Outcomes of Aortic Regurgitation After Percutaneous Transmitral Commissurotomy: Prospective Cohort

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Abstract

PURPOSE: The combined mitral stenosis (MS) and aortic regurgitation (AR) impose opposite loading conditions on the left ventricle. Physiologically, the relief of MS may increase the severity of AR.

METHODS: Participants were Filipinos 19 years or older, admitted because of severe MS with mild to moderate AR. The outcome of percutaneous transmitral commissurotomy (PTMC) was divided into two groups: (1) significant AR that included the increase in severity of AR: mild to moderate/severe or moderate to severe AR, and (2) the insignificant AR group, which included any decrease in the severity of AR: moderate to mild or persistence of mild or moderate AR. These groups were compared from baseline, 24 hours, 1 month, and 6 months using the same echocardiographic parameters. The numerical data between significant and insignificant tricuspid regurgitation were compared using nonparametric Mann-Whitney *U* test and categorical data using the χ^2 test.

RESULTS: A total of 43 participants were analyzed. At 24 hours post-PTMC, the significant AR group had significantly lower left ventricular end-diastolic dimension (3.83 vs 4.5, $P = 0.008$), left ventricular end-systolic dimension (2.33 vs 2.97, $P = 0.017$), right ventricular fraction area change (38.6 vs 48.7, $P = 0.025$), and left ventricular outflow tract (1.66 vs 2.02, $P = 0.020$) and higher systolic pulmonary arterial pressure (57 vs 32.4, $P = 0.008$). At 1 and 6 months, there were no significant differences in echocardiographic parameters between the significant and insignificant AR groups' left ventricular end-diastolic dimension (4.58 vs 4.5, 4.64 vs 4.57), left ventricular end-systolic dimension (3.1 vs 2.9, 2.9 vs 2.91), and systolic pulmonary arterial pressure (28 vs 34.7, 33.8 vs 32.4). Those with significant AR had a higher mean Wilkin score (mean, 10; $P = 0.007$) and subvalvular thickening (mean, 2.6; $P = 0.005$).

CONCLUSION: On short-term follow-up, the presence of mild to moderate AR before PTMC does not lead to severe AR. The outcomes regardless of the group showed a good functional class and no significant echocardiographic differences when compared.

KEYWORDS: rheumatic heart disease, mitral stenosis, percutaneous transmitral commissurotomy

INTRODUCTION

Rheumatic heart disease is prevalent in our country according to the Philippine Heart Association. It is seen in 1 to 2 per 1000 Filipinos. This reflects young individuals affected with the disease that may progress during adulthood if left untreated.[1] The mitral and aortic valves are most commonly affected. Approximately half of the patients with rheumatic mitral stenosis (MS) have some degree of aortic regurgitation (AR).[2] This combined multivalve lesion imposes an opposite loading condition on the left ventricle (LV).[3] Both left ventricular end-diastolic and end-systolic volumes are lower in combined MS and AR than with isolated AR.[4] Therefore, the increase in stroke volume typically associated with AR might be blunted in the presence of MS, and the clinical signs associated with increased pulse pressure might not be observed.[5] It is speculated that relieving the MS would increase the severity of AR. In a local unpublished retrospective study performed at the Philippine Heart Center, patients who underwent percutaneous transmitral commissurotomy (PTMC) due to severe MS with trivial to moderate AR, an abnormal left atrial volume index (LAVI), concomitant aortic stenosis, and mild AR were associated with composite outcomes of major adverse clinical events, valvular surgery, and development of infective endocarditis on phone call follow-up.[6] However, international retrospective studies showed that rheumatic MS with concomitant AR does not influence procedural success and inferior outcomes.[2,7,8] Therefore, this group of patients is a good candidate for PTMC. The gap in evidence concerning combined MS and AR can be addressed by providing more data on the natural history and impact of the intervention on the clinical and echocardiographic outcomes to better define our local indications for PTMC.

The aim of this study was to compare the clinical and echocardiographic parameters among significant and insignificant AR after PTMC.

