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EDITORS AND CONSULTANTS

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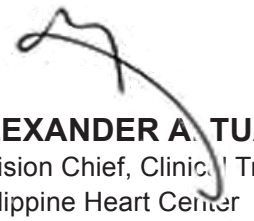
Editorial

WHAT'S LACKING?

Our vision is to make our institution, Philippine Heart Center, as the apex center for cardiovascular research. We must produce quality and relevant researches that will help clinicians in proving effective cardiovascular care not only among Filipino people but also worldwide. Our researches were done based on the problems OR issues that arises and originated from different areas of specialty but were cardiovascular related.

For the past years, our researches aimed on answering the targets of our institutions, that was primarily on global benchmarking of our experiences and those which will affect national policy. Data from the several outputs revealed that our institution was at par OR even better than the others do from other countries. Researches for policy impact needed further effort.

Included in this issue are some of this institution target related researches such as the outcome of PTMC, spectrum of Rheumatic Heart disease in our institution, and metabolic syndrome among pediatric patients and their cardiovascular risk assessment. Other articles tackled risk factor affecting outcome of diagnose IC procedure and intervention, and patient and doctor knowledge on treatment.



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Association of Obstructive Sleep Apnea (OSA) Risk with Post-Operative Complications Among Coronary Artery Bypass Graft (CABG) Patients

Karen Anne G. Bispo, MD; Ma. Encarnita Blanco-Limpin, MD; Jamaica Ross David, MD; Rommel D.R. Bayot, MD; Aileen G. Banzon, MD

Background **---** Obstructive sleep apnea (OSA) is commonly associated among patients with coronary artery disease but is frequently unrecognized. Post-operative complications among OSA patients include respiratory, cardiac and neurologic complications. Validated questionnaire, such as the STOP Bang questionnaire, can be used to determine patients who intermediate to high risk OSA. This study aims to determine the association of OSA risk using the STOP Bang questionnaire with incidence of post-operative complications among CABG patients.

Methods **---** This is a prospective cohort study that enrolled all patients referred for pulmonary pre-operative evaluation undergoing CABG were included in the study. A self-administered patients intermediate STOP Bang questionnaire was given to patients for determining who are risk (score 3-4) and high risk (score 5-8) for OSA. Post-operative complications were compared among with low risk for OSA (score 0-2).

Results **---** One hundred three patients were included in the study and mostly were males. Twenty-four patients developed post-operative complications and 10 (41.67%) were intermediate risk and 13 (54.17%) were high risk for OSA. Fifty-two (50.48%) and 19 (18.55%) out of 103 patients were intermediate and high risk for OSA (STOP Bang score 3-4 and 5-8, respectively) and 13 (54.17%) of these high risk for OSA developed post-operative complication which is statistically significant with a p value of 0.0002 and the most common complications observed were prolonged ICU stay, post-operative use of NIV, prolonged intubation.

Conclusion **---** Obstructive sleep apnea is a frequent condition usually not recognized, particularly among patients undergoing CABG. Identification of these patients using validated questionnaires such as the STOP Bang questionnaire can be used to prevent peri-operative and post-operative complications. Further studies with larger sample size and long-term follow-up is recommended. ***Phil Heart Center J 2022;25(1):1-7.***

Key Words: ■ obstructive sleep apnea (OSA) ■ coronary artery bypass graft (CABG) ■ post-operative complications ■ STOP Bang

Pulmonary post-operative complications occur commonly and it increases both the morbidity and mortality of patients. Post-operative pulmonary complications are classified as major and minor complications. Major post-operative pulmonary complications are as follows: (1) respiratory failure, (2) prolonged intubation (more than >48 hours on mechanical ventilation), and (3) development of pneumonia. Minor complications are as follows: (1) tracheo-bronchitis, and (2) atelectasis.

Prolonged intubation is one of the most important post-operative complications among patients undergoing coronary artery bypass graft. Prolonged intubation results to longer ICU stay, higher treatment cost and some of these patients will eventually need tracheostomy. There have been studies in determining the predictors of prolong intubation and some of them are history of hypertension, chronic obstructive pulmonary disease, and history of previous infective endocarditis.

1st place, Oral Presentation - Original Paper. 28th PHC Annual Research Paper Competition and Poster Presentation held on February, 2022 at Philippine Heart Center. Correspondence *to* ***Dr. Karen Anne G. Bispo.*** Division of Pulmonary and Critical Care Medicine. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

Therefore, an adequate pre-operative pulmonary evaluation is important in reducing such complications. There have been different pulmonary pre-operative evaluation designed to predict the occurrence of pulmonary post-operative complications (SPIVACK, Shapiro, etc.). These pre-operative assessment tools determines left ventricular function, comorbidities (history of congestion, smoking history, diabetes mellitus and angina), pulmonary function, derangements in the arterial blood gas which are used to predict pulmonary post-operative complications.

Obstructive sleep apnea (OSA) is commonly associated among patients with coronary artery disease but is frequently unrecognized. Post-operative complications among OSA patients include respiratory, cardiac and neurologic complications. If OSA, is not recognized among patients who will undergo CABG, they are at risk of developing complications such as unplanned re-intubations and post-operative cardiac events. Polysomnography is the gold standard diagnostic procedure to detect OSA. However, most of the patients undergoing CABG do not routinely undergo this procedure prior to their surgery, but validated questionnaire, such as the STOP BANG questionnaire, can be used to determine patientswho are moderate to severe and severe OSA.

This study therefore aims to determine the association of obstructive sleep apnea risk, using the STOPBANG questionnaire and the risk of developing post-operative complications among patients undergoing CABG.

Objectives: The general objective is to determine the association of OSA risk, using the STOP-BANG questionnaire with incidence of post-operative complications among CABG patients. While its specific objectives are: (1) to determine the low risk, intermediate risk and high risk for OSA using STOPBANG among CABG patients; (2) to determine and compare the post-operative complications among patients with low risk, intermediate and high risk for OSA among CABG patients. Occurrence of atrial fibrillation post-operatively, Prolonged intubation (>48 hours post-operative ICU re-admission, re-intubation, post-operative NIV use, ICU and in-hospital mortality; (3) to determine and compare the association of low risk, intermediate risk and high risk for OSA and the post-operative complications among CABG patients.

Null Hypothesis

There is no significant difference in the incidence of post-operative complications among patients with low risk, intermediate risk and high risk for OSA, who will undergo elective CABG at Philippine Heart Center.

Alternative Hypothesis

There is a significant difference in the incidence of post-operative complications among patients with low risk, intermediate risk and high risk for OSA, who will undergo elective CABG at Philippine Heart Center.

METHODS

This is a prospective cohort study, used in determining the association of Obstructive Sleep Apnea (OSA) with post-operative complications among Coronary Artery Bypass Graft (CABG) patients. Study was conducted at the Philippine Heart Center from August to December 2018.

This study included adults, more than 19 years old, who were referred to pulmonary service for pulmonary pre-operative evaluation prior to an elective CABG.While excluded in the study are patients who were diagnosed with OSA by polysomnography and with history of cerebrovascular disease.

Study Maneuver: All patients referred to pulmonary service for pulmonary pre-operative evaluation undergoing CABG were included in the study. A self-administered STOP-BANG questionnaire was given to patients for determining who are intermediate risk (score 3-4) and high risk (score 5-8) for OSA. Post-operative complications (occurrence of atrial fibrillation post-operatively, prolonged intubation, prolonged ICU and hospital stay, re-admission to ICU and in-ICU and in-hospital mortality) were

compared among patients with low risk for OSA (score 0-2).

Sample size: A minimum of 96 patients were required for this study based on 5% level of significance, 80% power and an effect size of 0.5859 from 0.75 ± 0.60 and 0.41 ± 0.56 duration of intubation measured in days for High and Low risk OSA[2], respectively.

Statistical analysis: Descriptive statistics was used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median and inter quartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Independent Sample T-test, Mann-Whitney U-test and Fisher's Exact/Chi-square test were used to determine the difference of mean, rank and frequency, respectively, between Any OSA and Moderate-to-Severe /Severe OSA. Odds ratio and corresponding 95% confidence intervals from binary logistic regression will be computed to determine significant predictors for Post-operative complications. All statistical tests were two tailed test. Shapiro-Wilk was used to test the normality of the continuous variables. Missing variables were neither be replaced nor estimated. Null hypotheses were rejected at 0.05 α-level of significance. STATA 13.1 will be used for data analysis.

RESULTS

A total of 173 patients were included in the study from August 2018 to December 2018. Seventy-three (73) of the 103 patients were males (70.87%) and 30 (29.13%) females. They were all assessed for OSA risk using the STOP BANG questionnaire prior to CABG. The mean ages of the patients were 61.35 ± 9.69 years and 61.38 ± 8.11 for without complications and with complications, respectively. Among the 103 patients, 32 (31.07%) were low risk for OSA, 52 (50.48%) were intermediate risk and 19 (18.55%) were high risk for OSA. Also, 24 patients developed post-operative complications and 13 (54.17%) were high risk for OSA.

Table 1 showed the baseline demographic and baseline characteristics of the patients who underwent CABG. The patients' age, gender, comorbidities (hypertension, DM, dyslipidemia, previous ACS) and ejection fraction were comparable between the two groups except for BMI and among former smokers.

Although most of the patients were males (70.87%), the occurrence of post-operative complications was comparable with females (p= 0.605). As shown in Table 1, patients with BMI of more than 35kg/m^2 were 15.6 more likely to have post-operative complications that patients with BMI of less than 35kg/m^2 (p= 0.024). Diabetic patients were 2.79 more likely to develop complications compare to those non-diabetic. Former smokers or those who quit smoking for 8 weeks were 65.17% less likely of developing post-operative complications. The rest of the demographic and clinical characteristics were comparable in both with or without complications.

Table 2 summarizes the post-operative complications noted in this study. Only 24 of the 103 patients recruited into the study developed post-operative complications. Among those who developed complications, the most common was prolonged ICU stay at 15.53% followed by NIV use (12.62%) and prolonged intubation, both at 11.65%.

The STOP BANG questionnaire was used in this study pre-operatively to identify the risk for OSA of patients who underwent CABG. As shown in Table 3, 19 (18.55%) out of 103 patients were high risk for OSA and 13 (54.17%) of these high risk for OSA developed post-operative complications with a crude OR of 67.17 (7.32 – 614.66).

Table 1. Baseline demographics and baseline characteristics of patients undergoing CABG.

	Total (n=103)	Without complications (n=79)	With complications (n=24)	Crude odds ratio (95% CI)	P-value
	Frequency (%)				
Age					
(Mean + SD)	61.36 + 8.90	61.35 + 9.69	61.38 + 8.11	1.00 (0.94–1.05)	0.992
Gender					
Male	73 (70.87)	57 (72.15)	16 (66.67)	0.77 (0.29–2.06)	0.605
Female	30 (29.13)	22 (27.85)	8 (33.33)	1.30 (0.48–3.45)	
BMI					
≥ 35	5 (4.85)	1 (1.27)	4 (16.67)	15.6 (1.65–147)	**0.016**
< 35	98 (95.14)	78 (98.73)	20 (83.33)	(reference)	
Comorbidities					
Hypertension	79 (76.70)	57 (72.12)	22 (91.64)	4.24 (0.92–19.58)	0.064
DM Type 2	49 (47.57)	33 (41.77)	16 (66.67)	2.79 (1.07–7.28)	**0.036**
Dyslipidemia	52 (46.48)	36 (45.57)	16 (66.67)	2.39 (0.92–6.22)	0.075
Smoking					
Non-smoker	37 (36.92)	24 (30.38)	13 (54.17)	(reference)	-
Smoker	3 (2.91)	2 (2.53)	1 (4.17)	0.92 (0.76 – 11.17)	0.950
Former	63 (40.78)	53 (67.09)	10 (41.67)	0.35 (0.13 – 0.90)	**0.030**
Previous ACS	72 (69.90)	55 (69.62)	17 (70.83)	1.06 (0.39 – 2.89)	0.910
LVEF					
≥ 55%	50 (48.54)	42 (53.16)	8 (33.33)	0.44 (0.17 – 1.15)	0.093
< 55%	53 (51.46)	37 (46.84)	16 (66.67)	2.27 (0.87 –5.91)	

Table 2. Outcomes of patients who underwent coronary artery bypass graft surgery.

Outcomes	Frequency (%)
Composite Outcomes	24 (23.30)
Atrial Fibrillation	10 (9.70)
Prolonged Intubation	12 (11.65)
Prolonged ICU stay	16 (15.53)
Prolonged hospital stay	11 (10.68)
Re-Intubation	4 (3.88)
Post-operative NIV	13 (12.62)
ICU re-admission	4 (3.88)
In- ICU and IN- hospital mortality	3 (2.91)

Table 3. Association of post-operative complications with OSA risk.

