Cardiovascular Topics

Characteristics and immediate outcomes of patients who underwent percutaneous balloon mitral valvuloplasty at the Jakaya Kikwete Cardiac Institute, Tanzania

Reuben K Mutagaywa, Maarten J Cramer, Pilly Chillo, Aileen Barongo, Engerasiya Kifai, Steven Chamuleau, Chete Eze-Nliam, Nelson B Vera, Deogratias Nkya, Alex Loth, Ben Alencherry, Stella Mongella, Henry Mayala, Peter Kisenge, Salehe Mwinchete, Alex B Joseph, Gideon Kwesigabo, Appolinary Kamuhabwa, Mazen Albaghdadi, Joanna Ghobrial, Mohamed Janabi

Abstract

Background: For rheumatic mitral stenosis (MS), a multidisciplinary evaluation is mandatory to determine the optimal treatment: medical, percutaneous balloon mitral valvuloplasty (PBMV) or valve surgery. Clinical and imaging evaluations are essential for procedural risk assessment and outcomes. PBMV interventions are increasingly available in Africa and are feasible options for selected candidates. Enhancing PBMV training/skills transfer across most of African countries is possible.
Objectives: The aim of this study was to provide insight into the clinical practice of patients with rheumatic MS evaluated for PBMV in a Tanzanian teaching hospital and to define the role of imaging, and evaluate the heart team and training/skills transfer in PBMV interventions.
Methods: From August 2019 to May 2022, 290 patients with rheumatic MS were recruited consecutively in the Tanzania Mitral Stenosis study. In total, 43 (14.8%) patients were initially evaluated for eligibility for PBMV by a heart team. We carried out the clinical assessment, laboratory investigations, transthoracic/oesophageal echocardiography (TTE/TEE) and electrocardiography.
Results: The median age was 31 years (range 11–68), and two-thirds of the patients were female (four diagnosed during pregnancy). Two patients had symptomatic MS at six and eight years. Nine patients had atrial fibrillation with left atrial thrombus in three, and two were detected by TEE. Nine patients in normal sinus rhythm had spontaneous echo contrast. The mean Wilkins score was 8.6 (range 8–12). With re-evaluation by the local and visiting team, 17 patients were found to have unfavourable characteristics: bi-commissural calcification (four), ≥ grade 2/4 mitral regurgitation (six), high scores and left atrial thrombus (three), left atrial thrombus (two), and severe pulmonary hypertension (two). Three patients died before the planned PBMV. Eleven patients were on a waiting list. We performed PBMV in 12 patients, with success in 10 of these, and good short-term outcomes [mean pre-PBMV (16.03 ± 5.52 mmHg) and post-PBMV gradients (3.08 ± 0.44 mmHg, $p < 0.001$)]. There were no complications.
Conclusions: PBMV had good outcomes for selected candidates. TEE is mandatory in pre-PBMV screening and for procedural guidance. In our cohort, patients with Wilkins score of up to 11 underwent successful PBMV. We encourage PBMV skills expansion in low- and middle-income countries, concentrating on expertise centres.

Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
Reuben K Mutagaywa, MD, reubenmutagaywa@yahoo.com
Pilly Chillo, MD
Deogratias Nkya, MD
Gideon Kwesigabo, MD
Appolinary Kamuhabwa, MD

Jakaya Kikwete Cardiac Institute, Dar es Salaam, Tanzania
Reuben K Mutagaywa, MD
Pilly Chillo, MD
Engerasiya Kifai, MD
Deogratias Nkya, MD
Alex Loth, MD
Ben Alencherry, MD
Stella Mongella, MD
Henry Mayala, MD
Peter Kisenge, MD
Salehe Mwinchete, MD
Alex B Joseph, MD
Mohamed Janabi, MD

Department of Cardiology, Division of Heart and Lung, University Medical Centre Utrecht,
Utrecht, The Netherlands
Reuben K Mutagaywa, MD
Maarten J Cramer, MD

Department of Paediatric and Child Health, Mwananyamala Regional Hospital, Dar es Salaam, Tanzania
Aileen Barongo, MD

Amsterdam Heart Centre, Department of Cardiology, Amsterdam University Medical Centre, Amsterdam, The Netherlands
Steven Chamuleau, MD

Department of Clinical and Interventional Cardiology, Cleveland Clinic; Heart, Vascular, and Thoracic Institute, Cleveland, USA
Chete Eze-Nliam, MD
Nelson B Vera, MD
Ben Alencherry, MD
Joanna Ghobrial, MD

NCH Heart Institute – NCH Healthcare System, Florida, USA
Mazen Albaghdadi, MD

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Rheumatic heart disease (RHD) is endemic in Tanzania; recently published data state the prevalence is around 17.9 per 1 000 population.[1] In Tanzania, RHD is the third most common cause of heart failure after hypertension and cardiomyopathies, including idiopathic dilated cardiomyopathy, peripartum cardiomyopathy and endomyocardial fibrosis.[2]

Rheumatic mitral stenosis (MS) in Africa shows a female predominance with presentation early in life.[3,4] Patients usually present in New York Heart Association (NYHA) functional class II–III, with atrial fibrillation (28%) and thromboembolic events (3.2%).[4,5] Clinically, patients may present with an irregular pulse, normal blood pressure, elevated jugular venous pulse, left parasternal lift and normal apex impulse. Auscultation reveals a low-pitched rumbling diastolic murmur.

Transthoracic echocardiography (TTE) is used to confirm the diagnosis, and assess the severity and prognosis of MS. It is used to describe valve morphology, assess valve function and cardiac chambers, and evaluate the feasibility and indications for intervention.[6] Transoesophageal echocardiography (TEE) is done to complement TTE pre-intervention, and specifically to rule out left atrial or left atrial appendage thrombus that may not be visible by TTE.