METHODS

The design is a prospective cohort study, that included all patients 19 years or older with rheumatic MS admitted at the Philippine Heart Center between January 2019 and October 2020 for PTMC due to symptomatic severe MS and concomitant mild to moderate AR with or without other associated valve lesions. Baseline clinical characteristics, anthropometric data, functional capacity, and two-dimensional transthoracic echocardiogram with Doppler (2DED) were obtained before the PTMC within admission after 24 hours, on outpatient at 1 and 6 months. An echocardiographic machine was used, using the latest Siemens model, and certified echocardiography sonographers performed the procedure. A sole designated level III echocardiographer served as the reader of the 2DED studies. The participants were asked to follow up using a phone call to arrange the meeting, with a window period of 1 week from the time of the original schedule for checkup and outpatient 2DED in our institution. The outcome of PTMC was divided into two groups: the significant AR group, which included any increase in severity of AR: mild to moderate/severe or moderate to severe AR, and the insignificant AR group, which included any decrease in severity of AR: moderate to mild or persistence of mild or moderate AR. These groups were compared from baseline, 24 hours, 1 month, and 6 months using the same echocardiographic parameters. For participants who were not able to follow up in our institution for checkup and outpatient 2DED, the 2DED evaluation is forfeited; however, they were asked to follow up with their local internal medicine specialist or cardiologist for assessment of functional capacity and anthropometric data. The approach and grading of valve lesions were based on established international guidelines.[9,10]

In this study, there are two groups: significant AR, which included increase in severity of AR: mild to moderate/severe or moderate to severe after PTMC, and insignificant AR, which included decrease in severity of AR: moderate to mild or persistence of mild or moderate AR after PTMC.

Data Organization, Editing, Processing, and Analysis

The data obtained were checked for completeness and categorized into four types per period of 24 hours, 1 month, and 6 months using Microsoft Excel (version 16.30; Microsoft Inc, Redmond, Washington):

(1) echocardiographic parameters of significant AR
(2) echocardiographic parameters of insignificant AR
(3) clinical characteristics of significant AR
(4) clinical characteristics of insignificant AR

The rechecking of data was done twice to ensure correctness and validity.