	With complications (n=24)	Without complications (n=79)	Crude odds ratio (95% CI)	P-value
	Frequency (%)			
Low risk	1 (4.17)	31 (39.24)	(reference)	-
Intermediate	10 (41.67)	42 (53.16)	7.38 (0.90 – 60.72)	0.063
High risk	13 (54.17)	6 (7.59)	67.17 (7.34 – 614.66)	0.0002

DISCUSSION

The aim of this study is to identify patients who are high risk for OSA among patients undergoing elective CABG and its association with post-operative complications. The study showed that 50.48% and 18.55% of the patients undergoing CABG at Philippine Heart Center are intermediate and high risk for OSA. Ten (41.67%) out of the 52 patients who were intermediate risk for OSA developed complications, although not statistically significant ($p = 0.063$) but 13 (54.17%) out of the 19 high risk for OSA developed complications which was statistically significant ($p = 0.0002$). Previously conducted studies showed that 20-70% of patients undergoing elective CABG are high risk for OSA using either the Berlin or the STOP Bang questionnaire.[13-15] The gold standard diagnostic procedure for diagnosing OSA is overnight polysomnography. However, OSA remains to be undiagnosed, resulting to underutilization of the said procedure and >80% of patients undergoing surgery are unaware of their sleep apneas.[16]

There have been validated questionnaires for screening of those who are high risk for OSA such as the Berlin questionnaire, the ASA checklist and the STOP BANG questionnaire. The Berlin questionnaire is the most widely used questionnaire in identifying patients at high risk for OSA and has the highest sensitivity of 86% and positive predictive value of 89%.[16, 17] The study utilized the STOP Bang questionnaire which was recently validated as a screening tool for OSA, pre-operatively.[16]

As discussed earlier, patients whose BMI is >35kg/m^2 are more likely to develop post-operative complications. In this study, five patients have a BMI of more than 35kg/m^2 and four had post-operative complications. However, studies have shown that obesity does not appear to be related to increase in incidence of post-operative complications.[18] According to Costa et.al, obesity is a risk factor to the development of wound dehiscence due to increase in subcutaneous tissue thickness. In another study, by Reis et.al that compared post-operative complication between malnourished and obese CABG patients, malnourished patients have impaired ability to manage stress, although not statistically significant. On the other hand, obesity is a risk factor to the development of OSA and obese patients are two times more likely to have OSA.[20] As cited in the study of Romero-Corral, obesity worsens OSA due to deposition of fat in the tissues surrounding the upper airway appears to result in a smaller lumen and increased collapsibility of the upper airway, predisposing to apnea. In addition, fat deposits around the thorax (truncal obesity) reduce chest compliance and functional residual capacity, and may increase oxygen demand.

Another significant finding in the study is that former smokers or those who stopped smoking for more than eight weeks are less likely to develop post-operative complications. Several studies have been made comparing recent smokers (quit smoking < 8weeks), former smokers (quit > 8 weeks) and smokers which showed no statistically significant difference on the occurrence of post-operative complications.[21] The cited study further concluded that there is no suggestion that quitting smoking shortly before surgery increases postoperative complications, however, it is strongly advised to encourage patients to quit smoking prior to surgery. Studies have been conducted on the association of smoking and OSA, however, results are inconclusive.[22] The effect of smoking on the pathophysiology of OSA are probably due to changes in sleep architecture, relaxation of the upper airway muscles and neural reflexes caused by nicotine, increased arousal threshold from sleep caused by nicotine, and increased upper airway inflammation due to smoke inhalation.[21-22]

As shown in the results, patients with high risk OSA were likely to develop post-operative complications. Among the 24 patients who develop complications, 52 (50.48%) and 19 (18.55%) are identified as intermediate and high risk for OSA, respectively using the STOP BANG questionnaire. Several studies have done to demonstrate the association of OSA and post-operative complications, however results have been inconclusive.[1] In a study

by Abdelsattar et.al, patients with untreated OSA are at increased risks for cardio-pulmonary complications after general and vascular surgery. Another study by Kaw et.al, showed that the incidence of postoperative desaturation, respiratory failure, postoperative cardiac events, and ICU transfers was higher in patients with OSA. However, Memtsoudis et.al, found an increase in complications but no impact of OSA on in-hospital mortality in an analysis of nationwide hospital discharge data.[1]

Among the complications observed in this study, prolonged ICU stay was the most frequent at 15.53%, followed by post-operative NIV use (12.62%), then atrial fibrillation (11.65%). In a study conducted by Amra et.al, prolonged ICU stay, atrial fibrillation and prolonged intubation were also observed, although not statistically significant except for prolonged intubation. Obstructive sleep apnea is known to increase pulmonary and cardiac complications.[26] Pulmonary post-operative complications associated with OSA patients are hypoxemia and hypercapnia.[24]

Non-invasive ventilator support can be used among hypoxemic and hypercapneic patients to improve gas exchange. Atrial fibrillation, is the most common cardiac dysrhythmia observed post-operatively. Possible mechanisms for the occurrence of atrial fibrillation are shared risk factors, autonomic instability, and atrial remodeling.[5]

There are limitations for this study. The sample size in the study is small since this is a preliminary data (71 out of 96 computed samples). Polysomnography was not used in this study. Finally, long- term outcomes were not assessed, that might be needed to consider in future studies.

CONCLUSION

This study showed that 71.83% of the patients who underwent CABG were categorized as intermediate to high risk for OSA. In these patients, there were associated post-operative complications such as prolonged ICU stay, post-operatively use of NIV, prolonged intubation and atrial fibrillation. Screening patients who will undergo CABG, especially those with BMI>35 and those who are currently smoking or at least smoked in the past 8 weeks, is beneficial as this may help prevent peri-operative and post-operative complications. Validated questionnaires like the STOP BANG questionnaire can be advantageous to minimize post-operative risk. Further studies with larger sample size and long-term follow up is suggested.

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Accuracy of Risks Calculator Predicting Post Operative Respiratory Failure and Prolonged Mechanical Ventilation After a Cardiothoracic Surgery in Philippine Heart Center

Gladys Judynil B. Daba, MD; Maria Encarnita Blanco-Limpin, MD; Aileen G. Banzon, MD

Background **---** Postoperative Respiratory Failure (PRF) is among the most common postoperative pulmonary complications.[2] It's usually defined as failure to wean from mechanical ventilation within 48 hours of surgery or in some studies reaching to 7 days or when there is unplanned intubation 30 days postoperatively after an extubation.[3,8]

Methods **---** This is a retrospective cross-sectional study at the Philippine Heart Center of 70 adult patients that underwent cardiothoracic surgery. Demographics and review of 5 preoperative risk factors namely ASA class, dependent functional status, emergency procedure, preoperative sepsis, and type of surgery were entered into a risk calculator and the returned percentage value was then recorded. Course in the ward was reviewed if patient had prolonged mechanical ventilation (PMV) or if patient had unplanned reintubation within 30days postoperatively, recorded as postoperative respiratory failure (PRF).

Results **---** There were 8 (11.43%) patients who had PRF and 23 (32.86%) patients who had PMV. Using the cut off value of 6.44% from the calculated risk score for predicting combined outcome, sensitivity was noted to be high at 96.6% with specificity of 87.8%, with a high negative predictive valve of 97.3% and accuracy of 91.4% at 95% confidence interval.

Conclusion **---** The risk calculator predicting postoperative respiratory failure and prolonged mechanical ventilation using the cut off of 6.44% has sensitivity of 96.6%, specificity of 87.8%, and an accuracy of 91.4%, thus, can be use to risk stratify patients who will undergo cardiothoracic surgery. ***Phil Heart Center J 2022;25(1):8-13.***

Key Words: ■ postoperative respiratory failure ■ pulmonary risk stratification

Postoperative pulmonary complications (PPCs) account for substantial proportion of risk related to surgery and anesthesia and are a major cause of postoperative morbidity, mortality and longer hospital stays with incidence varying from 2 to 19%.[1] Several studies documented PPCs such as respiratory failure, bronchospasm, pleural effusion, respiratory infection, atelectasis, aspiration pneumonia and pneumothorax.[2]

Postoperative respiratory failure (PRF) is among the most common postoperative pulmonary complications.[2] It's usually defined as failure to wean from mechanical ventilation within 48 hours of surgery or in some studies reaching to 7 days or when there is unplanned intubation 30 days postoperatively after an extubation.[3,8]

Gupta et al.[3] reviewed patients who underwent surgeries in the database of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) of 2007 and 2008, where their 2007 data set was used to formulate a model while their 2008 data set served as their validation set. They found out that PRF occurred in 3% of patients while 25% of these patients die within 30 days. Their study identified preoperative variables significantly associated with an increased risk

Finalist, Poster Presentation - Original Paper. 28th PHC Annual Research Paper Competition and Poster Presentation held on February, 2020 at Philippine Heart Center. Correspondence *to* ***Dr. Gladys Judynil B. Daba.*** Division of Pulmonary and Critical Care Medicine. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

for PRF and these included the American Society of Anesthesiologist (ASA) classification, dependent functional status of a patient, if procedure was an emergency or an elective, presence of preoperative sepsis, and the type of surgery. They used these identified variables to develop a risk calculator, which is available and can be downloaded online (*http://www.surgicalriskcalculator.com/prf-riskcalculator*). Their goal was to aid the surgical decision making of clinicians in identifying high-risk patients.

The aim of this study was to check the ability of the risk calculator in predicting PRF and prolonged mechanical ventilation (PMV) after a cardiothoracic surgery in Philippine Heart Center.

METHODS

A retrospective cross-sectional study was conducted after approval of the Philippine Heart Center Institutional Ethics Review Board (PHC IERB) of patients admitted from July 2017 to July 2018 who underwent CABG, valvular surgery, and aneurysmal repairs.

Study Population Selections: Patients admitted from July 2017 to July 2018, 19 years old and above, who underwent CABG, valvular surgery, and aneurysmal repairs. Excluded from the study were those patients who underwent procedures outside the operating room, and those with combined surgery either valve repair and CABG or aneurysm repair and CABG or valve and aneurysm repairs at one time.

Sample Size: A minimum of 70 patients were required for this study based on assumed 75% sensitivity, 50% prevalence and 15% width of confidence interval at 5% level of significance of risk calculator in predicting PRF and PMV.

Recruitment and Data Collection: Patients admitted from July 2017 to July 2018 who underwent cardiothoracic surgery were reviewed. Baseline demographic data and clinical characteristics that included age, sex, race, height, weight, body mass index, smoking history, and co-morbidities were obtained. Patient's course in the wards was reviewed for PRF or PMV. PRF was said to have occurred if patient was reintubated within 30 days of surgery. If the patient had to be reoperated for any reason and be reintubated as part of the anesthesia/surgery or if the patient self-extubated and had to be reintubated, it was not counted as reintubation. PMV was said to occur if patient was still on mechanical ventilation for > 48h postoperatively and was extubated without reintubation postoperatively.

The preoperative data was reviewed for the five risk factors described in the risk calculator namely: the patient's ASA class, functional status, emergency or elective procedure, presence of preoperative sepsis, and type of surgery done. The data for a given patient was entered to the risk calculator and the returned model-based percent estimate from the calculator was copied and recorded.

Statistical Analysis: STATA 13.1 was used for data analysis and in determining the cut off value for PRF and PMV. Descriptive statistics was used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion was used for categorical variables, median and inter quartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Independent Sample T-test, Mann-Whitney U test and Fisher's Exact/Chi-square test was used to determine the difference of mean, rank and frequency, respectively, between patients with and without PRF and PMV. Sensitivity, specificity, and likelihood ratios were used to determine the diagnostic accuracy of the risk calculator.

RESULTS

A total of 70 patients were included in the study. Table 1 presents the demographic and clinical characteristics of the patients who had outcome and without outcome. The mean age was 55 years old. The sex, race, BMI of patients in both groups was comparable. Among

the co-morbidities listed, CKD showed to be statistically significant (P-value 0.006) with 5 patients who all developed an outcome.

There were 8(11%) patients who developed postoperative respiratory failure among the 70 patients as shown in Table 2.

There were 23(33%) patients who developed prolonged mechanical ventilator use among the 70 patients as shown in Table 3.

As shown in Table 4, using the cut off value of 6.66% from the calculated risk score for predicting postoperative respiratory failure, sensitivity was noted to be at 75% with specificity of 72.6%, with a high negative predictive valve of 95.7% at 95% confidence interval.

As shown in Table 5, using the cut off value of 6.54% from the calculated risk score for predicting prolonged mechanical ventilation, sensitivity was noted to be at 78.3% with specificity of 80.9%, with a negative predictive valve of 88.4% and accuracy of 80%.

As shown in Table 6, using the cut off value of 6.44% from the calculated risk score for predicting an outcome, sensitivity was noted to be high at 96.6% with specificity of 87.8%, with a high negative predictive valve of 97.3% and accuracy of 91.4% at 95% confidence interval.

Table 1. Baseline Demographic and Clinical Characteristics.