Several two-dimensional (2D) echocardiography scoring systems have been created for evaluation of mitral valve anatomy and suitability for percutaneous balloon mitral valvuloplasty (PBMV) without demonstrating superiority,[7] including the most commonly used Wilkins score,[8] Echo score revisited[9] and Cormier score.[10] Limitations of the Wilkins score are the inability to differentiate fibrosis from calcification and the underestimation of commissural/subvalvular involvement.[11,12] However, the decision to perform PBMV is not solely dependent on the mitral valve score but also on clinical judgment. Studies have shown that in young patients or patients with fewer co-morbidities, PBMV gave a better survival rate despite a mean Wilkins score of 9.5.[13]

Guidelines recommend PBMV or mitral valve surgery for the management of clinically significant MS.[14,15] However, due to limited access to interventional cardiology and cardiothoracic surgery in low- and middle-income countries (LMICs), most of these patients are likely to be managed conservatively.[16] In Uganda, Okello *et al*.[17] demonstrated only 8% of patients requiring surgery and 1% requiring PBMV received those services. Instead, only medical therapy, including diuretics, beta-blockers, digoxin, calcium channel blockers and angiotensin converting enzymes inhibitors were prescribed. However, most of these medications only alleviate some of the symptoms but do not resolve the obstructive valve pathology.[18]

Additional medical therapy includes anticoagulation, indicated for the history of systemic embolism, thrombus in the left atrium, atrial fibrillation, dilated left atrium (diameter > 50 mm/indexed volume > 60 ml/m^2), and those that receive a prosthetic heart valve.[6,19] Secondary antibiotic prophylaxis for the prevention of recurrent attacks of acute rheumatic fever and progression of valve lesions is important.[20]

To optimise the evaluation and management of rheumatic MS, a heart team including cardiology, anaesthesiology, interventional cardiology and cardiothoracic surgery is a necessity.[14,15] To guide the choice of intervention (PBMV or surgery), this multidisciplinary approach incorporates clinical assessment, detailed imaging evaluation, procedural risk assessment and scoring systems. PBMV is a safe and cost-effective procedure, and provides excellent short- and long-term outcomes with improved haemodynamics, and symptomatic improvements in appropriately selected patients.[6,19,21,22]

Currently, most sub-Saharan African countries, including Tanzania, have access to a cardiac catheterisation laboratory and therefore PBMV is a feasible option. In August 2019, visiting teams from the United States started a mission in Tanzania to initiate, enhance and consolidate PBMV skills in the local cardiac interventional team. This study was conducted to determine the profiles of patients evaluated for PBMV due to rheumatic MS at Jakaya Kikwete Cardiac Institute (JKCI) during those workshop missions.

Methods

This was a prospective, single-centre, hospital-based, cross-sectional study of Tanzanian patients who were screened for PBMV at JKCI, the only institute offering the intervention in the country. All consecutive patients who were scheduled for PBMV due to severe rheumatic MS between August 2019 and May 2022 were enrolled in the study. We excluded patients with unfavourable clinical characteristics and mitral valve morphology and those with other forms of non-rheumatic valvular heart disease or other cardiac diseases.

Written, informed consent was obtained from all participants over 18 years. Assent was obtained from minors over 13 years of age in the presence of adult witness. For under 13 years, oral consent was provided by the guardian of the minor. The study was approved by the Directorate of Research and Publications of Muhimbili University of Health and Allied Sciences (P. MUHAS – REC-9-2019-059). Permission to conduct this study was obtained from JKCI (AB.157/334/01'A).

The sociodemographic, medical and co-morbidity history were obtained from all patients. NYHA functional class, Wilkins score and mortality information were also collected. All patients were clinically evaluated for the evidence of severe MS according to recognised clinical and echocardiographic criteria.[14,15,23] Several echocardiographic (SC 2000 Siemens Echo machine), electrocardiographic (General electronic Mac 400) and laboratory parameters were documented.

All of the echocardiographic images were reviewed by a heart team that comprised the local team and several members of the visiting team. All TTE was done with the patient in the left lateral decubitus position and with conventional views (parasternal long-axis, short-axis and apical four-chamber view). Two-dimensional and Doppler echocardiographic studies were performed according to the American Society of Echocardiography (ASE) guidelines.[24] TEE was also performed as previously described.[25]

The team took into consideration the following factors, apart from MVA ≤ 1.5 cm^2, when reaching a consensus on management

strategy: clinical assessment, such as symptomatic severity and co-morbidities, scoring systems (by Wilkins score) and procedural risk assessment, for example anatomical favourability and clinical favourability (pulmonary hypertension). We used the European Society of Cardiology (ESC) and the American Heart Association/American College of Cardiology (AHA/ACC)[14,15] definition of unfavourable anatomical characteristics: left atrial thrombus, Wilkins > 8, mitral regurgitation > grade 2, and bilateral commissural fusion to guide our decision. For unfavourable clinical characteristics the definition is: old age, NYHA functional class IV, severe pulmonary hypertension, atrial fibrillation and history of commissurotomy.[14,15] In this study, severe pulmonary hypertension was defined as a right ventricular systolic pressure > 70 mmHg measured from the maximum tricuspid regurgitation jet velocity, as previously described.[26]

A TEE was done on the day of PBMV to rule out left atrial or left atrial appendage thrombus. In four patients, the procedure was performed under local anaesthesia and moderate sedation, utilising TTE and fluoroscopy. In eight patients, TEE was used while the patient was under general anaesthesia and mechanical ventilation. While recognising that TEE adds to procedure time and complexity, the aim was to expose the local team to the two methods, fluoroscopy and TEE-guided approach.

Vascular accesses were right femoral vein with 8F sheaths upsized to 12F for the Inoue balloon, left femoral vein with 7F sheath for the Swan–Ganz catheter, and left femoral artery with 5F sheaths for angiographic pigtail catheter. Trans-septal puncture was done by an anterograde approach using a Brockenbrough needle via the trans-septal sheath and at anterior–posterior projection. Intravenous heparin at a dose of 100 IU/kg body weight was given immediately after septal puncture.

The Inoue balloon stepwise technique was used in all patients and performed as previously described.[27] Balloon sizing was based on patient height, as previously described.[28] The haemodynamic parameters were recorded before and after PBMV. A successful PBMV was defined as improvement in mitral valve area (MVA) to ≥ 1.5 cm^2 without complications, including mitral regurgitation of > 2/4 grade. One day after the procedure, echocardiography was done to evaluate the MVA and mitral regurgitation (MR). Fig. 1 shows the local team performing TEE before PBMV as part of pre-procedural patient preparation.

Fig. 1. A photograph showing pre-procedural TEE.

Statistical analysis

The collected data was checked for quality. Coding was done before entry. The analysis was done using Statistical Package for Social Sciences (SPSS) version 28.0. Continuous data are presented as mean with standard deviation (SD) when distributed normally, and as median with range when skewed. Categorical data are reported as counts and percentages. The chi-squared and Fisher's exact tests were used to compare categorical data. The *t*-test was used to compare the difference between continuous variables. A p-value < 0.05 was considered statistically significant.

