1.3

5.2. The new parameter MLS index

According to MVA all patients' data were gathered and classified according MVA using; both 2D and PHT; pre and post PBMV against MLS index pre and post PBMV to have a cut off values for MTVA and grading of mitral stenosis using MLS index:

There was a positive significant correlation between MVA using 2D planimetry and MLS index pre and post PBMV (r = 0.453) and (r = 0.668) respectively (p-0.0001).These results are similar to the results of both **Seow SC et al. 2006** and **Holmin C et al. 2007.**[24,26]

There was also a positive significant correlation between MVA using PHT and MLS index post PBMV (r = 0.768) (p = 0.0001) matching the results of **Seow SC et al. 2006.**[24]

When using MVA measured by 2D planimetry a ROC curve was generated and we could categorize moderate MS; by an MLS index greater or equal 10.1 mm with sensitivity and specificity' 60.4% and 54.1% respectively. For severe MS; a MLS index; below 9.05 mm had sensitivity and specificity 62.2% and 54% respectively.

When using MVA measured by PHT a ROC curve was generated and we could categorize mild MS; by an MLS index; equal to or greater than 11.75 mm with sensitivity and specificity 77.9% and 95% respectively. For moderate MS; an MLS index; equal to or greater than 10.15 mm had sensitivity and specificity 87.9% and 92% respectively. For severe MS; an MLS index; below or equal to 9.150 mm had sensitivity and specificity 93.9% and 91% respectively.

These results were similar to **Seow SC et al. 2006**[24] as they announced an MLS index of 12.5 mm for mild MS, 11.1 mm for moderate MS and 8.4 for severe MS with 92.3% sensitivity and 100% specificity.

Also these results were similar to **Holmin C et al. 2007.**[26] They found an MLS index of 12.00 mm for non-severe MS (mild and moderate) had 85% sensitivity and 89% specificity and an index of 8.0 mm for severe MS with 98% sensitivity and 96% specificity.

A MLS index above 11.75 mm and below 9.15 has excellent positive predictive value for detecting mild and severe MS respectively.[24–26]

6. Conclusion

- MLS index is an accurate and reliable measure of MS severity in the majority of patients with MS. Unlike planimetry, MLS index is technically easier particularly in poorly echogenic patient and with less-experienced echocardiographers.
- MLS index is feasible and provides a quick estimate of MS severity from standard 2D echocardiographic views without having to resort to tedious measurements especially in the setting of PBMV inside cath lab. The MLS index is complimentary and cannot be considered a substitute measure for MVA 2D planimetry and PHT.
- MLS index has no respect to the outcome of PBMV because MLS index is an anatomical parameter and doesn't show any relation with different grades of mitral regurgitation as it is not flow dependent.

Conflict of interest

Authors declare that there is no conflict of interest.