	With Outcome (n=29)	Without Outcome (n=41)	P-value
	Frequency (%); Mean ± SD; Median(IQR)		
Age	55.12 ±15.24	55.38 ±35	0.945
Gender			
Male	17(58.62%)	29(70.73%)	
Female	12(41.38%)	11(26.83%)	
Race			0.228
Asian	29(100%)	39(95.12%)	
Caucasian	0 (0%)	2(4.88%)	
BMI	24.46±2.87	24.35±3.37	0.887
Smoking history			0.434
Never Smoker	18 (62.07%)	20(48.78%)	
Former Smoker	9(31%)	19(46.34%)	
Current Smoker	2(6.90%)	2(4.88%)	
Co morbidities:			
Hypertension	16(55.17%)	21(51.22%)	0.744
Diabetes Mellitus	7(24.14%)	8(19.51%)	0.642
Bronchial Asthma	2(6.90%)	2(4.88%)	0.720
Malignancy	1(3.45%)	2(4.88%)	0.771
COPD	5(17.24%)	2(4.88%)	0.089
PTB	1(3.45%)	2(4.88%)	0.771
CKD	5(17.24%)	0(0%)	0.006
Cerebrovascular Disease	1(2.44%)	1(3.45%)	0.803

Table 2. Incidence of Postoperative Respiratory Failure among patients who underwent Cardiothoracic Surgeries

N=70	With PRF (n=8(11.43%)	Without PRF n=62(88.57%)	P-value
CABG	4(50.0%)	27(43.55%)	
Valvular surgeries	1(12.50%)	17(27.42%)	0.654
Aneurysmal repair	3(37.50%)	18(29.03%)	

Table 3. Incidence of Prolonged Mechanical Ventilato use among patients who underwent Cardiovascular Surgeries

N=70	With PRF n=23 (32.86%)	Without PRF n=47 (67.14%)	P-value
CABG	9(39.13%)	22(46.81%)	
Valvular surgeries	9(39.13%)	9(19.15%)	0.184
Aneurysmal repair	3(37.50%)	18(29.03%)	

Table 4. Diagnostic accuracy of Risk Calculator in predicting Postoperative Respiratory Failure using cut off 6.66

	With PRF (n=8)	Without PRF (n=62)	Total
	Frequency (%)		
≥ 6.66	6(75.00%)	17(27.42%)	23(32.86%)
< 6.66	2(25.00%)	45(72.58%)	47(67.14%)
Total	8(100%)	62(100%)	70(100%)
Sensitivity	75.00 % (34.9%-96.81%)	Positive LR	2.74 (1.55 - 4.83)
Specificity	72.58% (59.77%-83.15%)	Negative LR	0.34 (0.10-1.16)
PPV	26.09% (16.65%-38.41%)	Prevalence	11.43% (5.07 %-21.28%)
NPV	95.74% (87.03%-98.69%)	Accuracy	72.86% (60.90%-82.80%)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

Table 5. Diagnostic accuracy of Risk Calculator in predicting Prolonged Mechanical Ventilation using cut off 6.54

	With PMV` (n=23)	Without PMV (n=47)	Total
	Frequency (%)		
≥ 6.54	18(78.26%)	9(19.15%)	27 (38.57%)
< 6.54	5(21.74%)	38(80.85%)	43 (61.43%)
Total	23(100%)	47(100%)	70 (100%)
Sensitivity	78.26% (56.3 - 92.54%)	Positive LR	4.09 (2.19 - 7.64)
Specificity	80.85% (66.74% - 90.85%)	Negative LR	0.27 (0.12 - 0.59)
PPV	66.67% (51.69% - 78.90%)	Prevalence	32.86% (22.09% - 45.12%)
NPV	88.37% (77.56% - 94.35%)	Accuracy	80.00% (68.73% - 88.61%)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

Table 6. Diagnostic accuracy of Risk Calculator in predicting outcome using cut off 6.44

	With Outcome (n=29)	Without Outcome (n=41)	Total
	Frequency (%)		
≥ 6.44	28(96.55%)	5(12.2%)	33(47.14%)
< 6.44	1(3.45%)	36(87.80%)	37(52.86%)
Total	29(100%)	41(100%)	70(100%)
Sensitivity	96.55% (82.24 - 99.91%)	Positive LR	7.92 (3.47 – 18.05)
Specificity	87.80% (73.80% - 95.92%)	Negative LR	0.04 (0.01 – 0.27)
PPV	84.85% (71.06 - 92.74%)	Prevalence	41.43% (29.77% - 53.83%)
NPV	97.30% (83.95 -99.60%)	Accuracy	91.43% (82.27%-96.79%)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

DISCUSSION

This was a retrospective cross-sectional study of patients who underwent cardiothoracic surgery where respiratory failure was documented to have occurred in 44%. Also in our study, we wanted to be more specific regarding the outcomes, so we separated those who had postoperative prolonged mechanical ventilation from postoperative respiratory failure to mean that they were extubated but had unplanned reintubation within 30 days postoperatively. By sub-classifying we have found out that post-operative respiratory failure occured in 11% and the remaining 33% belonged to prolonged mechanical ventilation and 35% of these patients who had outcome died within 30 days.

The study of Gupta et al, where this risk calculator was developed, documented that post-operative respiratory failure including prolonged mechanical ventilation, occur in 3.1% of patients and 25% of these patients died within 30 days. But the patients here came from surgeries of different subspecialties. Also, one observation

they have was that the type of surgery performed had the largest difference in terms of risk for respiratory failure, which included aortic surgeries.[3] Importantly, thoracic aortic surgeries were also part of the sample population in our study.

Furthermore, in our study, majority of patients who underwent cardiothoracic surgery were hypertensive with mean age of 55 years old. The most important comorbidity noted to have an outcome was chronic kidney disease. In a study done by Baslanti, they concluded that both kidney injury and chronic kidney disease commonly occurred during hospitalization for major surgical procedures and were associated with up to four-fold increase in long-term cardiovascular specific mortality compared to patients with no kidney disease.[6]

Canver et al, in their study identified respiratory failure in patients who required longer than 72 hours of mechanical ventilation after CABG surgery where 5.6% developed respiratory failure. They found out that associated factors: sepsis, endocarditis, gastrointestinal bleeding, renal failure, mediastinitis, patients needing reoperation within 24 hours, and lastly, severe bleeding were significantly contributors for an increased risk of postoperative complications. They also concluded that postoperative extra cardiac organ impairment or systemic complication can influence respiratory failure after CABG.[7]

Prolonged mechanical ventilation is also known as delayed extubation. Although, there is still no concensus on its exact definition, but previous studies have used definitions ranging from extubation time of greater than 10 hours to greater than 7 days.[8] According to Totonchi, they have found that variables including gender, CKD, endocarditis, type of surgery and use of inotropes were significantly different between patients with and without PMV after an open heart surgery.

In the study conducted by Wong,[9] they have identified variables such as increased age, female gender, usage of intraortic balloon pump, inotropes, excessive bleeding and atrial arrhythmia as factors associated with delayed extubation.

In this study, PMV was defined as prolonged or delay of extubation of more than 48 hours. Our delayed extubation rate was high at 33%, although the definition of PMV and the study population in various studies have to be taken into consideration when comparing incidence rates. It has been shown that patients with emergent cardiac surgeries have a higher risk of delayed extubation compared to an elective surgery.[8] Delayed extubation was shown to have association with high in hospital morbidity, mortality, and bed occupancy costs in many studies.[8,10-11]

Gupta et al,[3] found that a patient with dependent functional status, with a higher ASA class, an emergency procedure, presence of preoperative sepsis were associated with PRF and they also observed that the type of surgery performed will give an impact on PRF that included aortic surgeries which are part of our study population. At the same time, these were also the 5 factors to be answered in the risk calculator, where an estimate of risk for PRF will be directly available once above data are supplied in the calculator. However, values alone are difficult to interpret so, in this study, we identified a cut-off value with the highest sensitivity and specificity in predicting PRF and PMV.

The risk calculator predicting postoperative respiratory failure using a cut off value of 6.66% has a sensitivity of 75% and specificity of 72.6% while in predicting prolonged mechanical ventilation using a cut off value of 6.54% has a sensitivity of 78.3% and specificity of 80.9%. However, we found that sensitivity and specificity of the risk calculator was highest when the two complications (PRF and PMV) were combined, referred in this study as outcome. Since, the calculator predicting an outcome (PRF and PMV) using the cut off value of 6.44% has higher sensitivity at 96.6%, with specificity of 87.8%, and an accuracy reaching 91.4%, we recommend its use than separating PMV from a PRF. Thus, for a patient with a score less than 6.44% from the risk calculator, weaning and early extubation could be facilitated.

LIMITATION OF THE STUDY

This was a retrospective study, so data was dependent to what was written in the charts and to charts that were retrieved.

CONCLUSION

The risk calculator predicting postoperative respiratory failure and prolonged mechanical ventilation using the cut off of 6.44% has sensitivity of 96.6%, specificity of 87.8%, and an accuracy of 91.4%, thus, can be use to stratify patients who will undergo cardiothoracic surgery and identify patients whom early extubation could be facilitated so as to reduce the length of ICU stay and mortality.

DISCLOSURE

The researcher is not personally or financially involved with any organization or company, which may have conflict of interest with the subject matter.

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Prevalence of Metabolic Syndrome Among Eight to Twelve Years Old Filipino Students Based on the Cardiovascular Risk Assessment Clinical Pathway for Children

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Background **---** Metabolic Syndrome (MetS) comprises of multiple cardiovascular disease risk factors. At present, there is no accepted universal definition of the metabolic syndrome for children and adolescents and no study reported prevalence of MetS in Filipino children.[2]

Method **---** A cross-sectional, population-based study. Included were 51 students who satisfied the inclusion/exclusion criteria. Demographic information was collected, physical examination was done, venous blood sample was taken and 2-D echocardiography was done at the school. Analysis of data were done.

Results **---** Sixty percent of Filipino children ages eight to twelve years old had Metabolic Syndrome. The prevalence of BP more than the 95th percentile for age and height was 33%, overweight/obesity at 37%, low HDL at 25%. Seventy percent had history of passive smoking while 73% had TV time of more than 2 hours. Passive tobacco and inactive lifestyle were significantly associated with metabolic syndrome ($p<0.0001$). The prevalence of LVPWd and LV mass for those who had at least three or more components of metabolic syndrome was 60.7%. Among them, 22.5% had abnormal relative posterior wall diameter and 25.0% had abnormal LV mass.

Discussion **---** The lack of universal definition of MetS among pediatric population limited the determination of its prevalence. Sixty percent of Filipino children had Metabolic Syndrome. Among the 31 subjects with MetS, abnormal relative posterior wall diameter and LV mass mass were noted. Thus, culmination of the pathology of metabolic syndrome occurs during childhood and early adulthood. Therefore, early recognition and early prevention of metabolic syndrome among pediatric population are of paramount importance for the reduction of morbidity and mortality as well as global burden of cardiovascular diseases in adulthood.

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Key Words: ■ MetS ■ pediatric metabolic syndrome

Metabolic Syndrome (MetS) comprises of multiple cardiovascular disease risk factors including obesity, hypertension, dyslipidemia, and abnormal glucose metabolism. At present, there is no accepted universal definition of the metabolic syndrome for children and adolescents. There are however, different definitions being used. In the United States, the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP-III) criteria, modified for children and adolescents was used.[1] The International Diabetes Federation (IDF) published a definition of MetS in children and adolescents. The prevalence in any group depends on the variables and cut points chosen because of its lack of universal criteria for diagnosis. At present, there has no study reported prevalence of MetS in Filipino children2. It is important to determine its prevalence among the young Filipino population who will be at risk for cardiometabolic diseases in the future.

Metabolic syndrome is commonly diagnosed during adulthood, several studies in the past reported that the process of atherosclerotic cardiovascular disease begins early in life and

2rd place, Oral Presentation - Original Paper. 28th PHC Annual Research Paper Competition and Poster Presentation held on February 2020 at Philippine Heart Center. Correspondence *to* ***Dr. Maricel Janice G. De Guzman.*** Department of Pediatric Cardiology. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

is progressive throughout the life span.[3-6] Identified potential risk factors for adult cardiovascular disease has been found to be present at a young age and that pediatricians must initiate the lifelong strategies to prevention. In adults, NCEP adopted the Framingham risk score to evaluate which patient are at highest 10-year risk of CVD and would benefit from more aggressive treatment.[8] No similar risk score available in children. A screening tool for metabolic syndrome would be a vital tool for the identification of those who are at risk in order to provide cardiovascular risk reduction. As lack of identification and treatment of those children leads to increased risk of CVD development for the next ten to twenty years.

The significance of the study is to identify usefulness of the cardiovascular risk assessment clinical pathway for children as a screening tool for metabolic syndrome. The optimal screening program would identify children with progressive atherosclerosis who are most at risk of MetS in adulthood. In order to provide those who are at risk of developing metabolic syndrome an early intervention and to provide means to modify and prevent the said risk factors. Furthermore, the data to be gathered in this study may be used to provide insights for health professionals and policy-makers about the extent of these problems in children. This research aims to prevent heart disease in young Filipinos and change the cardiovascular health of the Philippines.

REVIEW OF RELATED LITERATURE

Metabolic syndrome is a cluster of cardio vascular risk factors that collectively has a common pathophysiology related to insulin resistance. It may be an early indicator of chronic diseases such as diabetes mellitus and cardiovascular disease in adults.[9] There are already evidence that the individual risk factors in children is continuous into adulthood.[10] Hence, determination of its prevalence in young population is of utmost importance.