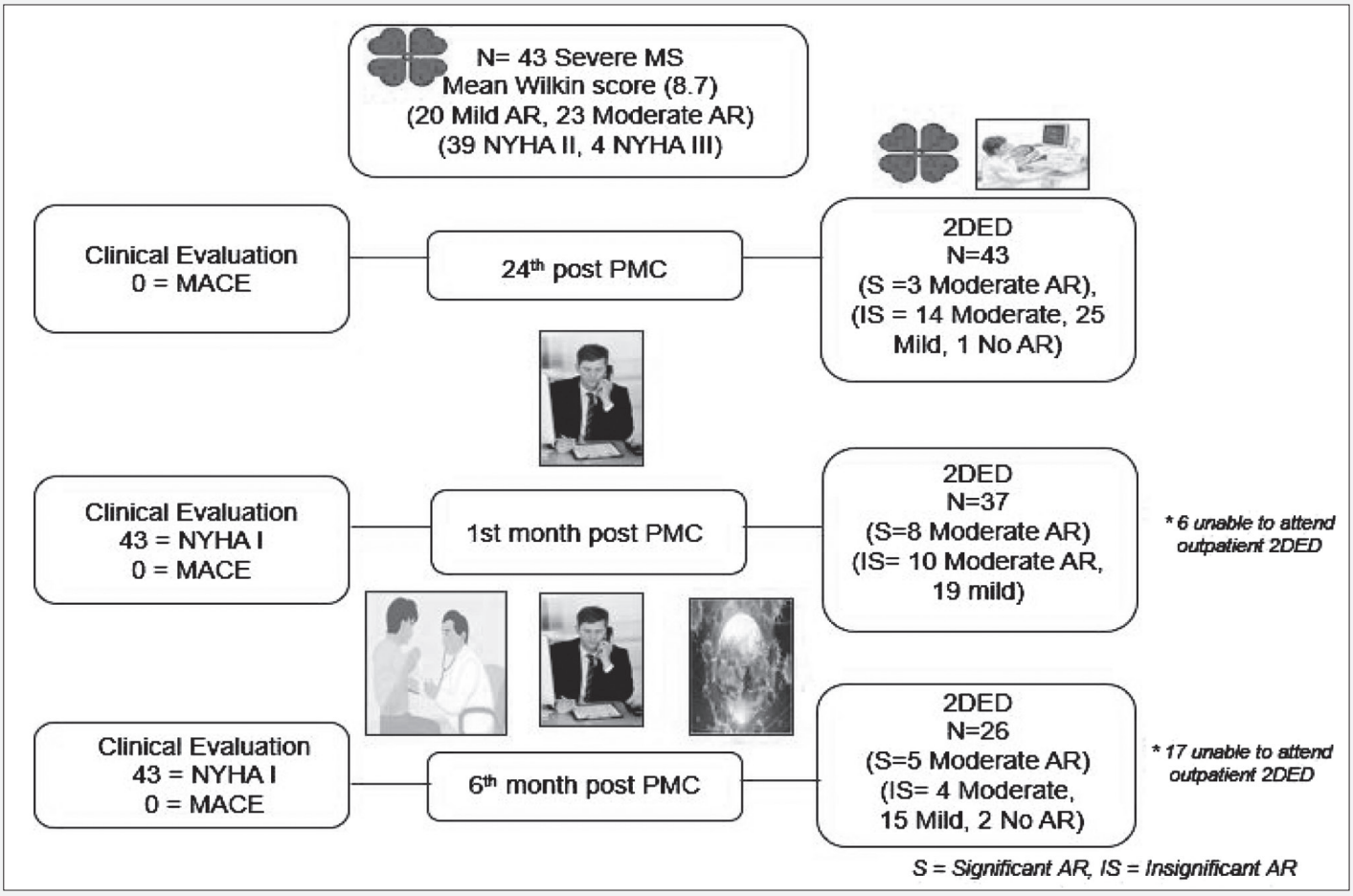
Statistical Analysis

All analyses were done using the Statistical Package for the Social Sciences (version 23; SPSS, Chicago, Ill). Numerical data are summarized as means and with their SD and interquartile ranges, whereas categorical data are presented as percentages. Comparison of numerical data between significant and insignificant valvular categories was done using nonparametric Mann-Whitney *U* test. Categorical data were compared using χ^2 test. All *P* values less than 0.05 were considered statistically significant. A minimum of 91 patients were required for this study based on prevalence of AR,[6] 10% half-width of confidence interval, and 5% level of significance.

RESULTS

From 2019 to 2020, the institution documented a total of 43 cases of severe MS with mild to moderate AR for PTMC (Figure 1). Their clinical profile is summarized in Table 1. The mean age was 40 ± 10.2 years, with female predominance (72.1%), mostly classified as New York Heart Association (NYHA) II (90.7%). More than half had sinus rhythm (51.2%), and (48.8%) had atrial fibrillation. The majority had a normal body mass index (79.1%). Three cases had a previous PTMC. The average interval time from diagnosis to the procedure is 26.5 months. Eight cases suffered a previous stroke (18.6%). The average total Wilkin score was 8.7. The mean scores for leaflet mobility,

Figure 1. Study flowchart



valve thickness, valvular subcalcification, and subvalvular thickening are displayed in Table 1.

The baseline echocardiographic parameters measured prior to PTMC showed normal mean values of left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left ventricular mass index, left ventricular relative wall thickness, right atrial volume index, right ventricular fraction area change, right ventricular dimension mid, pulmonary valve annulus, tricuspid valve annulus, left ventricular outflow tract (LVOT), and right ventricular outflow tract. The mean values of LAVI, pulmonary artery (PA) pressure, and mitral valve (MV) gradient were elevated, whereas MV planimetry is small as displayed in Table 2.

The echocardiographic parameters measured 24 hours post-PTMC showed that those with significant AR had statistically lower LVEDD (mean, 3.8 vs 4.5; $P = 0.008$), lower LVESD (mean, 2.33 vs 2.97; $P = 0.017$), lower right ventricular fraction area change (mean, 38.6 vs 48.7; $P = 0.025$), and lower LVOT readings (mean, 1.66 vs 2.02; $P = 0.020$). The PA pressure was higher (mean, 57 vs 32.4; $P = 0.008$) (Table 3).

The echocardiographic parameters measured 1 month post-PTMC showed that there was no significant difference in the parameters between those with significant AR and those with insignificant AR (all $P > 0.05$) (Table 4).

The echocardiographic parameters measured 6 months post-PTMC did not significantly differ between significant and insignificant AR. (all $P > 0.05$) (Table 5).

A comparative profile of cases of the baseline characteristics and the initial classification of significant and insignificant AR on 2DED at 24 hours post-PTMC to the clinical characteristics at 6 months was made (Figure 2). Those with insignificant AR had a statistically higher mean total Wilkin score (mean, 10 vs 8.6; $P = 0.007$), especially the score for subvalvular thickening (mean, 2.6 vs 2.1; $P = 0.005$). No differences were noted between the two groups in terms of age, sex distribution, NYHA classification, rhythm, height, weight, body mass index, previous PTMC, duration of time from diagnosis to PTMC, and the history of stroke (all $P > 0.05$).