References

1. WHO Technical Report, Series. Rheumatic fever and rheumatic heart disease: 1 November 2001. Geneva: WHO; 2004.
2. Ntusi NB, Mayosi BM. Epidemiology of heart failure in sub-Saharan Africa. Expert Rev Cardiovasc Ther. 2009;7:169.
3. Bocchi EA, Guimaraes G, Tarasoutshi F, et al.. Cardiomyopathy: adult valve disease and heart failure in South America. Heart. 2009;95:181.
4. Olson LJ, Subramanian R, Ackermann DM, et al.. Surgical pathology of the mitral valve: a study of 712 cases spanning 21 years. Mayo Clin Proc. 1987;62:22.
5. Horstkotte D, Niehues R, Strauer BE. Pathomorphological aspects: aetiology and natural history of acquired mitral valve stenosis. Eur Heart J. 1991;12:55.
6. Wood P. An appreciation of mitral stenosis: Clinical features. Br Med J. 1954;1:1051.
7. Rowe JC, Bland EF, Sprague HB, White PD. The course of mitral stenosis without surgery: ten- and twenty-year perspectives. Ann Intern Med. 1960;52:741.
8. Carroll JD, Feldman T. Percutaneous mitral balloon valvotomy and the new demographics of mitral stenosis. JAMA. 1993;270:1731.
9. Inoue K, Owaki T, Nakamura T, et al.. Clinical application of transvenous mitral commissurotomy by a new balloon catheter. J Thorac Cardiovasc Surg. 1984;87:394.
10. Lock JE, Khalilullah M, Shrivastava S, et al.. Percutaneous catheter commissurotomy in rheumatic mitral stenosis. N Engl J Med. 1985;313:1515.
11. Rajamannan NM, Nealis TB, Subramaniam M, et al.. Calcified rheumatic valve neoangiogenesis is associated with vascular endothelial growth factor expression and osteoblastlike bone formation. Circulation. 2005;111:3296.
12. Edler I. Ultrasound cardiogram in mitral valve disease. Acta Chir Scand. 1956;111:230.
13. Edler I. Ultrasoundcardiography in mitral valve stenosis. Am J Cardiol. 1967;19:18.
14. Otto CM. Valvular heart disease: mitral stenosis. Philadelphia Saunders. Vol. 252, 2nd ed. 2004. p. 255.
15. Bonow RO, Carabello BA, Chatterjee K, et al.. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients with Valvular Heart Disease): Developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. Circulation. 2006;114:184.
16. Inoue K, Feldman T. Percutaneous transvenous mitral commissurotomy using Inoue balloon catheter. Cathet Cardiovasc Diagn. 1993;28:119.
17. Wilkins GT, Weyman AE, Abascal VM, et al.. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. Br Heart J. 1988;60:299.
18. Feigenbaum H, Armstrong WF, Ryan T, et al. Feigenbaum's Echocardiography. Mitral valve disease. Lippincott Williams & Wilkins. Vol. 11, 6th ed.; 2005. p. 300.
19. Lung B, Vahanian A, Otto CM, Bonow RO, et al. Valvular heart disease: a companion to Braunwald's heart disease: rheumatic mitral valve disease. Vol. 221. Philadelphia: Saunders/Elsevier; 2009. p. 242.
20. Vahanian A, Baumgartner H, Bax J, et al.. Guidelines on the management of valvular heart disease: the Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. Eur Heart J. 2007;28:230.
21. Messika-Zeitoun D, Lung B, Brochet E, Himbert D, et al. Evaluation of mitral stenosis. Arch Cardiovasc Dis. 2008; 653:63.
22. Rifaie O, Abdel-Dayem MK, Ramzy A, Ezz-El-Din H, et al. Percutaneous mitral valvotomy versus closed surgical commissurotomy: up to 15 years of follow-up of a prospective randomized study. J Cardiol. 2009; 53:28–34.
23. Faletra F, Pezzano Jr A, Fusco R, Mantero A, 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;28:1190.
24. 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;19:102–106.
25. Fisher ML, Parisi AF, Plotnick GD, DeFelice CE, et al.. Assessment of severity of mitral stenosis by echocardiographic leaflet separation-. Intern Med. 1979;139:402.
26. Holmin C, Messika-Zeitoun D, Mezalek AT, Brochet E, 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;1119:24.
27. Duggal B, Bajaj M, Prabhu S, Mathew M. The mitral leaflet separation index for assessment mitral stenosis during percutaneous mitral commissurotomy: validation of the index in the immediate post PMC period. Echocardiography. 2012;9:10.
28. Drighil A, Bennis A, Mathewson JW, Lancelotti P, et al.. Immediate impact of successful percutaneous mitral valve commissurotomy on right ventricular function. Eur J Echocardiogr. 2008;536:41.
29. Bitigen A, Turkmen M, Karakaya O, Saglam M, et al.. Early effects of percutaneous mitral valvuloplasty on left atrial mechanical functions. Tohoku J Exp Med. 2006;285:9.
30. Vahanian A. Balloon Valvuloplasty Heart J. 2001;85(223):228.
31. Fawzy ME, Shoukri M, Al Buraiki J, Hassan W, et al.. Seventeen years' clinical and echocardiographic follow up of mitral balloon valvuloplasty in 520 patients, and predictors of long-term outcome. J Heart Valve Dis. 2007;16(454):60.
32. Boscarini M, Repetto S, Secchin G, Stifani A, et al.. Percutaneous mitral commissurotomy: immediate and short-term result. G Ital Cardiol. 1991;21(1185):94.