The metabolic syndrome in adults is generally defined as a cluster of cardiovascular risk factors namely central obesity, hyperglycemia, dyslipidemia and hypertension.[11] The cardiovascular risk factors tend to cluster, not only in adults, but also in children.[12] Metabolic syndrome is highly correlated to the following cardiovascular risk factors, namely obesity, hypertension, diabetes, hyperlipidemia, low HDL, smoking, sedentary lifestyle and parents with cardiovascular disease.

Obesity has been part of the global epidemic in both children and adults and is particularly associated with cardiovascular diseases, type 2 diabetes and hypertension.[13] Body mass index (weight in kilograms/height^2 in meters) classify overweight and obesity and is frequently used as a surrogate measure of fatness in children and adults. Both overweight and obesity affect heart structure and function. Obese individuals have large circulating volume that increased LV stroke volume, which in turn increases cardiac output. These changes result in ventricular alteration that ultimately lead to ventricular hypertrophy and enlargement, predisposing to heart failure. BMI is a strong predictor of cardiovascular disease.[14] Obesity is defined as BMI more than or equal to 95th percentile and overweight as BMI of more than or equal to 85% to les than 95th percentile. The mainstay for cardiovascular disease risk reduction is prevention of obesity in childhood and adolescents.

Hypertension is defined when measured blood pressure for children exceeds certain percentile values based on studies in normal populations. It is important to take into account age, sex and height in determining blood pressure percentile. Pre hypertension is defined as blood pressure between the 90th and 95th percentile for age, sex and height percentile or 120/80 mmHg, whichever is lower.[16] Hypertension is defined by systolic or diastolic blood pressure above the 95th percentile.[16] Children with an elevated BP is more likely to persist through adulthood because elevated blood pressure levels occur over time. Obesity, smoking and low levels of physical activity are factors that increase the likelihood of hypertension.[15] Prevalence of hypertension in adolescents are 3.2% and correlate with obesity.[16]

There are several population-based studies in patients with type 1 and type 2 diabetes that clearly suggests that hyperglycemia is a key risk factor for cardiovascular mortality with an increment of cardiovascular disease per increased of 1 unit (%) A1C of 18%.[17] In the Glucose Tolerance in Acute Myocardial Infarction study of patient with acute coronary syndrome, abnormal glucose tolerance was the strongest independent predictors of subsequent cardiovascular complications and death. Fasting plasma glucose was shown to be an independent predictor of cardiovascular events.[18]

Hyperlipidemia is link to atherosclerotic process in children and adolescents. The Bogalusa Heart Study and the PDAY Study both showed that early atherosclerotic lesions (fatty streak) and advanced lesions (fibrous plaques) are significantly related to elevations in total cholesterol, low density lipoprotein cholesterol (LDL-C), non-HDL cholesterol and low levels of HDL-C.[10] Approximately 70% of children with abnormal total cholesterol persisted with elevated levels in adulthood.[19] The National Health and Nutrition Examination Survey (NHANES) data from 1999-2006 indicated that the prevalence of abnormal lipid levels among all youths aged 12 to 19 years was 20.3%. But at present, there is lack of consensus on targeted versus universal screening for the management of dyslipidemia in children and youth. The American Academy of Pediatrics recommends targeted screening of children 2 years old and above with a family history of premature CVD or who have parents with dyslipidemia, whom family history is unknown or children who present with other CVD risk factors including hypertension, obesity and diabetes mellitus.[19]

Smoking or tobacco exposure has been link with CVD processes in adulthood. Prevention or cessation of smoking directed at children and youth is important for cardiovascular health promotion and risk reduction.[20]

Several observational studies of children and adolescents (4 to 18 years old) and young adults (19 to 21 years of age) showed link between increased time spent in sedentary activities with decreased levels of physical activity, adverse lipid profiles, increased levels of obesity and related cardiovascular risk factors.[21] Increase in physical activity reduces systolic and diastolic BP,[22] decreased BMI,[23] and improved cardio-metabolic risk profiles. Current recommendations for children 6 years of age and older are daily moderate to vigorous physical activitydaily with vigorous physical activity and muscle and bone-strengthening activities, of at least one hour, three days a week.[24] Also, decreased sedentary time (leisure screen time) to less than two hours per day is recommended. Limiting TV and electronic media usage to no more than 2 hours daily, and participating in at least 60 minutes of moderate vigorous physical activity daily.

In a study done by Donald et al., showed that parental cardiovascular disease independently predicted future offspring events in middle-aged adults.[25] A child with a positive parental history of CVD, particularly if premature at onset, is widely accepted risk factor for offspring cardiovascular events. The adverse association of cardiovascular risk factors in both children and adults with parental history of disease is well recognized hence cardiovascular screening programs have incorporated parental risk.

Metabolic syndrome has already been described by several studies and its prevalence has been reported by several authors.[26] However, there is no consensus yet on the definition of Metabolic Syndrome among pediatric population[27,28] Comparison across studies is problematic due to incongruent definitions used for metabolic syndrome. The lack of consensus on its definition is due to the fact that there are no reference values for different components to be used during childhood.[29]

There are several widely accepted definitions of the metabolic syndrome in children.[27] To name a few, a cohort study called IDEFICS (Identification and prevention of Dietary and Lifestyle induced Health effects in Children and Infants), classify children according to the

different components of the metabolic syndrome using reference values obtained in European children.[27] Another definition was done by Cook et al.[30] that corresponds to the NCEP (National Cholesterol Education Prgram) which was adapted to adolescents, but may be inappropriate if used for smaller children. The IDF (International Diabetes Federation) provided a definition of MetS adapted for children.[2] Viner et al. provided a definition based on obese children from UK and adolescents of different ethnicities to identify a high-risk group among the obese, which is frequently used by physicians.[2] All these definitions consider the following four major cardiovascular risk factors used for defining MetS: excess adiposity, blood pressure, blood lipids, blood glucose/insulin. According to these definitions, a child is diagnosed with MetS if a predefined criticalvalue is exceeded for three or more of these risk factors. Each definition has its own limitations.

In a population-based survey in eight European countries,[32] the prevalence of MetS using some definitions mentioned above showed 0.4 % by the definition proposed by IDF Consensus, 1.4 % by the definition of Cook et al, and 0.9% by the definition of Viner et al. The prevalence tends to be higherin girls as compared with boys. All classify a small percentage of thin or normal weight children as being affected by the metabolic syndrome and that it increased with weight category, and was highest among obese children. In that same study, it was noted that the contribution of the various components used for the definition of metabolic syndrome varies substantially between different definitions. In terms of hyperglycemia, the cut offs proposed by Cook et al and Viner et al result in a near negligible number of children classified as hyperglycemic. Thus, in both definitions, glucose and/or insulin levels contribute only small proportion to the prevalence of MetS. On the other hand, the IDF consensus Group showed minimal role of blood pressure, where the cutoff is exceeded only by a very small fraction of children. The proportion of different combinations of components of MetS according to IDEFICS cohort shows similar proportions for the different components of MetS, giving about equal chances for each of them to contribute to the overall prevalence of the MetS. The prevalence of Metabolic Syndrome among children in Asia Pacific Region is undetermined.[32] In 2017, a systematic review[32] on prevalence and trends of metabolic syndrome among adults in the Asia-Pacific region was done which showed a significant epidemic of MetS. The Philippines had a prevalence of 11.9% based on the national survey conducted in 2003.

A local study done by Dagooc et al,[33] determined prevalence of metabolic syndrome among Filipino children to be six percent. Furthermore, the prevalence of components of metabolic syndrome among Filipino children were 16.3 % on abdominal obesity, 13.5 % with hyperlipidemia, 11.5% with low HDL, 4.8 % had hypertension and 1 % had elevated fasting blood sugar.

Left ventricular hypertrophy is an independent risk factor for cardiovascular mortality and morbidity. According to the Framingham Heart Study,[34] LVH is the most important predictor of future cardiovascular disease. And the American College of Cardiology's Bethesda Conference has given LVH a category 1 risk factor for cardiovascular diseases. In a local study by Calveria-Barrion et al,[35] hypertension, high cholesterol, high LDL-C, and a family history of stroke were associated with thick left ventricular posterior wall. Furthermore, students with obesity and overweight, high LDL cholesterol, and fasting blood sugar were associated with high left ventricular mass index.

Objectives: The general objective is to determine the prevalence of metabolic syndrome and its component risk factors among Filipino children using the cardiovascular risk assessment clinical pathway for children as a screening tool for metabolic syndrome among eight to twelve years old Filipino children. While the specific objective are:

1. To determine the prevalence of Filipino children ages eight to twelve with metabolic syndrome
2. To determine the prevalence of cardiovascular risk factors among Filipino children ages eight to twelve years old level in terms of:
   a. Overweight/Obesity
   b. Hypertensive for age of at least > 95th percentile
   c. Diabetic for age (high random blood sugar)
   d. Hyperlipidemia (high random blood triglyceride)
   e. Low HDL
   f. Positive active/passive history of tobacco use
   g. Physically inactive/sedentary lifestyle
   h. Parents with cardiovascular disease
3. To determine the risk factors of metabolic syndrome:
   a. Positive active/passive history of tobacco use
   b. Physically inactive /sedentary lifestyle
   c. Parents with cardiovascular disease
4. To determine the relative posterior wall diameter and left ventricular mass by two-dimensional echocardiography for those who has at least three or more components of metabolic syndrome.

METHODS

Study Population

Inclusion Criteria:

1. Students ages eight to twelve with any one of the following:
   a. At least two (2) cardiovascular risk factors – hypertension for age and overweight or obese
   b. Presence of family history of heart attack or stroke occurred in family members less than 55 years of age
   c. Presence of parental hypertension, hyperlipidemia, and/or obesity maintained on medications
   d. Parent with definite Coronary Artery Disease (CAD)
   e. Previous history of Kawasaki Disease
2. Students with informed consent from parents to participate in blood extraction.

Exclusion Criteria: Students who had been previously diagnosed with Diabetes Mellitus Type I, Familial Hyperlipidemia.

Study Design: This is a cross-sectional, population based study wherein cardiovascular risk factors was determined among the subjects by using the clinical pathway - Cardiovascular Risk Assessment for Children.

Study Maneuver: An informed consent to conduct the study was secured from the school's principal. The study was conducted in La Verdad Christian School in Apalit, Pampanga from July 2019 to August 2019. The students included were those ages eight to twelve years old who met the inclusion criteria. An informed consent was secured from the parents or legal guardians from all subjects. A verbal assent for age 8 to 12 years old was obtained by the investigator and signed and personally dated by the subject and the person who conducted the informed consent discussion. A data collection form was used to gather data.

A basic demographic information was collected including age, sex, school (private or public), passive smoking, sedentary lifestyle and dietary ingestion. Age was presented in complete years (eight, nine, ten, eleven, twelve). The parents or legal guardians was asked about the family history of stroke or heart attack in family members < 55 years old, parental hypertension, parental hyperlipidemia, parental obesity and parent with definite coronary artery disease. The parents or legal guardians was asked if the child has Kawasaki Disease, Diabetes Mellitus I and Familial Hyperlipidemia.

A physical examination was done to all eligible subjects, to include anthropometric measurements. The following children's measures was taken: weight, height, and BP level. The body mass index (BMI) was calculated based on weight and height and apply the CDC growth charts for age and gender. An analog beam scale with height rod was used to measure the weight and height. At the beginning

of each measurement day at school, the child was asked to remove as much outerwear as possible. Regardless of the clothing worn, the child was asked to remove his/her shoes and was measured barefoot or wearing socks. Additionally, the child was asked to empty his or her pockets and remove all objects. The child was asked to remove eyeglasses, hair barrettes, and ties or rubber bands. A small box was provided at each measurement station for the child to place their personal items in until their measurements were complete. One measurement of weight and height was taken on each child. An aneroid sphygmomanometer with suitable cuff size for each subject was used to measure the blood pressure of the right arm in supine and sitting position after five minutes of rest. The mean of two measurements of Korotkoff phase I and the mean of two values of phase V will be recorded as systolic blood pressure and diastolic blood pressure respectively. Cardiac rate was counted manually using a stethoscope in full minute. Respiratory rate was counted in full minute.

A venous blood sample was taken from each subject by a medical technician of the tertiary hospital to measure random blood sugar and random total triglycerides and high-density lipoprotein.

A two-dimensional echocardiography was done at the school to those subjects that has at least three or more components of metabolic syndrome to measure relative posterior wall diameter and left ventricular mass. Z-score of the left ventricle posterior wall thickness was determined and left ventricular mass was indexed as LV Mass/Height raised to an exponential power 2.7, LV Mass to BSA raised to an exponential 2, and Z-score of LVM mass for lean body mass using the web-based calculators (*www.parameterz.com*).

Sample size computation: Using a G*power 3.1.9.2, a minimum sample size of 29 subjects are required for this study based on 9.642 odds ratio of obese adolescents to have hypertension, 5% level of significance and 90% power. The 9.642 odds ratio of having Hypertension among Obese adolescents was based on a study by Ujunwa FA[36] et al 2013.

Identification of Study Variables with definition of each variable:

I. Independent or exposure variables

A. *Socio-demographic characteristics:* Sex and age. Sex was presented as male or female. Age was presented in complete years as eight, nine, ten, eleven, twelve.

B. *Body Mass Index for Age Assessment:* calculated by dividing weight (kg) by height squared (m^2) and applying the CDC growth chart for age and gender.

