

Correspondence

Clinical outcomes by indexed mitral valve tenting on mitral stenosis undergoing percutaneous transvenous mitral commissurotomy

To the editor,

There is a propensity for atrial and ventricular remodeling by pressure overload followed by mitral stenosis (MS) [1]. Due to annular dilatation, the fusion of mitral valve (MV) leaflets causes it to take a shape of a tent in systole. Usually, the triangular area between the annulus and tented leaflets is called MV tenting area. MV tenting area can be assessed quantitatively by echocardiography and reflects left ventricular remodeling in patients with MV disease [2]. Several studies have demonstrated a positive association between the severity of MV tenting and unfavorable outcomes in patients with mitral regurgitation (MR) [3]. Recurrent MR, heart failure, and mortality occurred frequently with an MV tenting area of > 2.5 cm pre-operatively [4]. However, an association of MV tenting area with outcomes related to percutaneous transvenous mitral commissurotomy (PTMC) has not been studied in the literature. Hence, we hypothesize that, like patients with MR, the severity of MV tenting is associated with adverse outcomes in patients with MS undergoing PTMC.

In this study, we retrospectively reviewed 326 patients who underwent PTMC for MS from January 2017 to December 2021 at our institute (Abbas Institute of Medical Sciences, study ID # AIMS/007/22). One hundred and nineteen patients were excluded due to incorrect storage of echocardiographic data or insufficient image quality to measure tenting parameters (poor echo window, unclear MV dimensions, unclear MV annulus, angulated hearts with elongated PLAX views/4 chamber views). Therefore, a total of 207 patients with MS post-PTMC served as our study population. Individual patient consent was waived off due to the retrospective nature of the study. Patients that are suitable for PTMC are not discussed in heart team meetings and proceeded after echocardiographic suitability (Wilkin's score < 11). Patients with Wilkin's score of ≥ 12 are referred for surgery. Pre-procedural transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) are routinely performed within 24 hours before the procedure. Echocardiographic images were extracted from patient records and systematically analyzed by two independent investigators (W.A. and A.M.) who were blinded to each other's observations. Conflict among patient selection was resolved by consensus. Using a standard protocol, MV tenting was assessed in parasternal long-axis (PLAX) view according to the European Association of Echocardiography guidelines. The extent of tenting in MV was assessed by tenting area (cm^2). Annular diameter and tenting height were also measured in PLAX view during late systole in the anteroposterior diameter. The tenting area was adjusted with annular diameter and body surface area (BSA) to cater for variance in the body shapes and anatomical parameters between males and females. Clinical outcomes were defined as all-cause mortality and adverse cardiac events, consisting of MV replacement due to complication of PTMC, permanent pacemaker (for post-procedure conduction disturbances), or

repeat PTMC procedure for recurrence of MS. The primary endpoint was a composite of death and adverse cardiac events. All patients had a regular follow-up in the valvular heart disease clinic and their medical records were extracted. Moreover, all patients were contacted via telephone for a clinical outcome questionnaire interview.

We followed the model of post-hoc statistical analysis by von Stumm et al. to find out optimal BSA adjusted MV tenting area for clinical outcomes [3,4]. The tenting area was adjusted for BSA by simple division of variables after calculation of BSA by using the formula of Mosteller [5]. Furthermore, we calculated receiver operating characteristic (ROC) curves to calculate the optimal cut-off value for BSA and annulus-adjusted MV tenting area in our cohort. The optimal cut-off value was defined by Youden's J statistics. Continuous variables were expressed as mean and standard deviation (SD) and categorical variables were presented as frequency and percentages. Comparison of normally and abnormally distributed variables were performed by Student's *t*-test and Mann-Whitney test, respectively. Chi-square and Fisher's exact test was used for univariate analysis of categorical data. A Pearson correlation was used for correlation analysis. Overall endpoint survival and freedom of adverse cardiac events were compared using the log-rank test with the Kaplan-Meier method. Predictors of primary clinical endpoints were assessed by multivariate logistic regression analysis and a two-tailed *P*-value of < 0.05 was considered significant. Statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA.).