Results

Forty-three (14.8%) out of 290 patients enrolled in the Tanzania Mitral Stenosis (TAMS) study were evaluated for eligibility for PBMV at JKCI from August 2019 to May 2022 (Fig. 2). The interventions were done in August 2019 and May 2022, skipping the years 2020 and 2021 due to restrictions on travelling because of the COVID-19 pandemic.

Fig. 3 shows the map of Tanzania illustrating the residence of 290 patients enrolled in the TAMS study. Most of the patients were residing in the northern zone of the country.

As shown in Table 1, there was a female predominance (32, 74.4%). The median age of the patients was 31 years (range 11–68). Twenty-five (58.1%) patients were single, 21 (48.8%) had primary education, 23 (53.5%) were not employed, 38 (88.4%) were from outside Dar es Salaam, 24 (55.8%) had income < 42$ per month, 25 (58.1%) had a national health insurance, and 34 (79.1%) had lived in a clean environment during childhood.

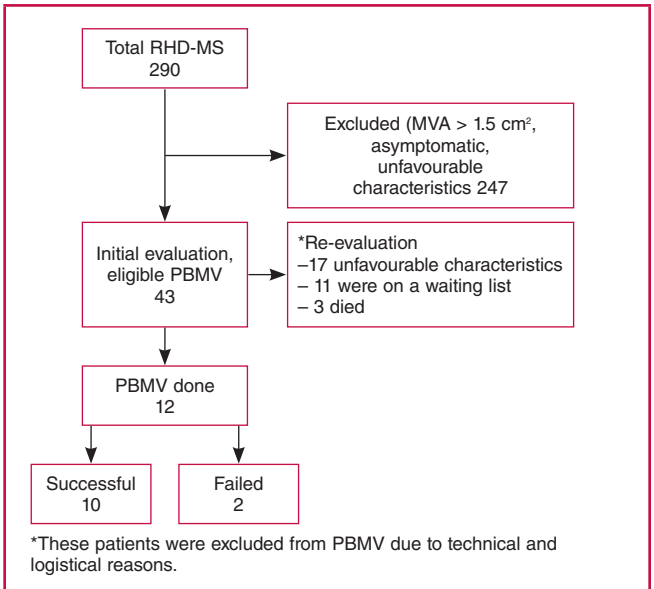

Fig. 2. A flow chart diagram showing patients' recruitment. RHD-MS, rheumatic heart disease–mitral stenosis; MVA, mitral valve area; PBMV, percutaneous balloon mitral valvuloplasty.

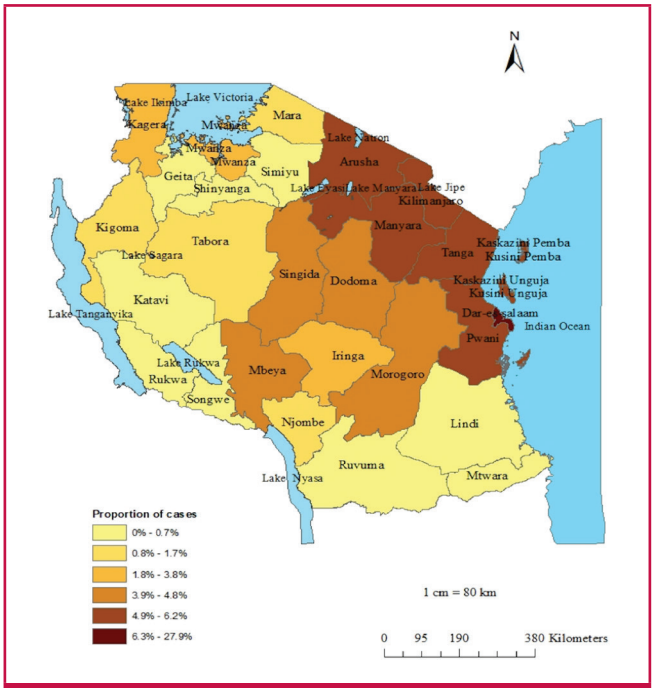

Fig. 3. A map of Tanzania showing the residence of 290 patients enrolled in the TAMS study.

Four (9.3%) patients were first diagnosed with RHD during pregnancy. The mean duration of symptoms before diagnosis was 43.26 ± 30.03 months. Two patients presented with symptomatic MS at the age of six and eight years, respectively. Nine (20.9%) patients had atrial fibrillation (AF) and all were on anticoagulants, four (9.3%) patients had a stroke, and seven (16.3%) had hypertension.

Table 1. Sociodemographic and clinical characteristics of patients evaluated for percutaneous mitral balloon valvuloplasty at JKCI from August 2019 to May 2022 (n = 43).

Variable	*Mean (± SD) or median (range)/frequency (%)*
Median age (years)	31 (11–68)
Female gender	32 (74.4)
Mean duration of symptoms (months)	43.26 ± 30.03
Proportion residing outside Dar es Salaam	38 (88.4)
Proportion not married	25 (58.1)
Proportion without health insurance	25 (58.1)
Proportion with monthly income < 42$	24 (55.8)
Proportion with primary education	21 (48.8)
Proportion with stroke	4 (9.3)
Proportion with hypertension	7 (16.3)
Proportion with atrial fibrillation	9 (20.9)
Proportion with NYHA class III–IV	12 (27.9)
Proportion on anticoagulants	11 (25.6)
Mean LVEF (%)	60.67 ± 8.73
Mean Wilkins score	8.63 ± 0.93
Mean RVSP (mmHg)	56.37 ± 21.60
Mean LA diameter (mm)	51.39 16 ± 8.98
Mean mitral valve area (cm^2)	0.89 ± 0.19
Mean transmitral pressure gradient (mmHg)	15.66 ± 4.25
Mean TAPSE	16 ± 2.93

NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; LA, left atrium.

The mean right ventricular systolic pressure derived from the tricuspid regurgitation velocity jet was 56.37 ± 21.60 mmHg. About a quarter were in NYHA functional class III–IV and nine (16.7%) had reduced left ventricular ejection fraction (LVEF). The mean mitral valve area was 0.89 ± 0.19 cm^2 and the mean transmitral pressure gradient was 15.66 ± 4.25 mmHg. The mean tricuspid annular plane systolic excursion (TAPSE) was 16 ± 2.93 (Table 1).