C. *Hypertension in the family history:* A family history of systemic arterial hypertension was considered positive when hypertension was reported in children's parents or grandparents

D. *Passive smoke:* Passive smoking was considered positive if the father, mother or caregiver is smoking

E. *Hyperlipidemia:* Triglyceride of children ages 0-9 years old, acceptable is < 75 mg/dL, Borderline 75-99mg/dL, High > 100 mg/dL; Tricglyceride of children 10-19 years old, acceptable < 90mg/dL, borderline 90-129 mg dL, High > 130mg/dL)

F. *Sedentary lifestyle:* history of breastfeeding, television viewing and gaming > 2 hours per day, school physical activity of at least one hour per week, moderate activity of at least 30 minutes.

II. Dependent or outcome variables Metabolic Syndrome was defined as subjects meeting at least three of the following criteria:

1. Systolic or diastolic blood pressure greater than the 95% percentile for age, sex, and height
2. Overweight or Obese
3. Low high-density lipoprotein cholesterol < 40mg/dL (<1.03 mmol/L)
4. Hyperlipidemia (Triglyceride 0-9 years old, acceptable is < 75 mg/dL, Borderline 75-99mg/dL, High > 100 mg/dL; 10-19 years old, acceptable < 90mg/dL, borderline 90-129 mg/dL, High > 130mg/dL)
5. Diabetic for age (Random blood sugar > 200 mg/dL (> 11.1 mmol/L)
6. Positive active/passive tobacco use
7. Physically inactive/Sedentary lifestyle

ANALYSIS OF DATA

Descriptive statistics were used to summarize the clinical characteristics of the subjects. Frequency and proportion was used for categorical variables, median and inter quartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Chi-square test was used to analyze categorical data univariately. Independent Sample T-test, Mann-Whitney U and Fisher's Exact/Chi-square test was used to determine the difference of mean, rank and frequency, respectively, between patients with and without METS. Ninety-five percent (95%) confidence intervals from binary logisticregression will be computed to determine significant factors of METS. All statistical tests were two tailed test. Shapiro-Wilk was used to test the normality of the continuous variables. Missing variables will neither be replaced nor estimated. Null hypothesis will be rejected at 0.05α-level of significance. STATA 13.1 was used for data analysis.

RESULTS

A total of 51 subjects were included in the study. Table 1 shows the distribution of subjects according to demographic characteristics. Their age ranged from 8 to 12 years with a mean age of 10.08 years. All came from private school. Thirty-three (64.7%) had family history of cardiovascular disease. Among them, 25 (67.6%) had a family history of hypertension, 1 (2.7%) had a family history of hyperlipidemia, and 1 (2.7%) had a family history of stroke. More than 50% had high triglyceride levels. Thirteen had overweight (25.49%) and 6 had obesity (11.79%). History of passive smoking was noted in 36(70.6%) while almost 73% had TV time of more than 2 hours.

Table 2 shows the distribution of Filipino children ages 8 to 12 years according to the different components of metabolic syndrome. Positive passive tobacco use was found with highest prevalence at 70.6% followed by physical inactivity or sedentary lifestyle with a prevalence of 66.7% then by hyperlipidemia with 64.7%. Thirty one (60.78%) manifested with at least 3 components hence were labeled as metabolic syndrome.

Table 3 shows the association of passive history of tobacco use, inactive lifestyle and parental CVD with metabolic syndrome. Positive passive tobacco was significantly associated with metabolic syndrome as shown by the p value of <0.0001. Significantly higher proportion of children with passive history of tobacco use had metabolic syndrome than those without with 77.8% and 0% respectively. Similarly, inactive lifestyle was found to be significantly associated also with metabolic syndrome ($p=0.002$). Moreover, parents with cardiovascular disease such as hypertension, hyperlipidemia, and stroke were all significantly associated with metabolic syndrome.

Table 4 showed the prevalence of left ventricular (LV) posterior wall diameter and left ventricular mass for those who has at least three or more components of metabolic syndrome risk. Of the 51 subjects included 31 (60.7%) had at least three or more components of metabolic syndrome. Among them, 7 (22.5%) had abnormal relative posterior wall diameter and 8 (25.0%) had abnormal LV mass.

Ethical Considerations: Before a subject's participation, an informed consent was obtained from a legally authorized representative by the investigator after adequate explanation of the aims, methods, anticipated benefits and potential risks of the study. The informed consent was signed and personally dated by the parents or legally authorized representative and the person who conducted the informed consent discussion. A verbal assent for age 8 to 12 years old was also obtained by the investigator and was signed and personally dated by the subject and the person who conducted the informed consent discussion. One copy of the informed consent was given to the legally authorized representative. The investigator shall preserve the confidentiality of all subjects taking part in the study. The investigator shall ensure that the subject's anonymity is maintained.

Table 1. Demographic Characteristics of Filipino Children Ages 8 to 12 Years Old

	Frequency (n=51)	Percentage	MetS (n=31)	No MetS (n=20)	P-value
Age (in years)					
Eight	1	2.0	0	1(0.05)	
Nine	11	21.6	6 (19.35)	5 (16.12)	
Ten	24	47.1	16 (51.16)	9(45.00)	
Eleven	13	25.5	7 (22.58)	5(25.00)	
Twelve	**2**	**3.9**	**2 (06.45)**	**0**	
Mean ± SD = 10.08 ± 0.85			10.19 + 0.83	9.9 + 0.85	0.229
Sex					0.267
Male	23	45.1	16 (51.61)	7 (35)	
Female	28	54.9	15 (48.39)	13 (65)	
Family history**					
Without	24	47.05	21 (67.74)	3 (15)	<0.001
With					
Hypertension	25	49.02	22 (70.97)	3 (15)	<0.001
Hyperlipidemia	1	1.96	1 (3.23)	0	1.000
Stroke	1	1.96	1 (3.23)	0	1.000
Hypertensive students					
Hypertensive	17	33.3	**17 (54.84)**	**0**	**<0.001**
Normal	**34**	**66.7**	14(45.16)	20	<0.001
BMI			20.35 + 3.27	15.59 + 1.82	
Normal	32	62.75	12 (38.71)	20 (100)	<0.001
Overweight	13	25.49	13 (41.94)		<0.001
Obese	6	11.76	6 (19.36)	0	
Triglyceride					
Acceptable	18	35.3	7 (22.58)	11 (55)	0.042
(Normal)	4	7.8	4 (12.90)	0	
Borderline	29	56.9	20 (64.52)	9 (45)	
High					
Low HDL	13	25.49	13 (41.94)	0	0.001
RBS					0.702
Normal	48	94.12	28 (90.32)	20 (100)	
Borderline	1	1.96	1 (3.23)	0	
High	2	3.92	2 (6.45)	0	
Passive smoker	36	70.59	31 (100)	5 (25)	<0.001
Sedentary Lifestyle	34	66.67	27 (87.10)	7 (35)	<0.001
Breastfeeding	27	52.94	11 (35.48)	16 (80)	0.004
TV Time > 2 hours	37	72.55	28 (90.32)	9 (45)	0.001

***with multiple response**

Table 2. Prevalence of Components of Metabolic Syndrome Among Filipino Children Ages Eight to Twelve Years Old Students

Components of Metabolic Syndrome	Frequency (n=51)	Percentage
Positive active/passive tobacco use	36	70.6
Physically inactive / sedentary lifestyle	34	66.7
Hyperlipidemia	33	64.7
Overweight/Obesity	19	37.3
Systolic or diastolic hypertensive for age at least > 95th	17	33.3
Low HDL	13	25.5
Diabetic for age	3	5.9
Metabolic Syndrome (w/at least 3 components)		
(+)	31	60.78
(-)	20	39.21

Table 3. Association of Passive History of Tobacco Use, Inactive Lifestyle and Parental CVD with Metabolic Syndrome

	Metabolic Syndrome		Total	p-value*
	(+) (n=28)	(-) (n=23)		
Positive passive history of tobacco use				
Yes	28 (77.8%)	8 (22.2%)	36	<0.0001 (S)†
No	0	15 (100%)	15	
Physically inactive/ sedentary lifestyle				
Yes	24 (70.6%)	10 (29.4%)	34	0.002 (S)†
No	4 (23.5%)	13 (76.5%)	17	
Parents with cardiovascular disease				
Yes	28 (84.8%)	5 (15.2%)	33	<0.0001 (S)†
No	0	18 (100%)	18	

*** p>0.05- Not significant; p ≤0.05-Significant**
† Chi-square test

Table 4. Prevalence of Left Ventricular (LV) Posterior Wall Diameter And Left Ventricular Mass For Those Who Has At Least Three Or More Components Of Metabolic Syndrome Risk

	With at least three components of metabolic syndrome (n=31)	Percentage
Relative Posterior Wall Diameter		
LVH	28 (77.8%)	8 (22.2%)
Normal	0	15 (100%)
LV Mass		
LVH	24 (70.6%)	10 (29.4%)
Normal	4 (23.5%)	13 (76.5%)

DISCUSSION

In the present study, it was determined that 60.78% of Filipino children ages eight to twelve years old had Metabolic Syndrome. Several studies determined prevalence of pediatric metabolic syndrome ranging from 0.2 to 38.9% and median prevalence of metabolic syndrome in children with normal weight 38% while obese and overweight 18% and 41.9%, respectively.[37] The median prevalence of metabolic syndrome[20] in the whole population was 3.3 % (range 0-19.2%), 11.9% (range 2.8 – 2.9%) in overweight children and 29.2% (range 10-66%) in obese populations.[38] For non-obese, non-overweight populations, the range was 0-1%. [38] The wide range of prevalence rate of Metabolic Syndrome among pediatric population was due to the lack of consensus on its definition. The cut-off points of reference value as well as the components that comprises metabolic syndrome were different among the widely used definition.

In a systematic review of 85 published papers,[38] it was noted that boys had higher accumulate fat around the waist as compared median metabolic syndrome prevalence compared to girls and in older compared with younger children. Higher tendency of boys to to females, possibly make them susceptible to MetS.[39,40] In this study, boys had median metabolic syndrome prevalence of 51.6% as

compared to girls with 48.39% with a mean age of 10.19 + 0.83. No significant difference in the proportion of males and females with metabolic syndrome with p-value 0.267.

Another striking data from this study is the prevalence of children with mean systolic BP greater than the 95th percentile for age, sex and height (54%). All 17 subjects had Metabolic Syndrome. Fifty-four percent of those with MetS had BP greater than the 95th percentile for age, sex and height. A cross sectional pediatric study conducted in Canada noted that obese adolescents had 7.6mm Hg higher systolic blood pressure than normal-weight youths, with BMI exerting the strongest effect on BP41. In a systematic review on cardiovascular risk factors present in childhood and their prevalence done by Anabel et al, it was noted that an increase in arterial blood pressure in pediatric population predicts hypertension in adulthood.[42] Therefore, accurate assessment of BP and treatment of hypertension in children and adolescents are essential for the prevention of future heart disease.

The prevalence of obesity among pediatric population represents the most common chronic disorder and had greatly increased in recent years. The 8th National Nutrition Survey[43] in 2013 revealed that the prevalence of overweight among Filipino children 5 to 10 years old had risen from 5.8% in 2003 to 9.1% in 2013. The 2011 Global School-based Health Survey also showed that about 13% of adolescents in the Philippines were overweight and obese.[39] About 90 % of obese children and adolescents had at least one feature of metabolic syndrome.[30] In this study, the prevalence of overweight and obesity was 37.3%.

Correlations between the plasma level of cholesterol and a decrease or delay in atherosclerotic disease by means of diet and lifestyle modification had been documented, such that for each 1% reduction in total cholesterol, a decreased of 2% occurrence of coronary artery disease was observed.[42] In a review studies done by Brotons et al[44] in 26 countries from 1975 to 1996 involving 60,494 children and adolescents aged 2-19 years, an average of 165 mg/dL cholesterol, 60mg/dL for HDL-cholesterol, and 67 mg/dL for triglycerides. In this study, low level of HDL was noted in 13 patients or 41.94% and 12.90% had borderline level of HDL. The prevalence of hyperlipidemia was 64%. Several studies confirmed the trend that children with lower family income and those that attend public schools have lower cholesterol levels than adolescents from higher-income families and private schools.[42] Whether breastfeeding during the first year of life confers protection against future increase in the levels of plasma lipids and mortality by atherosclerotic disease had not been fully elucidated.[45]

In this study, children with sedentary lifestyle were 66% and 70.6% among these children had MetS. Physically active lifestyle had been associated with lower systolic and diastolic BP, HDL, triglyceride, and glucose among school-aged children.[46] Physical exercise was inversely associated with MetS47. TV viewing had been suggested as a measure of sedentary behavior in school-age children.[48] In this study, children with TV time of more than 2 hours 70% and 90 % of these children were have MetS. Several studies had similar observation that metabolic syndrome was significantly higher in school-aged children who watched TV/played on the computer for more than 2 hours in a day.[48]

Clustering of risk factors were known to be associated with metabolic syndrome. Among the known cardiovascular risk factors being investigated were passive history of tobacco use, sedentary lifestyle and parental CVD which were significantly associated with metabolic syndrome. In a previous study done by Dagooc et al,[33] it demonstrated that the prevalence of the components of metabolic syndrome in children of parents with atherosclerotic disease was significantly higher than in children whose parents did not have atherosclerotic disease. This finding was line with the study of Park et al[49] on familial aggregation of the metabolic syndrome in Korean families with adolescents, which showed that the risk of metabolic syndrome in children was highly correlated with parental history of metabolic syndrome. It

implied the influence of genes and environments in the etiology of the metabolic syndrome.