Table 1. Baseline Characteristics of Severe Symptomatic Mitral Stenosis With Mild to Moderate Aortic Regurgitation, Philippine Heart Center, 2019–2020

	Frequency (%); Mean ± SD; Median (IQR)
Age, y	40 ± 10.2 (41)
Sex	
Male	12 (27.9)
Female	31 (72.1)
NYHA	
I	0
II	39 (90.7)
III	4 (9.3)
IV	0
Rhythm	
Sinus rhythm	22 (51.2)
Atrial fibrillation	21 (48.8)
Height	1.58 ± 0.08 (1.57)
Weight	55.6 ± 9.8 (55)
Body mass index	
Underweight	3 (7)
Normal	34 (79.1)
Overweight	6 (14)
Obese	0
Previous PTMC	3 (7)
Diagnosis to PTMC time, mo	26.5 ± 28.3 (12)
History of stroke/TIA	8 (18.6)
Wilkins score	8.7 ± 0.88
Leaflet mobility	2.1 ± 0.2
Valve thickness	2.2 ± 0.4
Valvular calcification	2.2 ± 0.4
Subvalvular thickening	2.1 ± 0.3

Percentage values in parentheses reflect vertical sum; IQRs are enclosed in parentheses after the mean.
IQR=interquartile range; NYHA=New York Heart Association; PTMC=percutaneous transmitral commissurotomy; TIA=transient ischemic attack.

Table 2. Baseline Echocardiographic Data of Severe Mitral Stenosis With Mild to Moderate Aortic Regurgitation, Philippine Heart Center, 2019–2020

	Mean	SD
No. of patients	43	—
Left ventricular end-diastolic dimension, cm	4.4	0.56
Left ventricular end-systolic dimension, cm	2.97	0.44
Left ventricular mass index	87.3	20.6
Left ventricular relative thickness	0.41	0.08
Ejection fraction by Simpson, %	60.8	7.1
Left atrial volume index, mL/m^2	60	19.4
Right atrial volume index, mL/m^2	25.3	15.0
Right ventricular fractional area change, %	46.9	7.2
Right ventricular dimension mid, cm	3.0	0.69
Systolic pulmonary artery pressure, mm Hg	51.6	26
Mitral valve planimetry, cm^2	0.75	0.18
Mitral valve gradient, mm Hg	14.5	5.3
Tricuspid valve annulus, cm	2.7	0.49
Pulmonic valve annulus, cm	2.2	0.33
Left ventricular outflow tract, cm	1.9	0.26
Right ventricular outflow tract, cm	2.3	0.45

DISCUSSION

Most of the participants belonged to the middle-aged group and are female. A long interval between the diagnosis of rheumatic heart disease with MS and the intervention of almost 2½ years was seen. The delay may be due to logistic factors from the participants and the health care system. In chronic AR, the symptoms tend to occur after a long period when there is considerable cardiomegaly or left ventricular dysfunction.[12] The proximal and more severe lesion of MS predominates; hence, the functional class was limited because of exercise intolerance whenever tachycardia occurs. The participants were on functional classes II and III despite medical treatment of diuretics and β-blockers. Almost half of the participants have

Table 3. Comparison in Echocardiographic Data of Significant and Insignificant AR 24 Hours After PTMC, Philippine Heart Center, 2019–2020

	Significant AR	Insignificant AR	*P**
	Mean ± SD		
No. of patients	3	40	
Left ventricular end-diastolic dimension, cm	3.83 ± 0.47	4.5 ± 0.42	**0.008**
Left ventricular end-systolic dimension, cm	2.33 ± 0.47	2.97 ± 0.43	**0.017**
Left ventricular mass index	68.7 ± 17.1	89 ± 26	0.19
Left ventricular relative thickness	0.43 ± 0.08	0.40 ± 0.09	0.56
Ejection fraction by Simpson, %	63.6 ± 9.3	63.4 ± 5.8	0.95
Left atrial volume index, mL/m^2	40.6 ± 14.2	53.5 ± 22.5	0.34
Right atrial volume index, mL/m^2	25.6 ± 22.1	23.7 ± 10	0.77
Right ventricular fractional area change, %	38.6 ± 15	48.7 ± 6.5	**0.025**
Right ventricular dimension mid, cm	3.6 ± 1.0	2.9 ± 0.60	0.077
Systolic pulmonary arterial pressure, mm Hg	57 ± 30.8	32.4 ± 13.2	**0.008**
Mitral valve planimetry, cm^2	1.36 ± 0.25	1.6 ± 0.27	0.13
Mitral valve gradient, mm Hg	8.6 ± 3.2	5.3 ± 2.7	0.052
Tricuspid valve annulus, cm	2.6 ± 0.49	2.7 ± 0.44	0.67
Pulmonic valve annulus, cm	2.46 ± 0.23	2.2 ± 0.34	0.21
Left ventricular outflow tract, cm	1.66 ± 0.21	2.02 ± 0.24	**0.020**
Right ventricular outflow tract, cm	2.5 ± 0.26	2.28 ± 0.33	0.28