A total of 207 patients (mean age 41 ± 7 years, 125 females) were analyzed. Baseline patient characteristics are tabulated in Table 1. Pre-procedural and post-procedural MV parameters are tabulated in Supplementary Table S1. Atrial fibrillation (AF) was found in 25 (30.48%) males and 36 (28.8%) females. The mean left ventricular ejection fraction (LVEF) and Wilkin's score was $45 \pm 10\%$ and 9 ± 3 , respectively. Eighty-five (41.06%) patients were in New York Heart Association (NYHA) class II symptoms and 122 (58.93%) in class III. The mean valve area was $0.9 \pm 0.6 \text{ cm}^2$ by planimetry with mean pressure gradients of 8.32 ± 2.64 mmHg. There was no statistical difference between males and females in the mean valve area (*P*-value = 0.262) but pressure gradients were higher in females (8.34 ± 1.58 vs. 9.15 ± 1.22 , *P*-value = 0.043) and pulmonary artery systolic pressures were higher among males (45.33 ± 7.45 vs. 43.84 ± 8.42 , *P*-value = 0.037). Pre-operative assessment of MV tenting parameters revealed a mean tenting area of $3.28 \pm 0.74 \text{ cm}^2$ and an annular diameter of 36.42 ± 6.32 mm (Table 2). Mean BSA was $1.8 \pm 0.3 \text{ m}^2$. The all-cause mortality over 54 month's follow-up was 3/207 (1.44%) and 14/207 (6.76%) patients experienced an adverse cardiac event including MR requiring MV replacement ($n = 7$), pacemaker insertion for heart block ($n = 3$), tamponade ($n = 2$), ventricular septal defect ($n = 1$), and myocardial infarction ($n = 1$)

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Table 1
Baseline characteristics.

Patient characteristics	All (n = 207)	Tenting area/BSA			Tenting area/annular diameter			Sex difference		
		>1.5 cm ² /m ² (n = 112)	≤1.5 cm ² /m ² (n = 95)	P-value	>0.81 cm/cm (n = 109)	≤0.81 cm/cm (n = 98)	P-value	Males (n = 82)	Females (n = 125)	P-value
Age (years)	41 ± 7	41 ± 7	42 ± 8	0.947	42 ± 10	40 ± 4	0.572	41 ± 7	39 ± 10	0.33
Females (%)	125(60.38)	72(58)	53(42)	0.031	63(50.4)	62(49.6)	0.981	-	-	-
BSA (m ²)	1.8 ± 0.3	1.9 ± 0.2	2 ± 0.3	0.058	1.9 ± 0.3	2 ± 0.3	0.467	2 ± 0.2	1.7 ± 0.1	0.041
AF (%)	64(30.91)	34(30.35)	29(30.52)	0.934	31(28.44)	28(28.57)	0.913	25(30.48)	36(28.8)	0.036
Creatinine (mg/dL)	1.2 ± 0.9	1.2 ± 0.9	1.4 ± 0.8	0.127	1.2 ± 1	1.3 ± 0.8	0.223	1.2 ± 0.8	1.1 ± 0.9	0.35
LVEF (%)	45 ± 10	43 ± 11	48 ± 12	0.032	46 ± 9	42 ± 12	0.018	47 ± 11	45 ± 9	0.02
Wilkins score	9 ± 3	9 ± 3	9 ± 2	0.966	8 ± 2	10 ± 3	0.049	9 ± 2	9 ± 3	0.96
NYHA Class (%)										
II	85(41.06)	41(36.6)	35(36.84)	0.921	38(34.86)	34(34.69)	0.896	24(29.26)	37(29.6)	0.95
III	122(58.93)	71(63.39)	60(63.15)	0.958	71(65.13)	64(65.3)	0.932	58(70.73)	88(70.4)	0.98
Mitral valve parameters										
Area by planimetry (cm ²)	0.9 ± 0.6	0.9 ± 0.5	1.1 ± 0.3	0.335	1 ± 0.4	1.2 ± 0.2	0.751	0.8 ± 0.6	0.9 ± 0.4	0.262
Mean pressure gradient (mmHg)	8.32 ± 2.64	8.11 ± 2.24	8.26 ± 2.53	0.175	9.11 ± 1.7	8.93 ± 2.14	0.079	8.34 ± 1.58	9.15 ± 1.22	0.043
PASP (mmHg)	42.16 ± 9.45	43.27 ± 8.53	45.67 ± 9.97	0.021	43.82 ± 9.91	43.75 ± 8.5	0.814	45.33 ± 7.45	43.84 ± 8.42	0.037

Table 2
Pre-procedural tenting parameters.

Tenting parameters	All (n = 207)	Males (n = 82)	Females (n = 125)	P-value
Annular diameter (mm)	36.42 ± 6.32	38.73 ± 6.15	36.48 ± 5.17	0.001
Annular diameter adjusted to BSA (cm/m ²)	20.47 ± 2.9	19.85 ± 2.63	21.56 ± 2.49	0.005
Tenting height (mm)	10.52 ± 1.98	11.75 ± 2.65	10.21 ± 1.96	0.025
Tenting height adjusted to BSA (mm/m ²)	6.5 ± 1.4	7.2 ± 1.3	6.5 ± 1.3	<0.001
Tenting area (cm ²)	3.28 ± 0.74	3.62 ± 1.27	2.93 ± 0.88	<0.001
Tenting area adjusted to BSA (cm ² /m ²)	1.63 ± 0.48	1.64 ± 0.51	1.71 ± 0.44	0.009