In a previous local study done by Barion et al, it was established that hypertensive and obese students had a strong risk of having thick left ventricular wall diameter. And both hypertension and obesity could predict elevated left ventricular mass and thickened left ventricular posterior wall diameter. The three multi-risk combination of obesity, hypertension and high LDL was able to predict an increase in left ventricular mass index and left ventricular posterior wall diameter. In that same study, a strong association between the occurrence of thick LV posterior wall diameter and hyperlipidemia was established. In this study, among the 31 subjects with MetS, 22.0% had abnormal relative posterior wall diameter and 25% had abnormal LV mass. LV mass should be evaluated for children with hypertension, to determine if left ventricular hypertrophy (LVH) is present. LV hypertrophy is the most useful mark for hypertensive target organ abnormality. When present, it indicates a more aggressive treatment.

CONCLUSION

The prevalence of metabolic syndrome among Filipino students ages eight to twelve years of metabolic syndrome found positive active or passive tobacco use with highest prevalence at 70.6% followed by physical inactivity or sedentary lifestyle with a prevalence of 66.7% then by hyperlipidemia with 64.7%. The prevalence of BP more than the 95th percentile for age and height was found at 33 %, overweight/obesity at 37%, low HDL at 25%. Sixty percent manifested with at least three components of MetS. The results showed that a positive active or passive history of tobacco use and having parents with cardiovascular disease were significant predictors of metabolic syndrome among Filipino children ages 8 to 12 years old. Among the 31 subjects with old was 60 percent. Prevalence of components MetS, 22.0% had abnormal relative posterior wall diameter and 25% had abnormal LV mass. It is elucidated in this study that the culmination of the pathology of metabolic syndrome occurs during childhood and early adulthood. Therefore, early recognition and early prevention of metabolic syndrome among pediatric population are points of paramount importance for the reduction of morbidity and mortality as well as global burden of cardiovascular diseases in adulthood.

RECOMMENDATION

Follow up research should be done in a larger population, with both public and private schools. Future study be done with comparison of prevalence using the commonly accepted definition of metabolic syndrome i.e definition by Cook et al, Viner et all, IDEFICs and the cardiovascular clinical pathway used in this study.

Disclosure of Conflict of Interest:

This study is not in collaboration with any pharmaceutical company or sponsors. The researcher will not receive any incentive or compensation for the review. The data gathered will be considered confidential.

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Association of Smoking with the Presence of Myocardial Perfusion Defects

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Background **---** Smoking is a modifiable risk factor for coronary artery disease (CAD). Myocardial perfusion scintigraphy is widely used to assess the extent and severity of CAD. This study aims to determine the association between smoking and myocardial perfusion defects.

Method **---** Myocardial perfusion scans of 420 patients were reviewed. The patients were classified according to their smoking status: current smokers (n = 53), former smokers (n = 119), and never smokers (n = 248). Perfusion scores, namely the summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS), and left ventricular ejection fractions post-stress (SLVEF) and at rest (RLVEF) were compared.

Result **---** Compared to never smokers, both current and former smokers have more total perfusion defects an more reversible perfusion defects, having greater SSS [F (2, 417) = 24.60, p < 0.0001], and SDS [F (2, 417) = 28.64, p = 0.0001]. Former smokers, but not current smokers, have more irreversible perfusion defects than non-smokers, having higher SRS [t (366) = 3.12, p = 0.006]. Both former and current smokers also have decreased LV wall function, with lower SLVEF [F (2, 417) = 18.34, p < 0.0001] and RLVEF [F (2, 417) = 20.42, p < 0.0001] than non-smokers.

Conclusion **---** Smoking is associated with increased extent and severity of myocardial perfusion defects and with reduced LV ejection fractions. ***Phil Heart Center J 2022;25(1):27-34.***

Key Words: ■ smoking ■ smoking cessation ■ coronary artery disease ■ mypcardial perfusion scintigraphy

Smoking is a modifiable risk factor for coronary artery disease (CAD). Among smokers worldwide, cardiovascular disease is the leading cause of death.[1] Conversely, smoking cessation leads to improved cardiovascular outcomes.[2,3]

Rheumatic fever (RF) and rheumatic heart disease (RHD) is prevalent in our country. In a study done by Lue et.al in 1979, RF and RHD Myocardial Perfusion Scintigraphy (MPS) has been used in the past to study and predict outcomes among patients CAD in general, and also specifically smokers with CAD. Piccini[4] found that the extent of perfusion defects was associated with the risk for sudden cardiac death. Furuhashi[5] retrospectively studied patients with CAD and found that both smoking status and the summed difference score (SDS) on MPS predict cardiovascular events such as cardiac death, non-fatal MI, unstable angina requiring hospitalization, congestive heart failure requiring hospitalization, and late revascularization. MPS was also used to quantify the effect of smoking cessation in an experimental set-up. Mahmarian[6] performed scans at baseline, mid-treatment with transdermal nicotine patches, and after treatment. Relative to baseline, the patients showed decreased smoking intensity (number of cigarettes smoked per day), decreased size of perfusion defects, and increased treadmill exercise duration.

This study investigated the association of smoking history and myocardial perfusion defects. We studied adult Filipino patients referred for MPS, determined their smoking history, and related this to the perfusion and gated SPECT parameters on MPS.

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METHODS

This cross-sectional study included 420 adult patients referred to the Division of Nuclear Medicine of the Philippine Heart Center for stress (tread-mill or dipyridamole) MPS with either thallium-201 or technetium-99m sestamibi for the assessment of coronary artery disease and/or myocardial ischemia.

Inclusion criteria is the study included patients, age 19 and above, referred for stress (exercise/pharma-cologic) MPI for the evaluation of CAD and/or assessment of myocardial ischemia, with prima facie clinical, electrocardiographic and/or echocardiographic evidence suggestive of CAD, or with CAD confirmed by scintigraphy itself, or byangiography. While excluded the study were:

1. Patients with no evidence of CAD by clinical examination, angiography, electro-cardiography, echocardiography, and myocardial scintigraphy.
2. Patients referred for viability study only.
3. Patients who underwent revascularization within two months prior to MPI.
4. Patients with valvular or aortic surgery within two months prior to MPI.
5. Critically-ill patients.
6. Patients with documented cardiomyopathy.
7. Pregnant patients
8. Patients with incomplete database/records for data on smoking status and/or smoking history or myocardial scintigraphic parameters due to an inadequate study.

This was a retrospective review of patient who had undergone stress myocardial perfusion scintigraphy at the Philippine Heart Center. Images were obtained using the Philips Forte and processed using the Philips Forte JETS tream software, The decision to refer the patient for imaging, including the choice of stress and on existing medical records. Information such as demographic data, anthropometric data, risk factors, smoking status and smoking history, and medications were obtained from the cardiac interview form. Myocardial perfusion parameters were obtained after the scans were re-processed and reviewed. These information were recorded in a prepared data collection form.

Based on their databases, patients were classified according to their smoking status, using the consensus definitions adopted by the World Health Organization,[1] Centers for Disease Control and Prevention (CDC), National Health Interview Survey (NHIS), and U.K. National Health Service Centre for Coding and Classification (NHS CCC).[1] The definitions were:

1. Ever smokers are adults who have smoked at last 100 cigarettes in their lifetime. An ever-smoker may be further classified as a;
   a. Current smoker: an adult who has smoked more than 100 cigarettes in his or her life-time and who currently smokes, with the last episode of smoking within the last 28 days of the interview.
   b. Former smoker: an adult who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of the interview and had not smoked in the past 28 days.

2. Never smoker: an adult who has never smoked, or who has smoked less than 100 cigarettes in his or her lifetime; in layterms, a non-smoker.

Also in accordance to consensus, former and current smokers' exposure to tobacco will be quantified in pack-years, using the following equation:

number of pack-years = (packs smoked per day) x years as a smoker

This definition was developed to establish the association between tobacco exposure and lung cancer, but has been successfully used in relation to other tobacco-related pathologies, including coronary artery disease.[1] The duration of smoking cessation was measured in years since smoking cessation, or quit-years.[1]

Dependent variables: ***Visual analysis of MPS with gated SPECT***

Myocardial perfusion scans were interpreted in consensus readings, with readers blind to patient's smoking status. The widely adopted American College of Cardiology/American Heart Association (ACC/AHA) using the 17-segment SPECT model and five-point semi-quantitative scoring was used in the visual analyses. In this scheme,[7] the left ventricle was divided into 17 myocardial segments. The uptake of Thallium-201 or Tc-99m Sestamibi in each segment was assigned a score of 0 for normal, 1 for mildly decreased, 2 for moderately decreased, 3 for severely decreased, and 4 for absent uptake. The summed stress score (SSS) was calculated by adding each of the seventeen segments' scores during the stress study. Similarly, the summed rest score (SRS) was calculated by adding each segment's score during the rest study. The SRS subtracted from the SSS yielded the summed difference score (SDS). Scores reflected the severity of CAD. A higher SSS denoted more extensive and/or more severe perfusion defects. SSS of 0-3 was considered within normal, 4-8 mildly abnormal, 9-13 moderately abnormal, and those greater than 13 were severely abnormal. The SDS was a measure of the degree of reversibility of such defects and was thus indicative of ischemia. SDS less than 2 indicated the absence of signifi-cant ischemia, 2-4 mild ischemia, 5-8 moderate ischemia, and greater than 8 indicated severe ischemia. Gated SPECT was also reviewed and measures of LV function, LV ejection fraction post-stress (S-LVEF) and at rest (R-LVEF), were recorded.

Confounding variables: Data on other diseases and events that influenced the development and natural history of CAD were also collected to better determine the association between perfusion defects and smoking. These were: hypertension, diabetes, previous acute coronary syndrome, and previous reperfusion more than 2 months prior to the scintigraphy. These were also derived from the patients' records.

Adequate Sample Size: In the aforementioned study by Furuhashi et al,[5] SDS was seen to be most predictive of poor outcomes. Overall standard deviation in their study was 1.7 and between-groups mean difference of 0.9 was found; 61% of their sample were ever-smokers. Based on these numbers, and an alpha set at 5% and power at 80%, a sample of 56 ever-smokers was predicted to be adequate to detect differences between never-smokers and ever-smokers. At an alpha of 1% and a power of 90%, 106 ever-smokers with smoking history was predicted to be adequate. Sample size requirements were cal-culated using STATA v13.0 (1985-2013; College Station, TX: StataCorp).

Statistical Analysis: Patients were classified into three groups: current smokers, former smokers, and never smokers. Homogeneity of baseline characteristics was tested between groups using analysis of variance (ANOVA), Pearson's chi-square, and Kruskal-Wallis tests as appropriate. The dependent measures for comparison were summarized as means and standard deviations. The three groups were compared using analysis of variance (ANOVA), with $p \leq 0.05$; if $p \leq 0.05$, with a Tukey HSD post-hoc analysis performed as needed. Associations between the dependent variables and smoking burden were determined using Spearman's rho, with additional moderator analyses performed to determine the interaction between smoking burden and smoking cessation. Analyses were performed using STATA v13.0 (1985-2013; College Station, TX: StataCorp).

Ethical considerations: The study was conducted in compliance withthe ethical principles set forth in the Declaration of Helsinki. Prior to study initiation, there was review and approval of the study protocol and subsequent amend-ments by the Philippine Heart Center Institu-tional Ethics Review Board (PHC IERB).

The investigator applied for a waiver of written consent as the study involved retro spective chart reviews. As all data for the

study had been extracted and/or was in the patient's medical records, no more than minimal risk is conferred by enrollment in this study. This waiver did not adversely affect the rights and welfare of the patients. Moreover, the study could not be done without this waiver.

The investigator preserved the confidentiality of all subjects taking part in the study and ensured that each subject's anonymity was maintained.

RESULTS

Baseline Characteristics: Overall, current smokers were younger than both former smokers and never smokers (*Table 1*). Current and former smokers were more likely to be male than never smokers. Height, weight and abdominal circumference, but not BMI, were also increased among former and current smokers, likely reflecting the predominance of males in these groups. Smoking burden was not significantly different between current and former smokers, with 22.33 and 25.55 pack-years of smoking respectively. Former smokers quit a mean of 12.99 years, with more of them having a short duration of smoking cessation. Current smokers were less likely to be hypertensive than former and never smokers but were more likely to have had an MI. Former smokers were more likely to be diabetic and to be on aspirin than both current and never smokers. Both current and former smokers were more likely to be dyslipidemic and to have wall motion abnormalities on echocardiography, than never smokers.

Data are presented as mean ± standard deviation or as number (%), as appropriate. Boldface denotes statistically significant associations with reference to never smokers, with p-values presented in the last column.

Data are presented as mean ± standard deviation. Boldface denotes statistically significant associations with reference to never smokers, with p-values presented below.