*Significant P values if P < 0.05 (in bold font), Mann-Whitney U test.
AR=aortic regurgitation; PTMC=percutaneous transmitral commissurotomy.

atrial fibrillation, and a great number suffered from transient ischemic attack or stroke, and is related to the severity of MV obstruction and the patient's age.[13] Few participants were in the underweight or overweight group. The assessment of nutritional status and whether it affects the outcome of the procedure are yet to be explored. The baseline high valve score of 8.7 connotes unfavorable outcome[14] and may be associated with the multivalve involvement of AR.

The baseline echocardiographic parameters demonstrated that the average values of left ventricular volume, function, left ventricular mass index, left ventricular relative wall thickness, and LVOT were all normal. A form of LV remodeling will most likely not manifest either as it is expected because proximal obstruction of MS led to a decreased flow on the receiving LV chamber. Eccentric hypertrophy is a form of adaptation, commonly seen in isolated significant AR, which is less likely unless concomitant conditions are present.[15] Severe MS reflected a very small MV planimetry, high MV gradient, and dilated LAVI. Its hemodynamic consequence of a dilated tricuspid valve annulus and increased systolic pulmonary arterial pressure were also present.

The mechanism for which PTMC exerts its valvular improvement is through commissural separation, and fracture of nodular calcium, a reduction of MV gradient, increased MV planimetry, and cardiac output were expected.[12] At the 24 hours post-PTMC, the echocardiographic data revealed only 3 of 43 participants with significant AR. However, the significant AR group had paradoxically smaller LVEDD, LVESD, and LVOT; an expected lower right ventricular fractional area change; and higher PA pressure. This may be due to less effective relief of obstruction as seen with lower MV planimetry, higher MV gradient, and systolic pulmonary arterial pressure. On further

Table 4. Comparison in Echocardiographic Data of Significant and Insignificant AR From 24 Hours to 1 Month After PTMC, Philippine Heart Center, 2019–2020

	Significant AR	Insignificant AR	*P**
	Mean ± SD		
No. of patients	8	29	
Left ventricular end-diastolic dimension, cm	4.58 ± 0.53	4.5 ± 0.47	0.70
Left ventricular end-systolic dimension, cm	3.1 ± 0.35	2.9 ± 0.46	0.30
Left ventricular mass index	98 ± 25.5	89.1 ± 22.8	0.34
Left ventricular relative thickness	0.40 ± 0.07	0.39 ± 0.08	0.70
Ejection fraction by Simpson, %	61.5 ± 4.3	62.9 ± 4.6	0.44
Left atrial volume index, mL/m^2	55.5 ± 30.5	55.3 ± 21.4	0.98
Right atrial volume index, mL/m^2	22 ± 5.5	24.6 ± 12.3	0.56
Right ventricular fractional areas change, %	49.1 ± 7.2	49.8 ± 7.4	0.81
Right ventricular dimension mid, cm	2.9 ± 0.43	2.88 ± 0.55	0.86
Systolic pulmonary arterial pressure, mm Hg	28 ± 9.3	34.7 ± 17.3	0.30
Mitral valve planimetry, cm^2	1.43 ± 0.32	1.44 ± 0.31	0.96
Mitral valve gradient, mm Hg	5.03 ± 1.65	6.39 ± 2.65	0.18
Tricuspid valve annulus, cm	2.65 ± 0.48	2.76 ± 0.48	0.55
Pulmonic valve annulus, cm	2.05 ± 0.23	2.18 ± 0.35	0.31
Left ventricular outflow tract, cm	2.0 ± 0.23	1.97 ± 0.27	0.82
Right ventricular outflow tract, cm	2.11 ± 0.19	2.3 ± 0.36	0.15

*Significant *P* values if $P < 0.05$, Mann-Whitney *U* test.
AR=aortic regurgitation; PTMC=percutaneous transmitral commissurotomy.

follow-up, during the first and sixth months after PTMC, the echocardiographic data revealed a minority of 8 of 37 and 5 of 26 participants who had significant AR. Temporary, comparable differences were seen only on the 24th hour, which then started to plateau and equalized at 1 and 6 months in both groups.