during follow-up. Overall cardiac adverse event-free survival (4.5 years) was 93.24% (OR 0.071; 95 %CI: 0.013 – 0.152; p-value = 0.03) by Kaplan-Meier analysis. MV tenting area adjusted to BSA of > 1.5 cm²/m² was associated with 4.5 years’ mortality (OR 0.56; 95 %CI: 0.12 – 0.88; P-value = 0.002). This is shown in Fig. 1. There was significant correlation of tenting area with BSA (Pearson r = 0.208, P-value = 0.03) and annular diameter (Pearson r = 0.771, P-value = 0.005). In the multivariate analysis, BSA-indexed MV tenting area was identified as an independent indicator of the primary endpoint (OR 1.03; 95% CI: 0.98 – 1.07; P-value = 0.036). Other predictors of the primary endpoint were AF, Wilkins score, PASP, and LVEF. This is shown in Table 3.

In this study, we aimed to investigate the association between severity of pre-procedural MV tenting area, indexed to BSA and mitral annulus diameter, and adverse clinical outcomes in patients with MS who underwent PTMC. Both indexing factors correlated well with MV

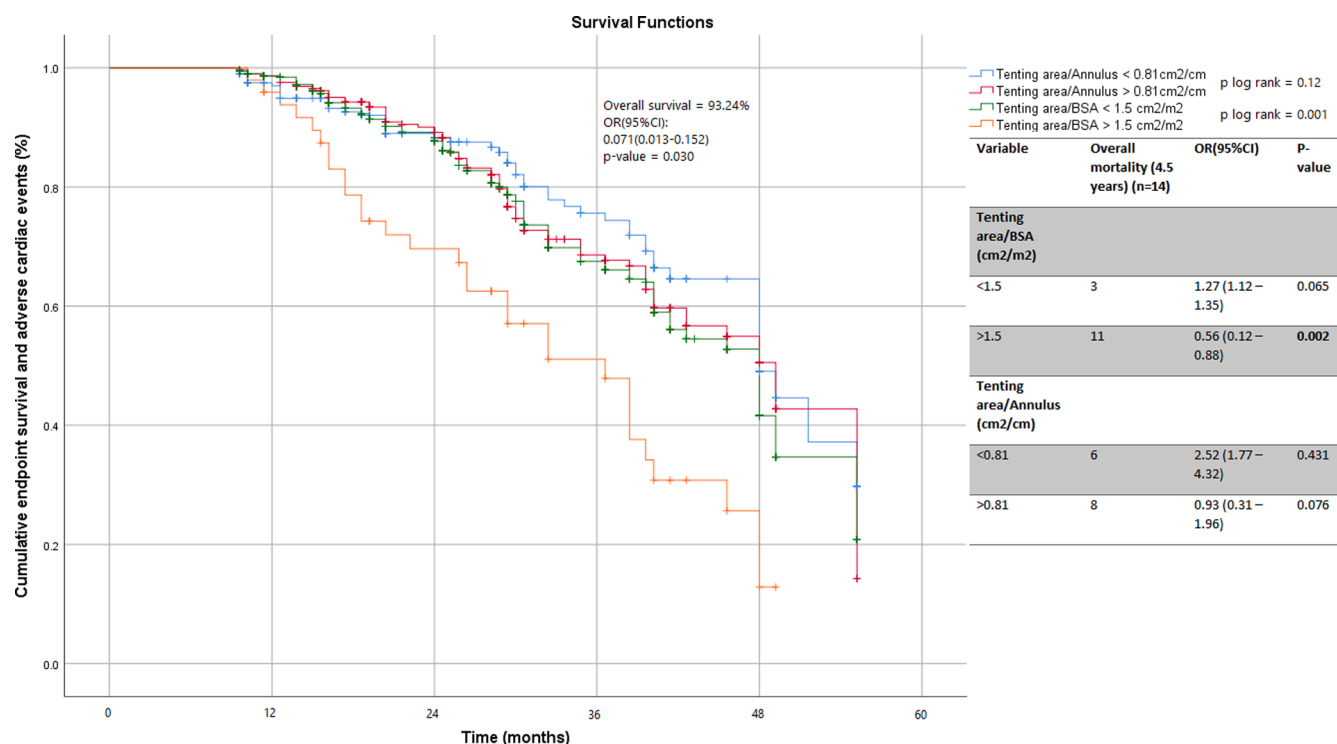


Fig. 1. Univariate Kaplan-Meier analysis of the composite of survival and freedom of cardiac adverse events using tenting area adjusted for body surface area (A) and annular diameter (B).

Table 3
Predictors of mortality or adverse cardiac events.