Current and former smokers were more likely than never-smokers to have higher SSS and SDS (*Table 2*). Former smokers, but not current smokers, have significantly higher SRS than never-smokers. Both former and current smokers had lower SLVEF and RLVEF than never-smokers. Differences between former and current smokers in terms of these parameters were not statistical significant.

Boldface denotes statistically significant associations with reference to never smokers, with p-values presented below.

Among ever smokers, there were weak but significant monotonic relationships between smoking burden and all perfusion scores, and between smoking burden and LV function post-stress (*Table 3*). Among current smokers, pack-years had a significant weak positive correlation with SRS [rs (51) = 0.3489, p = 0.0105]. Other scintigraphic parameters were not significantly associated with pack-years. Among former smokers, there were significant moderate correlations between pack-years and SSS [rs (117) = 0.3462, p = 0.0001] and, pack-years and SDS [rs (117) = 0.3278, p = 0.0003] but not between pack-years and the other parameters. The duration of smoking cessation had small and inverse associations with all three perfusion parameters, none of which were statistically significant. There were small and positive associations with both measures of LV function, which were statistically significant. However, when moderator analysis was applied, stronger associations were found between smoking burden corrected for smoking cessation and all three perfusion scores [for SSS rs (117) = 0.6419, p < 0.0001; for SDS rs (117) = 0.6427, p < 0.0001; for SRS rs (117) = 0.6137, p < 0.0001] and the LV ejection fraction at rest [rs (117) = 0.2342, p = 0.0103]. The association with SLVEF fell short of statistical significance.

Table 1. Baseline characteristics by smoking status among 420 patients referred for MPS

	Overall n=420	Current Smokers n=53	Former Smokers n=119	Never Smokers n=248	Sig
Age	57.8 ± 12.6	54.3 ± 10.8	59.9 ± 10.0	57.5 ± 12.6	0.0136
Male	298 (71.0%)	48 (90.6%)	107 (89.9%)	143 (57.7%)	< 0.001
BMI	26.6 ± 4.4	26.7 ± 4.5	27.1 ± 4.4	26.3 ± 4.3	0.278
Height (cm)	163.5 ± 8.5	166.8 ± 7.5	166.1 ± 7.6	161.7 ± 8.6	< 0.001
Weight (kg)	70.9 ± 13.3	73.9 ± 12.7	74.6 ± 13.5	68.5 ± 12.9	< 0.001
Abdominal Circumference (cm)	88.7 ± 12.2	89.6 ± 14.4	91.6 ± 11.1	87.2 ± 12.0	0.0102
Pack-Years		22.33 ± 18.36	25.55 ± 21.41	N.A.	0.3454
1-10 pack-years		14 (26.4%)	39 (32.8%)		
11-20 pack-years		18 (34.0%)	32 (26.9%)		
21-33 pack-years		12 (22.6%)	14 (11.8%)		
>34 pack-years		9 (17.0%)	34 (28.5%)		
Quit Years		N.A.	12.99 ± 11.00	N.A.	N.A.
0.25-4 quit-years		N.A.	33 (27.7%)	N.A.	N.A.
5-10 quit-years			32 (26.9%)		
11-20 quit-years			30 (25.2%)		
21-50 quit-years			24 (20.2%)		
Treadmill	221 (52.6%)	27 (50.9%)	57 (47.9%)	137 (55.2%)	0.405
METs	9.6 ± 4.7	11.1 ± 4.6	8.9 ± 3.3	9.5 ± 5.2	0.1228
%PMHR	88.1 ± 18.2	87.5 ± 18.3	88.4 ± 14.4	88.1 ± 19.7	0.9792
Thallium-201	286 (68.1%)	37 (69.8%)	87 (73.1%)	162 (65.3%)	0.312
Hypertension	318 (75.7%)	31 (58.5%)	90 (75.6%)	197 (79.4%)	0.005
Diabetes Mellitus	169 (40.2%)	15 (28.3%)	61 (51.3%)	93 (37.5%)	0.007
Dyslipidemia	161 (38.5%)	23 (43.4%)	50 (42.4%)	88 (35.6%)	0.034
Previous MI	62 (14.8%)	13 (24.5%)	20 (16.8%)	29 (11.7%)	0.047
Previous Revascularization	70 (16.7%)	8 (15.1%)	25 (21.0%)	37 (15.0%)	0.331
Typical Chest Pain	87 (20.8%)	12 (22.6%)	24 (20.2%)	51 (20.7)	0.932
Atypical Chest Pain	118 (28.1%)	16 (30.2%)	33 (27.7%)	69 (27.8%)	0.936
Heart Failure Symptoms	125 (29.8%)	13 (24.5%)	41 (34.5%)	71 (28.6%)	0.35
Ischemia on ECG	176 (44.7%)	25 (48.1%)	46 (42.2%)	105 (44.7%)	0.777
Wall Motion Abnormality	91(42.5%)	15 (50.0%)	31 (50.0%)	45 (36.7%)	0.0158
Beta-Blocker	160 (38.1%)	20 (37.4%)	46 (38.7%)	94 (37.9%)	0.989
ARB/ACEI	239 (56.9%)	27 (50.9%)	67 (56.3%)	145 (58.5%)	0.597
CCB	156 (37.1%)	14 (26.4%)	50 (42.0%)	92 (37.1%)	0.148
Statin	268 (63.8%)	29 (54.7%)	84 (70.6%)	155 (62.5%)	0.108
Nitrates	79 (18.8%)	11 (20.8%)	29 (24.4%)	39 (15.7%)	0.13
ASA/Clopidogrel	257 (61.2%)	30 (56.6%)	85 (71.4%)	142 (57.35%)	0.026
OHA	138 (32.9%)	12 (22.6%)	48 (40.3%)	78 (31.5%)	0.057
Insulin	25 (6.0%)	3 (5.7%)	11 (9.2%)	11 (4.4%)	0.174

Table 2. Smoking history and scintigraphic measures of perfusion and LV function

	Overall n=420	Current Smokers n=53	Former Smokers n=119	Never Smokers n=248
SSS	7.7 ± 11.0	10.6 ± 11.0	12.5 ± 13.4 < 0.001	4.7 ± 8.6
SDS	4.6 ± 7.1	7.2 ± 9.0 < 0.001	7.7 ± 8.9 < 0.001	2.5 ± 4.6
SRS	3.1 ± 7.6	3.4 ± 7.4 0.505	4.8 ± 9.1 0.006	2.2 ± 6.6
S-LVEF	56.2 ± 17.0	49.0 ± 17.4 < 0.001	51.1 ± 17.6 < 0.001	60.2 ± 15.5
R-LVEF	52.7 ± 15.8	45.6 ± 15.0 < 0.001	47.7 ± 16.0 < 0.001	56.6 ± 14.6

Table 3. Association between smoking burden and scintigraphic measures of perfusion and LV function.

	Current Smokers Pack-Years n = 53	Former Smokers n = 119			Ever Smokers Pack Years n = 172
		Pack-Years	Quit Years	PY/QY	
SSS	0.1647 0.2386	0.3462 0.0001	-0.1687 0.0666	0.6419 < 0.0001	0.2977 < 0.0001
SDS	-0.0365 0.7951	0.3278 0.0003	-0.1321 0.1521	0.6427 < 0.0001	0.2203 0.0037
SRS	**0.3489** **0.0105**	0.1710 0.0630	-0.1580 0.0862	0.6137 < 0.0001	0.2209 0.0036
S-LVEF	-0.1320 0.3461	-0.1630 0.0766	0.1888 0.0398	0.1650 0.0729	-0.1519 0.0467
R-LVEF	-0.0073 0.9588	-0.1609 0.0804	0.2079 0.0233	0.2342 0.0103	-0.1163 0.1287

DISCUSSION

Smoking is associated with increased extent and severity of myocardial perfusion defects and with reduced LV ejection fractions. Compared to non-smokers, ever-smokers have higher summed scores, indicative of more severe and/or more extensive perfusion defects. Among ever smokers, greater smoking burden is associated with more extensive and more severe perfusion defects. Among former smokers, smoking burden and smoking cessation taken together is more strongly associated with extent and severity of perfusion defects compared to these factors taken individually.

Although there have been past studies on the cardiovascular effects of smoking and smoking cessation, most have focused on different populations (e.g., elderly Japanese[5], women[8], young Hispanics in the United States[9]), on different outcomes (e.g., death[2, 3, 4, 10], heart failure[3, 10], or abnormal echocardiographic data[9]), or have used different designs (e.g., experimental[6], prospective cohort[8]). Similar to the existing literature, this study shows non-linear monotonic relationships between the smoking burden and markers of disease (i.e., reduced myocardial perfusion and LV function)[8,9]. The moderator analyses, however, show stronger associations between smoking burden corrected for smoking cessation and perfusion. This indicates that smoking burden and smoking cessation, when taken together, predict myocardial perfusion defects better than smoking burden alone. This suggests that smoking cessation reduces perfusion defects and that magnitude of this protective effect depends on the smoker's cumulative smoking burden upon quitting as well as on the duration of smoking cessation. Again, this is concordant with findings that smoking cessation reduces and, if maintained for a sufficient duration, could eliminate the increased risk for death and heart failure among former smokers[3,8,10].

Compared to past studies, this study does not demonstrate marked differences between former smokers and current smokers. This may be because the patients in this study presented with more extensive disease. For example, SSS in the sample was 7.7 ± 11.0 versus Furuhashi's[5] 4.2 ± 5.1. Other factors

that may have prevented us from demonstrating a difference between former and current smokers include the following: 1. a small number of ever-smokers in the study (only 41% versus Furuhashi's[5] 61%); 2. an even smaller number of current smokers in the study, and who were also younger (mean age of 54.3 years old) than the former smokers (59.9 years old); 3. the comparable smoking burden between the two groups (25.55 vs 22.33 pack-years), and; 4. the relatively short duration of quit-years relative to the studies which demonstrated reduced risk among former smokers (12.99 vs. > 15 quit-years in Ahmed[3]).

The pathophysiological processes underlying the deleterious effects of smoking on myocardial perfusion have been studied. Smoking has many detrimental biological effects, chief of which is the generation of free radicals that damage coronary arteries and myocardium. Secondarily, cigarettes contain nicotine, the component responsible for the addictive potential of cigarettes and a pharmacologic stimulant. As a stimulant, it increases myocardial oxygen demand by increasing the heart rate, blood pressure and cardiac output. Recurrent damage through multiple exposure to free radicals in the setting of increased demand, may cause weak vessels unable to cope with increased demand upon stress. This leads to reduced perfusion in the myocardial segments subtended by these vessels. At first, these perfusion defects (reflected by the SSS) may be reversible, indicative ischemia (reflected by the SDS), but over time may lead to myocardial infarction (reflected by the SRS). These episodes of reduced perfusion in turn may lead to remodeling and enlargement of the left ventricle with reduction of LV ejection fraction[11]. The larger effect sizes seen in the interaction of smoking and smoking cessation with myocardial perfusion data may be due in part to perfusion derangements occurring earlier in the course of CAD progression, compared to abnormalities in overall ejection fraction.[12]

This study has several strengths, among which is the use of myocardial perfusion parameters. There are also several limitations, mainly due to the retrospective nature of the study. Our pool of patients was limited to those referred by their attending physicians, and thus vulnerable to selection bias and has likely resulted in a skewed sample. Thus, there were inadequate numbers in interesting subsets such as female smokers. Furthermore, the increased proportion of males among ever-smokers likely contributes to the lower LV ejection fractions among smokers, as normal values for males are lower than those for females. Our data on smoking status was vulnerable to recall bias on the part of the informant and on what had been recorded in the cardiac interview form and existing medical hospital records. Other measures of smoking burdensuch as cigarettes per day (smoking intensity) and duration of smoking were not included in the analyses as these data were not routinely recorded in the cardiac interview. Data on related exposure, such as passive smoking and the use of smokeless tobacco were also not included. There was also no available data to correct for the influence of alcohol consumption, lack of physical activity, and unhealthy diet—lifestyle factors that are known to co-vary with smoking. Moreover, because this was a cross-sectional study, it is not known whether the large perfusion defects seen among smokers translates to increased risk for cardiac mortality and morbidity.

These data show that when evaluating patients for CAD work-up, smoking status is a significant risk factor and increases the likelihood of finding myocardial perfusion defects. Further research could be done on whether these myocardial perfusion findings predict MACE and may rightly be used as surrogate markers for them. Focus could be given to certain subsets (e.g., women, post-revascularization patients) with adequate samples to make regression analyses appropriate.

CONCLUSION

Smokers have more extensive and more severe myocardial perfusion defects and reduced left ventricular function, which vary in proportion to smoking burden.

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Association of Knowledge on Anticoagulation with Time in Therapeutic Range in Patients on Chronic Warfarin Treatment

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Background **---** Knowledge of anticoagulation therapy is an important factor in optimizing anticoagulation control. This study seeks to determine the gaps of knowledge in our locality and determine the association of good knowledge with anticoagulation control.