At most, there was a moderate AR and no progression to severe AR in both groups. Although not statistically significant, those in the significant AR group had a larger LVEDD, LVESD, and LVOT on the 1st and 6th month period. Although according to standard categorization, it will still fall under normal. Unfortunately, two cases had severe mitral regurgitation as a procedural complication; despite the presence of AR, neither pulmonary edema nor congestion occurred. A chronically enlarged left atrium with increased LAVI from MS may have ameliorated the abrupt rise of LA pressure seen in acute MR.

The baseline characteristics and the classification of 3 significant and 39 insignificant AR patients at 24 hours post-PTMC showed a significantly higher unfavorable valve score in the significant AR group, 10 compared with 8.6. The driver for the increased score was in the subvalvular thickening. The Wilkin score is the most validated parameter that predicts immediate and long-term morbidity and mortality.[14] The incorporation of AR severity with the prediction of events may better elucidate the course of the disease as a whole. Both groups had a classification of NYHA I at 1 and 6 months post-PTMC. There were no major cardiovascular events encountered such as heart failure, stroke, or infective endocarditis. The improvement of the functional class was seen in NYHA II–III at baseline. The majority returned to work or tolerated a successful noncardiac surgery. These findings support the previous findings that concomitant AR undergoing PTMC does not yield inferior outcomes as reflected by the clinical and echocardiographic parameters in this study..

Table 5. Comparison in Echocardiographic Data of Significant and Insignificant Tricuspid Regurgitation From 1 to 6 Months After PTMC, Philippine Heart Center, 2019–2020

	Significant AR	Insignificant AR	*P**
	Mean ± SD		
No. of patients	5	21	
Left ventricular end-diastolic dimension, cm	4.64 ± 0.83	4.57 ± 0.43	0.80
Left ventricular end-systolic dimension, cm	2.9 ± 0.51	2.91 ± 0.46	0.95
Left ventricular mass index	101.6 ± 40.2	84.5 ± 21.2	0.19
Left ventricular relative thickness	0.40 ± 0.10	0.38 ± 0.09	0.58
Ejection fraction by Simpson, %	63.2 ± 5.3	62.3 ± 4.9	0.73
Left atrial volume index, mL/m^2	52.4 ± 13.7	57.1 ± 26.1	0.69
Right atrial volume index, mL/m^2	29.6 ± 3.1	23.2 ± 10.3	0.19
Right ventricular fractional area change, %	49.6 ± 3.2	48.6 ± 8.1	0.80
Right ventricular dimension mid, cm	2.56 ± 0.37	2.7 ± 0.47	0.49
Systolic pulmonary arterial pressure, mm Hg	33.8 ± 4.9	32.4 ± 9.9	0.77
Mitral valve planimetry, cm^2	1.38 ± 0.30	1.44 ± 0.19	0.56
Mitral valve gradient, mm Hg	6.18 ± 2.5	6.49 ± 3.4	0.89
Tricuspid valve annulus, cm	2.7 ± 0.25	2.66 ± 0.56	0.88
Pulmonic valve annulus, cm	2.12 ± 0.44	2.1 ± 0.31	0.95
Left ventricular outflow tract, cm	2.02 ± 0.17	1.96 ± 0.18	0.52
Right ventricular outflow tract, cm	2.26 ± 0.33	2.27 ± 0.31	0.94

*Significant *P* values if $P < 0.05$, Mann-Whitney *U* test.
AR=aortic regurgitation; PTMC=percutaneous transmitral commissurotomy.

LIMITATIONS AND RECOMMENDATIONS

The unfortunate effects of the COVID pandemic had brought the cases down of elective PTMC procedure; hence, an adequate sample size to represent both groups was not obtained. The dropout rates for the acquisition of 2DED data were 14% at 1 month and 39% at 6 months. The lockdown instituted to the different parts of our country precluded the participants from the scheduled date of 2DED at our institution. The percentage that belonged to the significant AR group was 7% at 24 hours, 22% at 1 month, and 19% at 6 months. The high dropout rates may have altered the true incidence of each group. We recommend a larger sample size and low dropout rates to predict the factors of outcome for each group. Also, the determination of factors associated with or predictive of functional class or major cardiovascular events would have a greater impact on management.

CONCLUSION

On short-term follow-up, the presence of mild to moderate AR prior to PTMC does not lead to severe AR. The outcomes regardless of group showed good functional class and no significant echocardiographic differences when compared.