TTE was done on all patients while TEE was done on 29 patients (Table 2). Nine patients were in AF, of whom three patients had LA thrombus. Only one of these patients had detectable left atrial thrombus on TTE while the other

Table 2. Characteristics of the patients evaluated for PBMV (n = 43)

Case no	*Age*	*Gender*	*Wilkins score*	*ECG rhythm*	*TTE LA thrombus*	*TEE LA thrombus*	*Spontaneous echo contrast*	*Disposal*	*Status*
1	16	F	8	Sinus	No	No	No	PBMV	Done
2	62	F	8	AF	Yes	–	Yes	PBMV	Re-scheduled†
3	42	F	8	AF	No	No	No	MVR*	Done
4	28	F	8	Sinus	No	No	No	PBMV	Failed
5	30	F	8	Sinus	No	–	No	PBMV	On waiting list
6	18	F	8	Sinus	No	–	No	PBMV	On waiting list
7	20	F	8	Sinus	No	–	No	PBMV	On waiting list
8	35	F	8	Sinus	No	No	No	PBMV	Done
9	42	F	8	AF	No	Yes	Yes	PBMV	Re-scheduled†
10	43	F	8	Sinus&	No	No	Yes	PBMV	On waiting list
11	19	M	8	Sinus	No	No	No	MVR#	Scheduled
12	25	F	8	Sinus	No	-	No	PBMV	On waiting list
13	35	F	8	Sinus	No	No	No	PBMV	Done
14	49	F	8	AF	No	–	No	PBMV	On waiting list
15	11	F	8	Sinus	No	–	No	PBMV	Died before op
16	19	M	8	Sinus	No	–	No	PBMV	On waiting list
17	20	F	8	AF	No	–	No	PBMV	On waiting list
18	62	M	8	AF	No	–	No	MVR*	Scheduled
19	19	M	8	Sinus	No	No	No	MVR*	Done
20	13	F	8	Sinus&	No	No	Yes	PBMV	Died before op
21	17	F	8	Sinus&	No	No	Yes	PBMV	Failed
22	33	F	8	Sinus	No	Yes	Yes	MVR*	Done
23	39	F	8	Sinus	No	Yes	Yes	MVR*	Scheduled
24	30	F	8	Sinus	No	-	No	PBMV	On waiting list
25	31	F	9	Sinus	No	No	No	PBMV	Done
26	16	M	9	Sinus	No	–	No	PBMV	On waiting list
27	24	F	9	Sinus	No	No	No	PBMV	Done
28	47	F	9	AF	No	No	Yes	PBMV	Done
29	68	F	9	AF	No	No	Yes	MVR#	Done
30	45	F	9	Sinus	No	No	Yes	PBMV	Done
31	48	F	9	Sinus&	No	No	Yes	PBMV	Died before
32	42	F	9	Sinus&	No	No	Yes	PBMV	Done
33	49	F	9	AF	No	Yes	Yes	MVR*	Scheduled
34	45	F	9	Sinus	No	No	No	MVR*	Done
35	60	M	9	Sinus	No	–	No	MVR*	Done
36	61	F	9	Sinus	No	No	No	MVR*	Done
37	15	F	10	Sinus	No	–	No	PBMV	On waiting list
38	28	F	10	Sinus&	No	No	Yes	MVR*	Done
39	16	F	10	Sinus	No	No	No	MVR*	Done
40	20	M	10	Sinus&	No	No	Yes	PBMV	Done
41	17	M	11	Sinus&	No	No	Yes	PBMV	Done
42	35	F	11	Sinus&	No	No	Yes	MVR*	Done
43	20	M	12	Sinus	No	No	No	MVR*	Scheduled

ECG, electrocardiography; TTE, transthoracic echocardiography; TEE, transoesophageal echocardiography; LA, left atrial; AF, atrial fibrillation; PBMV, percutaneous ballooon mitral valvuloplasty; MVR, mitral valve regurgitation.
*Unfavourable anatomy, #unfavourable clinically, &smoke in normal sinus rhythm, †LA thrombus alone.

two patients required TEE for detection. Fig. 4 shows the echocardiography of a patient with a left atrial thrombus in AF.

As depicted in Table 2, 34 patients were in normal sinus rhythm, of whom two patients had left atrial thrombus on TEE but not on TTE. These two patients with normal sinus rhythm had left atrial volume index (LAVI) of 88 and 90 ml/m^2, respectively. Nine patients in normal sinus rhythm had left atrial spontaneous echo contrast (LASEC) of moderate to severe intensity (Fig. 5). The mean left atrial size for the occurrence of spontaneous echo contrast was 55.34 ± 11.24 mm. All patients with left atrial thrombus had associated LASEC.

A careful evaluation revealed that 15 patients had unfavourable anatomical characteristics characterised by: bi-commissural calcification (four patients), ≥ grade 2/4 mitral regurgitation (six patients), high scores and left atrial thrombus (three patients), and left atrial thrombus (two patients). Two patients had unfavourable clinical characteristics (severe pulmonary hypertension). Among these, 10 underwent mitral valve replacement (MVR), five were on schedule for MVR, and two (with left atrial thrombus) were re-scheduled for PBMV. Three patients died before the planned PBMV, presumably due to progressive heart failure. Eleven patients were on a waiting list for PBMV (Table 2).

Table 3 shows the individual outcomes of patients who underwent PBMV. The procedure was done in 12 patients, of whom 10 (83.3%) were successful. There were no immediate post-procedural complications. The two patients in whom the procedure failed had a score of 8 each. Of the two failures, one was a problem with septal puncture and the other one was due to difficulties crossing the mitral valve orifice.

Table 4 shows the MVA improvement and the haemodynamic changes produced by PBMV. The mean pre-PBMV was 16.03 ± 5.52 mmHg and the mean post-PBMV was 3.08 ± 0.44 mmHg ($p < 0.001$). PBMV resulted in a significant decrease in mitral gradient, left atrial and pulmonary arterial pressures and an increase in the MVA. There was a significant symptomatic improvement among all patients, attaining NYHA functional class I.