Variable	P-value	OR	95 %CI
Predictors of adverse cardiac events			
AF	0.027	1.67	1.04 – 2.87
Wilkins score	0.005	0.85	0.64 – 1.05
PASP	0.038	2	1.45 – 3.85
Predictors of mortality			
LVEF	0.007	0.97	0.95 – 0.99
BSA-adjusted tenting area (>1.5 cm ² /m ²)	0.036	1.03	0.98 – 1.07

tenting area, however, only the BSA-adjusted tenting area was a predictor of clinical outcomes after PTMC at a median follow-up of 4.5 years. The use of indexed MV tenting parameters is limited in its predictive value in defining clinical outcomes of MR. To the best of our knowledge, this is the first study to determine the association of the severity of MV tenting area and clinical outcomes in MS after PTMC.

Only a few studies have addressed BSA-indexed MV tenting area, and that too for functional MR. Indexation of annular diameter is a novel parameter with only two studies demonstrating the association of annulus-indexed MV tenting area with clinical outcomes of functional MR after annuloplasty [3,4]. We were unable to find any prior data on these parameters being used in patients with MS. Given the results of our findings, we believe that MV annular geometry has a limited role in describing the primary endpoint prediction. Furthermore, the impact of gender had been widely evaluated in patients undergoing PTMC [6]. However, in our study, gender is not a predictor of adverse cardiac events after PTMC.

This study has all the limitations of a single-center retrospective study design. Exclusion of high patient cohort was a problem due to insufficient echocardiographic data, therefore; a larger sample size could not be analyzed. Echocardiographic follow-up was not included due to attrition bias, as most of the follow-up echocardiography is done by external outpatient physicians who may or may not use a standardized protocol to quantify MV tenting parameters or degree of MR after PTMC. Furthermore, using of ROC curve for cut-off point analysis neglects the time dependency of outcome events. Therefore, a prospective study should be carried out to confirm our current findings.

In summary, there is a need for incorporating conventional parameters of MV apparatus for PTMC with the novel techniques like the indexed MV tenting area to further understand the key pathophysiology of adverse events in patients with MS and PTMC. Therefore, it is our observation that the MS treatment algorithm should include indexed echocardiographic values of the MV tenting area to allow an individualized treatment and predict a treatment response after PTMC in short-term and long-term results. In our study, BSA-adjusted MV tenting area > 1.5 cm²/m² was found to be a reliable indicator that predicts survival and adverse cardiac events in patients with MS undergoing PTMC.

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcha.2022.101025>.

References

- [1] M. Garbi, M.J. Monaghan, Quantitative mitral valve anatomy and pathology, *Echo Res. Pract.* 2015 Sep 1;2(3):R63-72. doi: 10.1530/ERP-15-0008. Epub 2015 Jul 7. PMID: 26693344; PMCID: PMC4676476.
- [2] D.M. Dudzinski, J. Hung, Echocardiographic assessment of ischemic mitral regurgitation, *Cardiovasc Ultrasound.* 21 (12) (2014 Nov) 46, <https://doi.org/10.1186/1476-7120-12-46>. PMID: 25416497; PMCID: PMC4277822.
- [3] M. von Stumm, F. Dudde, T. Holst, T. Sequeira-Gross, J. Pausch, L. Müller, C. R. Sinning, H. Reichenspurner, E. Girdauskas, Predicting clinical outcome by indexed mitral valve tenting in functional mitral valve regurgitation, *Open Heart.* 8 (1) (2021 Jan), e001483, <https://doi.org/10.1136/openhrt-2020-001483>. PMID: 33495382; PMCID: PMC7839912.
- [4] M. von Stumm, F. Dudde, S. Gasser, T. Sequeira-Gross, J. Pausch, C. Sinning, H. Reichenspurner, E. Girdauskas, Prognostic value of mitral valve tenting area in patients with functional mitral regurgitation, *Interact Cardiovasc Thorac Surg.* 30 (3) (2020 Mar 1) 431–438, <https://doi.org/10.1093/icvts/ivz291>. PMID: 31808513.
- [5] R.D. Mosteller, Simplified calculation of body-surface area, *N Engl J Med.* 317 (17) (1987 Oct 22) 1098, <https://doi.org/10.1056/NEJM198710223171717>. PMID: 3657876.
- [6] C. Liu, T. Chen, W. Zeng, S. Wang, Y. Xiong, Z. Liu, T. Huang, Reevaluating the prognostic significance of male gender for papillary thyroid carcinoma and microcarcinoma: a SEER database analysis, *Sci Rep.* 7 (1) (2017 Sep 12) 11412, <https://doi.org/10.1038/s41598-017-11788-8>. PMID: 28900207; PMCID: PMC5595899.

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