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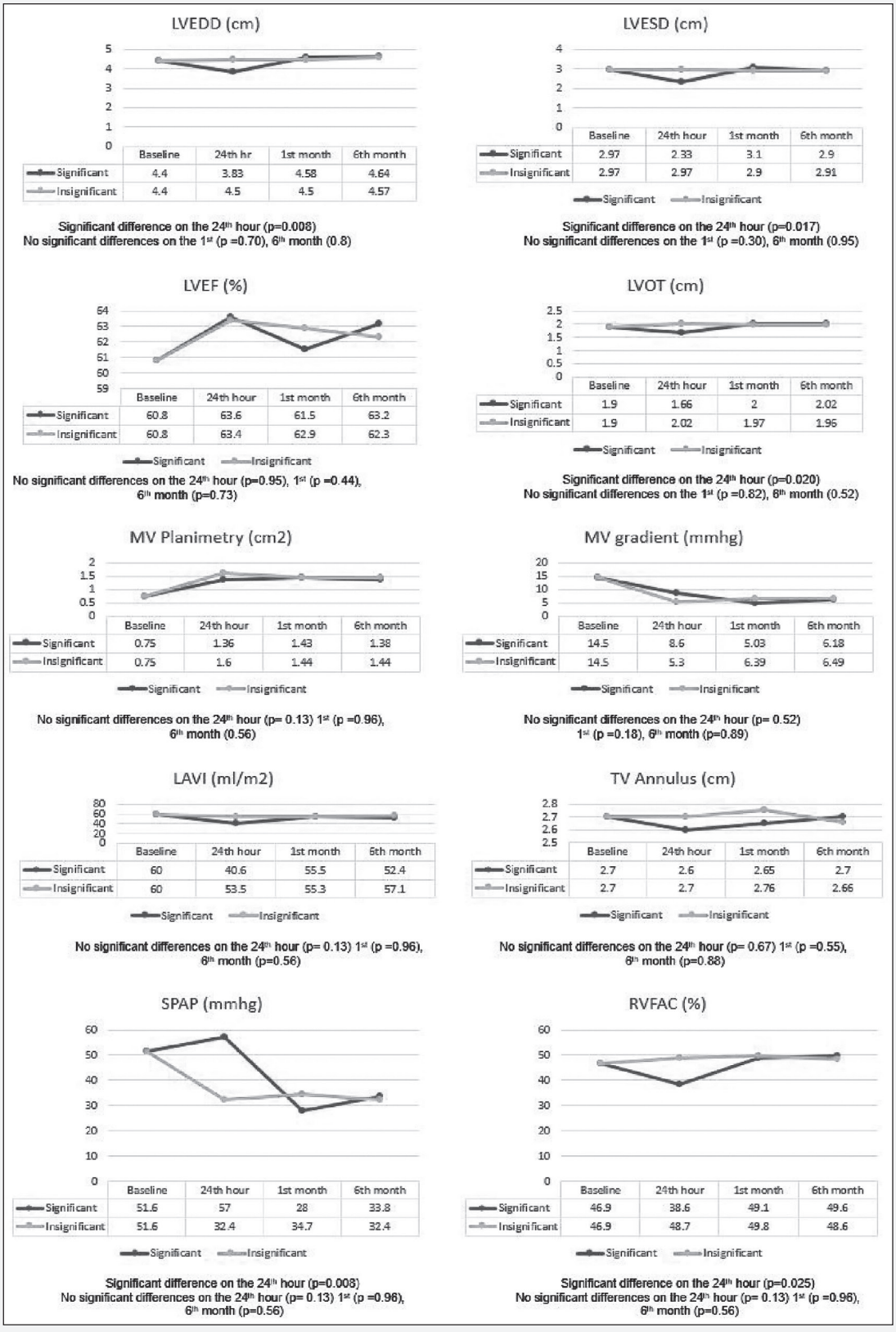
Table 6. Comparison in Characteristics of Significant and Insignificant AR From 24 Hours to 6 Months After PTMC, Philippine Heart Center, 2019–2020