With regard to the Wilkins score, improvements in MVA by planimetry in the two groups [1.6 (0.88) vs 1.63 (1.88), $p = 1.00$] and in haemodynamics, such as mitral gradient [8.5 (2.6) vs 14

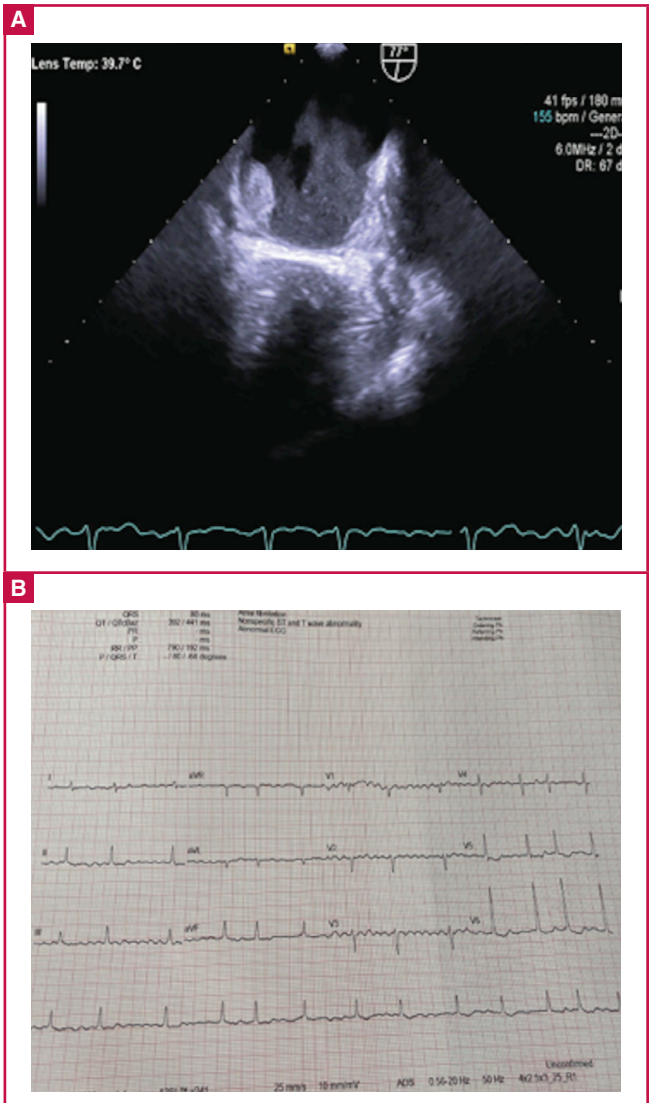

Fig. 4. Echocardiographic and electrocardiographic images taken from a patient with left atrial thrombus (A) in atrial fibrillation (B).

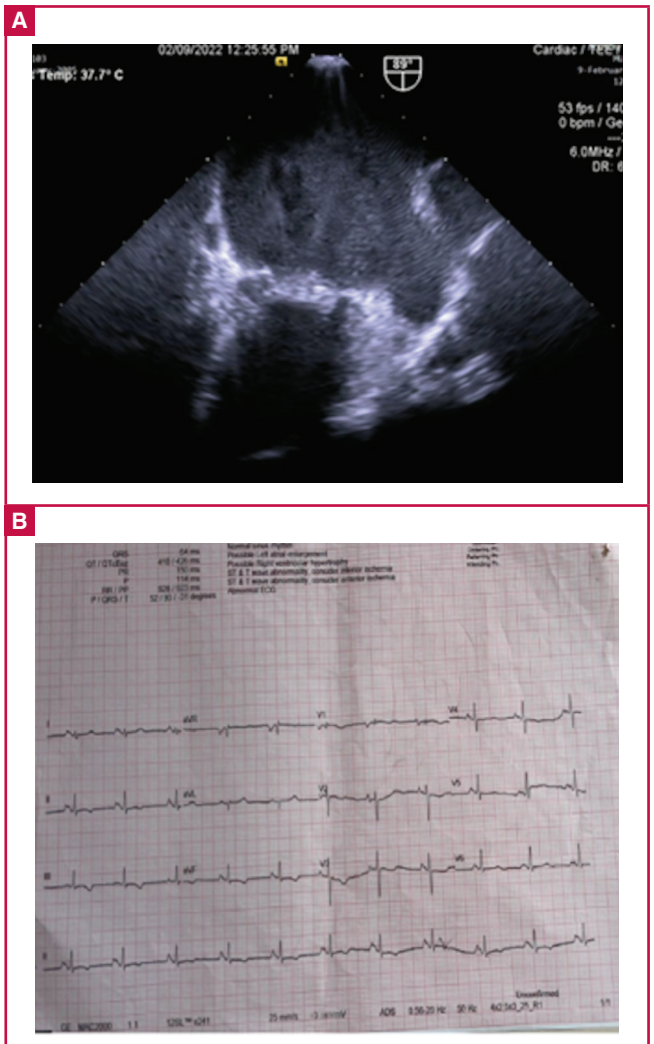

Fig. 5. Echocardiographic and electrocardiographic images taken from a patient with left atrial severe spontaneous echo contrast 'smoke' (A) in normal sinus rhythm (B).

Table 3. Outcome of patients who underwent PBMV at JKCI from August 2019 to May 2022 (n = 12).

Case no	*Wilkins score*	*LA size (mm)*	*Pre-PBMV transmitral gradient (mmHg)*	*Post-PBMV transmitral gradient (mmHg)*	*Pre-PBMV MR*	*Post-PBMV MR*	*Compli-cations*
1	8	44	11	3	Trace	Mild	None
4	8	46	14	–	Mild	–	Failed
8	8	46	14	3.5	Trace	Mild	None
13	8	44	12	3	Trace	Mild	None
21	8	58	16	-	Trace	–	Failed
25	9	60	21.2	3.5	Mild	Mild	None
27	9	46	10.9	3	Trace	Mild	None
28	9	50	10	2	Mild	Mild	None
30	9	47	17	3	Mild	Mild	None
32	9	45	18.2	3	Mild	Mild	None
40	10	42	12	3	Mild	Mild	None
41	11	58	28	3.4	Mild	Mild	None

PBMV, percutaneous ballooon mitral valvuloplasty; LA, left atrial; MR, mitral regurgitation. – Not done.

Table 4. Comparison of pre- and post-PBMV parameters of patients who underwent successful PBMV at JKCI from August 2019 to May 2022 (n = 10).

Parameter	*Pre-PBMV*	*Post-PBMV*	p-*value*
Mean mitral valve area (cm^2)	0.87 ± 0.16	2.25 ± 0.46	< 0.001
Mean mitral valve pressure gradient (mmHg)	16.03 ± 5.52	3.08 ± 0.44	< 0.001
Mean left atrial pressure (mmHg)	22.66 ± 3.89	8.00 ± 2.31	< 0.001
Mean pulmonary arterial pressure (mmHg)	38.40 ± 13.59	33.50 ± 11.29	< 0.001

PBMV, percutaneous ballooon mitral valvuloplasty.

Table 5. Pre- and post-PBMV median (range) differences in improvement between groups

	Wilkins score		
Variable	*≤ 8 (n =3)*	*9–11 (n = 7)*	*p-value*
MVA improvement (cm^2)	1.60 (0.88)	1.63 (1.18)	1.000
MV gradients improvement (mmHg)	–8.50 (2.60)	–14.00 (16.60)	0.117
LAP improvement (mmHg)	–2.00 (2.00)	–4.00 (8.00)	0.117
PAP improvement (mmHg)	–5.00 (6.00)	–2.00 (20.00)	0.517

MVA, mitral valve area; MV, mitral valve; LAP, left atrial pressure; PAP, pulmonary artery pressure; PBMV, percutaneous balloon mitral valvuloplasty.

(16.6), $p = 0.117$], left atrial pressure [2 (2) vs 4 (8), $p = 0.117$] and pulmonary artery pressure [5 (6) vs 2 (20), $p = 0.517$] were similar, as shown in Table 5.

In the two mission visits, four local interventional cardiologists were supervised in performing PBMV. Fig. 6A shows the local team performing PBMV at JKCI catheterisation laboratory in May 2022. Fig. 6B shows the balloon inflated across the mitral valve.

Discussion

This single-centre, prospective study reports the first investigation of patients' eligibility for PBMV and the immediate post-PBMV outcomes in Tanzania. The study further defines the role of the heart team and training/skills transfer in PBMV interventions. Lastly, we highlight the presentation of female gender in RHD.

The main findings are: (1) TEE is mandatory in pre-PBMV screening to rule out left atrial thrombus as TTE does not always detect it, and for procedural guidance; (2) the ESC and AHA/ACC guidelines[14,15] need reconsideration for a good outcome of PBMV (cut-off Wilkins score ≤ 8). In our cohort, patients with Wilkins score of up to 11 underwent successful procedures; (3) PBMV had good short-term outcomes in the selected patients,

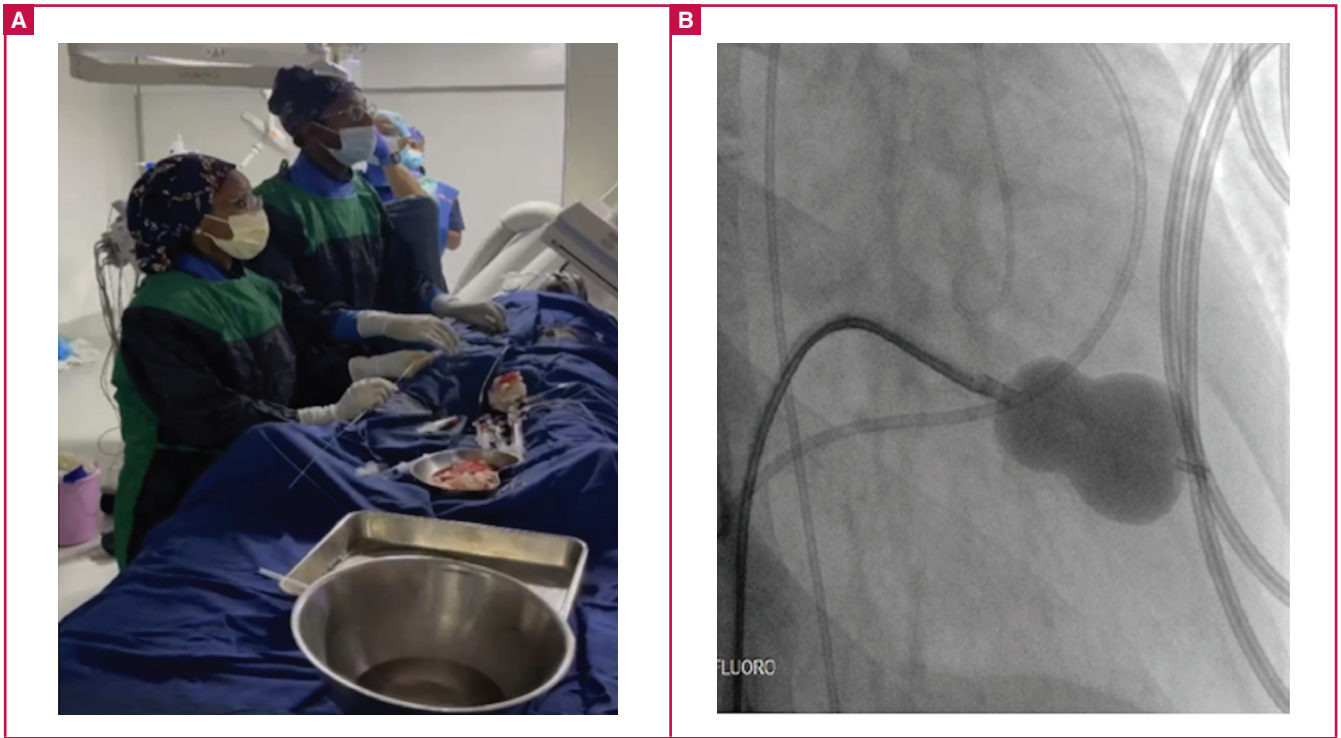

Fig. 6. A photograph showing the local team performing PBMV (A) and the balloon inflated across a stenosed rheumatic mitral valve (B).

which underscores the importance of appropriate patient selection in a multidisciplinary valvular heart team; and (4) in Tanzania, MS has a female predominance with presentation early in life.

These findings are encouraging and lower the bar for performing PBMV in a large group of RHD-MS patients, given its short procedural time and short recovery period allowing the patient to return to family or work more promptly if needed. Our findings are an example of well-planned development, which if sustained, can make significant differences in the diagnosis, treatment and outcomes of patients with rheumatic MS in LMICs.