Characteristics	Significant AR	Insignificant AR	*P**
	Mean ± SD		
Age (years)	39.3 ± 16.9	40.1 ± 19.1	0.90
Sex§			0.26
Male	0	12 ± 100	
Female	3 ± 9.7	28 ± 90.3	
NYHA§			—
I	3 ± 7	40 ± 93	
II	0	0	
III	0	0	
IV	0	0	
Rhythm§			0.57
Sinus rhythm	2 ± 9.1	20 ± 90.9	
Atrial fibrillation	1 ± 4.8	20 ± 95.2	
Height, m	1.61 ± 0.19	1.58 ± 0.57	0.51
Weight, kg	59.3 ± 18.8	59.1 ± 9.7	0.97
Body mass index†			0.70
Underweight	0	1 ± 100	
Normal	3 ± 10	27 ± 90	
Overweight	0	11 ± 100	
Obese	0	1 ± 100	
Previous PTMC	0	3 ± 100	0.62
Diagnosis to PTMC time, mo	25.3 ± 22	26.6 ± 28.9	0.94
History of stroke/transient ischemic attack§	0	8 ± 100	0.39
Wilkins score (total)	10 ± 0	8.6 ± 0.84	0.007‡
Leaflet mobility, mean ± SD	2 ± 0	2.1 ± 0.26	0.63
Valve thickness, mean ± SD	2.6 ± 0.57	2.2 ± 0.40	0.09
Valvular calcification, mean ± SD	2.6 ± 0.57	2.2 ± 0.40	0.06
Subvalvular thickening, mean ± SD	2.6 ± 0.57	2.1 ± 0.30	0.005‡

*Significant difference if $P < 0.05$ (in bold font).
†Mann-Whitney *U* test.
‡See the Appendix for the definitions of body mass index categories.
§χ^2 Test.
AR=aortic regurgitation; NYHA=New York Heart Association; PTMC=percutaneous transmitral commissurotomy.

Figure 2. Echocardiographic parameters from baseline to 6 months of follow-up.



EF=ejection fraction; LAVI=left atrial volume index; LVEDD=left ventricular end-diastolic dimension; LVESD=left ventricular end-systolic dimension; LVOT=left ventricular outflow tract; MV, mitral valve; RVFAC=right ventricular fraction area change; SPAP=systolic pulmonary arterial pressure; TV=tricuspid valve.

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APPENDIX

1. New York Heart Association (NYHA) Classification: assessment of functional capacity done by a cardiologist or internal medicine specialist categorized as I (no limitation of physical activity), II (slight limitation of physical activity), III (marked limitation of physical activity), IV (heart failure at rest).
2. Body mass index: calculated as the weight in kilograms divided by the square of the height in meters, categorized as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (≥30 kg/m^2).
3. Left ventricular internal dimension: normal diastolic dimension (LVEDD) in centimeters: (4.2–5.84) in males, (3.78–5.22) in females; normal systolic dimension (LVESD) in centimeters: (2.5–3.98) in males, (2.16–3.48) in females.[11]
4. Left ventricular (LV) remodeling: based on the measurement of left ventricular mass index (LVMI), normal is ≤115 in males, ≤96 in females, and relative wall thickness (LVRT) normal is ≤0.42. Concentric remodeling (normal LVMI and increase LVRT), eccentric hypertrophy (increase in LVMI, normal LVRT), and concentric hypertrophy (increase in LVMI and LVRT).[11]
5. Ejection fraction (EF): reference range is (52–72) in males and (54–74) in females.[11]
6. Left atrial volume index (LAVI): measured in milliliters per meter squared; normal (16–34), mild dilatation (35–41), moderate dilatation (42–48), and severe dilatation >48.[11]
7. Right atrial volume index (RAVI): measured in milliliters per meter squared; normal is (15–27) in females and (18–32) in males.[11]
8. Right ventricular fractional area change (RVFAC): normal is >35%.[11]
9. Right ventricular dimension mid (RVD): measured in centimeters at the two-dimensional echocardiogram and midlevel; normal is (1.9–3.5).[11]
10. Systolic pulmonary arterial pressure (SPAP): measured in millimeters of mercury; normal (18–34), mild (35–59), moderate (60–79), and severe (>80).[11]
11. Mitral valve (MV) planimetry: measured in centimeters squared; mild (>1.5), moderate (1–1.5), and severe (<1.0).[11]
12. MV mean gradient: measured in millimeters of mercury; mild (<5), moderate (5–10), and severe (>10).[11]
13. Tricuspid valve annulus: measured in centimeters; normal is (1.3–2.8).[11]
14. Pulmonic valve annulus: measured in centimeters normal is (1.7–2.3).[11]
15. Left ventricular outflow tract: measured in centimeters; normal is (1.8–2.4).[11]
16. Right ventricular outflow tract: measured in centimeters; normal is (2.1–3.5) in females and (1.7–2.7) in males.[11]

Values in parentheses reflect horizontal sum. Significant $P < 0.05$, χ^2 test.