In this study, left atrial thrombi were present in five patients, four of which could not be detected with a TTE but only with a TEE. This finding highlights the importance of pre-PBMV TEE. Similarly, other studies have reported that the sensitivity of TTE in detecting a thrombus in the left atrium or its appendages (posteriorly located) in patients with RHD was 32–50%.[23,29] The sensitivity and specificity of TEE in identifying left atrial thrombi was 99% in another study.[29]

Among patients with left atrial thrombus, two were in normal sinus rhythm (their left atrial volume indexes were 88 and 90 ml/m^2). It is possible that these patients in sinus rhythm may have experienced paroxysmal AF owing to the dilated left atrium. In this cohort, one patient with left atrial thrombus had a history of stroke. Similarly, previous studies have shown the risk of arterial–systemic embolism is increased by left atrial thrombus and LASEC, particularly in left atrial thrombi with irregular surfaces and LASEC with moderate to severe intensity.[23,30-33]

In our study, all patients with left atrial thrombus had associated LASEC. Previously, it has been reported that LASEC increased the risk of left atrial thrombi and hence the expression 'when there is smoke, there is fire'.[34,35] In this study, nine patients in normal sinus rhythm had moderate- to severe-intensity left atrial spontaneous echo contrast (so-called 'smoke'). The mean size of the left atrium for the occurrence of LASEC was 55.34 ± 11.24 mm.

Left atrial thrombus (and ≥ grade 2/4 mitral regurgitation, bilateral commissural fusion) absolutely contra-indicate eligibility for PBMV.[14,15] However, depending on certain clinical circumstances, experienced operators may deviate from these guidelines.[23] For example, the approach for patients with left atrial thrombus is controversial.[11] While most operators agree with the ACC/AHA guidelines to avoid PBMV,[14,15] others argue that the risk of dislodging a thrombus is reduced by the low profile and manoeuverability of the Inoue balloon when done in experienced hands.[36]

Indications for anticoagulation are: history of systemic embolism, thrombus in the left atrium, prosthetic heart valve, AF or left atrium > 50 mm diameter/left atrium volume > 60 ml/m^2.[14,15] However, controversy exists on whether patients with rheumatic MS in normal sinus rhythm based on enlarged left atrium or LASEC should be anticoagulated.[14,15,37,38] Patients with left atrial thrombus should be given a four-to-six-week pre-PBMV treatment with warfarin.[11]

There is an unmet need for alternative anticoagulation strategies (apart from vitamin K antagonists) in patients with moderate to severe MS and prosthetic heart valves because the new oral anticoagulants are neither safe nor effective, as evidenced by the Randomized Evaluation of Dabigatran in Patients after Heart Valve Replacement (RE-ALIGN) trial.[39] Indeed, the INVestigation of rheumatiC AF Treatment (INVICTUS) trial results, which have just been published, have shown that rivaroxaban is outmatched by vitamin K antagonists for rheumatic AF.[40]

Findings from the INVICTUS trial underscore a need to improve anticoagulation control in LMICs, for instance, by ensuring the availability of point-of-care international normalised ratio (INR) devices at different levels of health facilities, including primary healthcare. Currently, in sub-Saharan Africa, there are great challenges with anticoagulation, with wide variation in its use and time in the therapeutic range of 27–56%.[41,42]

In our study, the mean Wilkins score was 8.6 ± 0.9, with a range of 8–12. Seven patients had a score ≥ 10, implying an 'unfavourable' Wilkins score. However, we obtained successful results in 10/12 patients with no immediate post-procedural complications. The improvement in the MVA and haemodynamics were similar between patients with Wilkins scores ≤ 8 and those with scores of 9–11. Similarly, previous studies[13,43,44] have shown that in a population of young patients or those with fewer co-morbidities, PBMV gave a better survival rate despite an unfavourable Wilkins score (mean score of 9.5).

In our cohort, the patients were young and with no co-morbidities. That is an important observation in selecting a candidate for PBMV, as it should not solely rely on Wilkins score. In addition, Almeida *et al.*[45] have reported that PBMV is safe and effective in patients with rheumatic MS in patients with Wilkins scores ≤ 8 and 9–11; and with similar improvement in the MVA. Recently, Carvalho *et al.*[46] reported no difference in all-cause/composite of all-cause mortality between the two groups after a follow up of 10 years.

Another study from Khartoum by Suliman *et al.*[47] that comprised patients with an average Wilkins score of 9 showed good immediate PBMV outcomes, similar to our findings. In its original description, a Wilkins score ≥ 12 predicted poor results with PMBV.[8] In one large analysis, approximately 60% of patients with Wilkins scores 9–11 achieved a successful result with PMBV.[48] Wilkins score ≥ 12 achieved significant improvement in MVA, although full success was uncommon (30%).

PBMV relies on the mechanism of commissural splitting.[14,15] The ideal valve anatomy would have commissural fusion, pliable leaflets and limited subvalvular apparatus calcification.[23] If there is minimal commissural fusion, a successful result is unlikely.[8] In patients with RHD, commissural fusion is the hallmark. On the contrary, in the Western world, most patients with significant MS are older with degenerative, calcified, less-pliable leaflets, making PBMV unsuitable.[14,23]

Our study showed that PBMV has good short-term outcomes in selected patients. In countries where RHD is endemic, PBMV is an alternative to mitral valve surgery, offering a similar survival rate despite a lower event-free duration, and its main advantage over surgery is the lower cost. Ambari and his colleagues[48] have recently presented survival data of patients with rheumatic MS after PMBV in a LMIC, showing that PBMV was non-inferior to mitral valve surgery in terms of survival.

On the contrary, in high-income countries, PBMV is still performed occasionally, not only because of the lower incidence of RHD but also because they are strict with the scoring system in selecting appropriate patients predicting safety and success.[49]

Furthermore, in high-income countries there is a higher level of skill and techniques among cardiothoracic surgeons, such as using minimally invasive techniques, which have been shown to provide quick recovery and long-term survival.[50]

PBMV is important in an LMICs where haemodynamically severe MS presents earlier in life, and young patients have thickened valve leaflets, presenting with or without concurrent regurgitation.[51] It is also a bridging therapy to open-heart surgery for MS patients during pregnancy, postponement of valvular replacement for women to finish their childbearing time (in avoidance of anticoagulation), or in patients who cannot withstand open-heart surgery, such as those with significant co-morbidities, frail elderly, irreversible pulmonary hypertension and severe left ventricular systolic dysfunction.[8,11] Apart from the risk imposed by warfarin on pregnancy, managing a patient with a mechanical heart valve in resource-constrained countries is challenging in terms of anticoagulants and monitoring of the INR.[52,53] Other advantages are those related to its lower cost, lower morbidity rate, and lower procedure-related mortality rate.[6,19,21,22,54]

In the current study, among the 12 patients who underwent PBMV, five (41.7%) had a Wilkins score ≤ 8 and seven (58.3%) had a score of 9–11. There was a procedural technical failure in two patients, both of whom had a score of 8. This implies that the success of PBMV is not solely dependent on the score. In one patient there was a failure to cross a severely stenosed valve, and failure of septal puncture in the second.

Similarly, previous studies have reported the failure rate ranging from one to 17%.[55] The often-reported causes of failure are the inability of atrial septal puncture or to correctly position the balloon across the valve.[55] Unfavourable anatomy such as predominant subvalvular stenosis or severe valve stenosis can also result in failures.[55] Usually, the commonest reason for failure to cross the valve is when the septal puncture is either too posterior or too anterior.

In our cohort, these procedures were done under the supervision of experienced operators and TEE guidance, and therefore the techniques were correct. In a patient in whom we failed to puncture the septum despite correct positioning of a sharp Brockenbrough needle at the fossa ovalis, we speculate that could have been due to the extended rheumatic/inflammatory process involving the septum. In the second patient in whom we failed to cross the mitral valve orifice despite attempting several manoeuvres, the huge left atrium could have been the reason.

Intracardiac echocardiography (ICE) is nowadays considered the imaging modality of choice to guide puncture of the septum, however, the device is expensive, hence limiting its application in most settings.[55] Recent studies suggest improved visualisation of the septum and assessing of tenting during puncture of the septum by use of the real-time 3D TEE.[55] One of the failed PBMV in our cohort was converted to mitral valve surgery and the other one was on the waiting list for the same. Ten patients who underwent a successful PBMV were on a regular clinical follow up.

Our findings are important to Africa as a whole because Tanzania, being the host of the East African Centre of Excellence for Cardiovascular Sciences (EACoECVS), identified RHD as a priority disease due to its high morbidity and mortality rates in Africa.[2,56,57] Therefore, the lessons learnt will be useful to the East African community and the rest of Africa. The strategies of involving the heart team in selecting patients and eventual steps resulted in good short outcomes among patients who underwent PBMV.

Our collaboration with the USA, which was implemented in Uganda a few years ago, albeit a different approach, proved to be effective.[58] Similarly, several approaches to enhance PBMV skills in Africa have been suggested, for instance, using 3D and 4D echocardiography.[47] This is because 3D echocardiography has been shown to assess the mitral valve anatomy with accuracy, and guide atrial septal puncture, giving a clinician a better view to provide good PBMV outcomes.[55,59,60] However, the high cost of balloons in resource-limited countries and the setting where many patients do not have health insurance needs consideration. In this study, half of the patients had a monthly income of less than 42$. Activity such as a recent PBMV workshop alongside the Tokyo International Conference on African Development (TICAD 8) in Tunisia, whereby one young cardiologist per African country was supported to attend, is an example of a forum to discuss challenges related to PBMV in Africa.[61]

In our study, there was a female predominance (74.4%). Similarly, other previous RHD studies[62–70] have shown that the disease is more common in females than males. The reasons for these differences are not known.[65,71,72] Intrinsic factors such as genetically mediated immunological factors that predispose women to autoimmune disease have been implicated.[73] Extrinsic factors, such as child-rearing, which might result in repeated exposure to group A streptococcus and limited access to healthcare, where males are given more priority than females when they fall ill, also have been implicated.[71,72]

Recently, prothymosin-alpha has been associated with a potential mediator of gender predisposition in RHD.[74] In the current study, two female patients aged 11 and 13 years presented with symptomatic rheumatic MS at six and eight years, respectively. Similarly, other studies report that MS in Africa shows a female predominance with presentation in early life.[3,4] These findings underscore a need for screening (as a cost-effective measure) for sub-clinical RHD among the at-risk population, as recommended by the World Heart Organisation (WHO), as an effective way to detect the disease at an early stage when secondary prophylaxis can be administered.[75]

A recent publication of a clinical trial from Uganda confirmed the prevention of progression of sub-clinical RHD disease among children given secondary prophylaxis.[76] In the current study, four (9.3%) patients were first diagnosed with RHD during pregnancy. They all had uneventful spontaneous vertex deliveries before intervention. Similarly, other African studies have shown that it is not uncommon to discover patients with RHD during pregnancy and delivery, most presenting with heart-failure symptoms.[42,77] In Africa, RHD in pregnancy is increasingly being detected, accounting for up to 30% of heart diseases in pregnancy and it is associated with poor outcomes for the mother and baby.[42,78,79]

The 2018 ESC guidelines on the management of cardiovascular diseases during pregnancy recommend performing risk assessment in all women of childbearing age with cardiac diseases using the modified WHO classification (class I–IV) of maternal risk.[80] Pregnancy is contra-indicated in patients who fall into class IV. Another important observation from this study is that most of the patients recruited in the TAMS study came from the northern zone of the country. Similarly, anecdotal data

shows that RHD is prevalent in the northern part of Tanzania. However, this observation needs proper investigation in disease mapping as it could be a potential source of information for use in preventative measures.

Strengths and limitations

The study has several advantages. First, being a prospective study, there was a potential for follow up of these patients. Second, it provides baseline data for future comparisons. Third, lessons learnt could benefit the East African region and beyond. However, the small sample size did not allow detailed analysis. Nevertheless, we have described several parameters known to influence PBMV outcomes.

Owing to the possible effect of the small number of patients who underwent PBMV on skills transfer to the local team, our team has several strategies. First, to continue collaborating with the visiting team; the latest mission was conducted from 23 to 26 October 2022 in which five PBMV were performed. Second, two cardiologists will be going to Cleveland, USA, for a six-month visit in order to strengthen their skills. This approach has been done in Uganda and proved to be successful.[58] Third, our catheterisation laboratory is equipped with a system that is supporting remote proctoring of interventional procedures. This will allow ongoing supervision of a local team by our collaborators. Lastly, our team was involved in the Africa PBMV workshop held in Tunisia from 24 to 25 August 2022.[61] The workshop aimed at building sustainable PBMV programmes across African countries.

Conclusion

TEE should be carried out on all patients before PBMV to rule out left atrial thrombus. Despite a higher Wilkins score, PBMV can be completed successfully in patients with rheumatic MS who have been carefully screened by the heart team. Patients in AF and with a left atrium > 55 mm should be anticoagulated. The ESC and AHA/ACC guidelines (Wilkin score ≤ 8) for a good outcome of PBMV need reconsideration. PBMV services should be available in catheterisation laboratories in Africa. Enhancing and consolidating PBMV skills among the local team should be undertaken.

Our findings are an example of a well-planned development that, if sustained, can make significant differences in the diagnosis, treatment and outcomes of patients with rheumatic MS in low- and middle-income countries.

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