Methods **---** This cross-sectional study enrolled patients from a warfarin clinic at a tertiary hospital. Anticoagulation knowledge was assessed using a validated Anticoagulation Knowledge Tool (AKT) comprising 28 questions. Patients who scored more than 24 points (maximum of 35 points) was considered to have good anticoagulation knowledge. INR results in the past year was obtained and Time in Therapeutic Range (TTR) was computed by the Rosendaal Method. Spearman correlation analysis was used to investigate the association between anticoagulation knowledge and TTR.

Results **---** A total of 98 patients were interviewed. The mean AKT score was 24.70 ± 4.7 with 56% having good anticoagulation knowledge. The mean TTR was 48.96 ± 23.81 with only 34% having good anticoagulation control (TTR > 60%). TTR increases the odds of having good knowledge (OR 1.04 CI 1.02-1.04, p < 0.001) while Time under Therapeutic range (TUR) decreases the odds of having good knowledge (OR 0.97 CI 0.96 – 0.99, p = 0.002). Patients with good anticoagulation control have a 4.61 odds (CI 1.75-12.13) of having good knowledge. There was a significant positive association between patient's oral anticoagulation knowledge tool scores and TTR (R = 0.2832, p=0.005).

Conclusion **---** The gaps in the knowledge of anticoagulation uncovered in this study should be addressed in order to optimize anticoagulation control. This study was able to demonstrate that good anticoagulation knowledge was significantly associated with better anticoagulation control. ***Phil Heart Center J 2022;25(1): 35-44.***

Key Words: ■ warfarin ■ anticoagulation knowledge ■ anticoagulation control

Warfarin is an essential part of treatment in order to prevent stroke in patients with atrial fibrillations, valvular heart diseases, rheumatic hearts and hypercoaguable states.[1] However, warfarin has a narrow therapeutic margin and may result to a number of complications especially bleeding.[2] The use of warfarin requires long term follow up and monitoring of INR. Even with the advent of direct oral anticoagulant agents (DOACs) which have been proven to be as effective as warfarin with a lower risk for bleeding, the use of warfarin remains to be popular especially in developing countries because of its relative cheaper cost and it's indication in patients with valvular atrial fibrillation and those with metallic prosthetic valves.

Several factors are known to influence anticoagulation control with warfarin including dietary restrictions, alcoholic consumption, drug interactions and compliance.[2] Knowledge of these factors along with the possible side effects of warfarin is important in order to achieve the desired therapeutic outcome while preventing complications.[3] It has been shown that better knowledge and higher satisfaction were more likely to have higher warfarin refill adherence and to have good INR control.[4] Many studies have explored the association of knowledge of warfarin therapy with anticoagulation control but with conflicting results.[4–12] Most of these studies, however, have not use validated tools for assessing warfarin knowledge.[4,7,8,13–17]

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To date there are three validated tools for assessing warfarin knowledge: Anticoagulation Knowledge Assessment (AKA) by Briggs et al,[3] Oral Anticoagulation Knowledge test (OAK) by Zeolla et al,[13] and the Anticoagulation Knowledge Tool (AKT) by Obamiro et al.[18] The latter was the latest to be developed and was validated to also include the newer direct oral anticoagulation agents.

In the Philippines, only a small percentage of patients are found to be in the therapeutic range while majority had sub therapeutic levels.[19] To date there has been no other study investigating the level of knowledge using a validated tool in the locality.

Objectives: This study aims determine the association of knowledge on anticoagulation with time under therapeutic range among patients who are on chronic warfarin therapy.

1. to determine knowledge of anticoagulation among patients taking chronic warfarin therapy in the outpatient clinic at a Tertiary Hospital
2. to determine the time under therapeutic range of patients taking chronic warfarin therapy.
3. to determine the association between good knowledge and time under therapeutic range.

METHODS

The study was done with the approval from the institution's committee of research and ethics. An informed consent was obtained from the participants prior to their enrollment into the study.

Tis a cross - sectional analytical study was employed. The study took placed at the warfarin clinic at the outpatient department and private clinics of a tertiary hospital over one year (August 2017 - August 2018). The warfarin clinic caters to patients on chronic warfarin therapy who require regular INR monitoring and warfarin therapy adjustment. On an average, 30-50 patients are seen per day.

Included in the atudy were male and female patients who were at least 19 years old seen at the outpatient warfarin clinic and private clinics, have been taking warfarin for at least 1 year, and were able to give written consent were included in this study. Patients who refuse to participate in the study were excluded.

Sample Size Computation: A minimum of 97 patients were required for this study was based on 5% level of significance, 95% power and 0.356 correlation coefficient on the association of knowledge and warfarin adherence.[5]

Study Maneuver: After obtaining permission, the validated Anticoagulation Knowledge Tool (AKT)[18] was used for this study (Appendix A). The AKT is composed of 20 general questions and 8 questions specific to patients taking warfarin. A maximum of 1 point was allocated for each correct answer except for Question Items 6, 18, and 19 in Section A and Question Item 6b in Section B. A maximum score of 2 was given for item 6 in Section A, 1 point each for answers related to thromboembolism and for minimizing bleeding. For items 18 and 19, 1 point was given for each correct sign of side effects and each correct approach to reduce the risk of bleeding. Lastly, for the item 6b, 1 point was allocated for each food substances that was mentioned. A maximum total of 35 points can be obtained from both sections.

The study was explained to eligible patients on follow-up in the warfarin clinic and an informed consent was obtained. The primary investigator facilitated the interview and asked the participants questions from the questionnaire in Filipino. An approved script was used during the interview. The primary investigator then filled up the data collection form with the participants answer.

Subsequently, the patient's charts and records were reviewed to obtain clinical and demographic characteristics, and INR results in the preceding one year period.

Identification of Study Variables

A. *Socio-demographic Profile* - refers to the characteristic of the population namely for

the purposes of this study: age, sex, education level, social service class, monthly income and previous information on warfarin. Education level is the highest educational attained by the patient (i.e. elementary, high school, college, vocational or post graduate). The social service class (A, B, C, D) is the bracket in which social services has assigned to the patient and was obtained from the patient's white card. Previous information on warfarin refers to whether the patient received or can recall any educational materials or lectures for warfarin therapy.

B. *Clinical Data* was obtained from the review of patient's charts. This included the indication of anticoagulation therapy, length of anticoagulation therapy and number of INR determinations over the past year.

C. *Anticoagulation Knowledge Tool (AKT)* Score is the total of correct points with a maximum obtainable score of 35. A patient has good knowledge of anticoagulation therapy if the AKT score is greater than 24 points (> 70%).

D. *Time in Therapeutic Range (TTR)* - is the percentage of time the patient is within therapeutic range (INR 2.5 – 3.5 for metallic prosthetic valves, INR 2.0 – 3.0 for other indications). TTR was calculated by the Rosendaal Method which uses a linear interpolation approach to impute daily INR values. TTR was then taken as the percentage of daily INR values that fell within the therapeutic range over the total days that was monitored. INR values were not included if it was three months apart or included days were warfarin was withheld for dental pro cedures. Good anticoagulation control was considered when TTR is more than 60%.

Plans for Analysis: Descriptive statistics was used to summarize data. Logistic regression was used to determine the odds ratio (95% CI) of having good knowledge (AKT > 24 points) for the following selected socio-demographic and clinical characteristics: age, sex, monthly income, socioeconomic class, and duration of warfarin. Association between AKT scores with TTR will be determined by Pearson's R at 5% levelof significance using Sofa stats version 1.4.6.

RESULTS

A total of 98 patients were interviewed in this study. A summary of the sociodemographic and clinical characteristics of these patients are shown in Table 1.

Table 1. Sociodemographic and Clinical Characteristics of the Study Population

Characteristics	N = 98
Age, Years Mean +/- SD	49.39 ±12.77
Sex (%)	
Male	42 (43 %)
Female	56 (57 %)
Educational Level (%)	12 (12 %)
Primary	56 (57 %)
Secondary	30 (31 %
Tertiary	
Social Service Bracket (%)	0
A	2 (2%)
B	1 (1 %)
C1	6 (6 %)
C2	30 (31 %)
C3	58 (60 %)
D	
Monthly income	71 (72 %)
Unemployed	19 (19 %)
< 10,000	5 (5%)
10,000-19,999	3 (3 %)
> 20,000	
Received previous Information on Warfarin Therapy (%)	
Yes	30 (31%)
No	68 (69 %)
Primary Indication of Anticoagulation Treatment (%)	
Congenital Heart Disease	2 (2 %)
Cardiomyopathy	13 (13 %)
Prosthetic Metallic Valve Replacement	26 (27 %)
Rheumatic Severe MS Atrial f ibrillation	39 (40 %)
Non-Valvular AF	16 (16 %)
Cardioembolic Stroke	2 (2 %)
Length of Anticoagulation Therapy	
1-2 years	55 (56 %)
2.1 – 5 years	20 (20 %)
Greater than 5 years	23 (23 %)
Number of INR determination in the past year, Mean +/- SD	10.37 ± 4.1
Mean TTR +/- SD	48.96 ± 23.81
Proportion of patients with Good TTR (>60%), (%)	33 (34 %)

The mean age of the patients was 49.39 ± 12.77 years old. Among the patients, 42/98 (43%) were male and 56/98 (57%) were female. Majority of the study population finished secondary education 56/98 (57%) and were mostly unemployed 71/98 (72%). The most common indication for warfarin therapy was atrial fibrillation in severe mitral stenosis 39/98 (40%), followed by prosthetic metallic valve replacement 26/98 (27%) and nonvalvular atrial fibrillation 16/98 (16%). Other indications included cardiomyopathy with or without an LV thrombus 13/98 (13%), congenital heart disease 2/98 (2%) and cardioembolic stroke 2/98 (2%). More than half of the population, 55/98 (56%) have been taking warfarin for the past 1 – 2 years with majority receiving no previous information on warfarin therapy, 68/98 (69%).

The mean number of INR determinations in a year was 10.37 ± 4.1 and the mean time in therapeutic range was 48.96% ± 23.81% for this cohort. Only about one third of the population 33/98 (34%) had a TTR of more than 60%.

Of the 98 patients, 55 (56%) had good knowledge or were able to achieve a score of more than 24. The mean total score was 24.70 ± 4.7 (*Table 2*). An overview of the percentages of correct responses to the 28 questions of the Oral Anticoagulation Knowledge Tool is shown in Appendix A.

Table 2. Anticoagulation Knowledge Test (AKT) Scores and Good Knowledge

Anticoagulation Knowledge Test	SCORE
Mean Section A Subtotal Score ± SD (Max 26 pts)	17.79 ± 3.7
Mean Section B Subtotal Score ± SD (Max 9 pts)	6.92 ± 1.7
Mean Total ± SD (Max 35 pts)	24.70 ± 4.7
Patients with Good Knowledge (score of more than 24), (%)	55 (56%)

All patients correctly responded to Question 1 (what is the name of your anticoagulant). More than 90% of respondents were able to correctly answer Question 4 (frequency of the medication), Question 7 (regular timing of the medication), Question 15 (informing another health professional before undergoing a procedure), Question 23 (importance of INR monitoring), Question 26A (any food interactions) and Question 26B (types of foods). Five questions were answered correctly by less than 50% of the study population with the lowest proportion in Question 22 (Latest INR results) and Question 27 (Vitamin that affects warfarin therapy), 15% and 21% respectively. The percentage of correct response for each question is presented in Appendix A.

Presented in Table 3 are the univariate odds of having good knowledge of anticoagulation therapy for selected sociodemographic characteristics and anticoagulation control. Age, sex, educational level, previous warfarin information, length of warfarin therapy and number of INR determinations in a year did not significantly increase the odds of having good knowledge. TTR [Odds Ratio (OR) 1.04 Confidence Interval (CI) 1.02-1.04] increased the odds of having good knowledge by 4% for every unit increase. On the other hand, the odds of good knowledge decreased by 2.6% for every unit increase in time below therapeutic range (TBR) [OR 0.97 CI 0.96-0.99]. Patients with good control (TTR > 60%) have increased odds [OR4.61 CI 1.75-12.13] of having good knowledge.

Table 3. Univariate Odds Ratio of Having Good Knowledge of Anticoagulation for Selected Sociodemographic and Clinical Parameters of Patients who are on Chronic Warfarin Therapy

Parameters	Odds Ratio (95% CI)	p-value
Age	1.01 (0.98 – 1.05)	0.418
Male	0.55 (0.24 – 1.23)	0.143
Educational Level		
Secondary	1.61 (0.45 – 5.70)	0.456
Tertiary	2.80 (0.70 – 11.08)	0.142
Received Information on Warfarin Therapy	0.85 (0.36 – 2.02)	0.712
Length of Warfarin Therapy	1.00 (0.996 – 1.008)	0.532
Number on INR determinations in a year	1.08 (0.98 – 1.20)	0.129
Time in Therapeutic Range	1.04 (1.02 – 1.06)	< 0.001*
Time above Therapeutic Range	0.99 (0.96 – 1.02)	0.443
Time below Therapeutic Range	0.97 (0.96 – 0.99)	0.002*
Good Control (TTR > 60%)	4.61 (1.75 – 12.13)	0.002*

*significant p < 0.05

There was a significant positive association between patient's oral anticoagulation knowledge tool scores and TTR (R = 0.2832, p=0.005) and is shown in Figure 1.

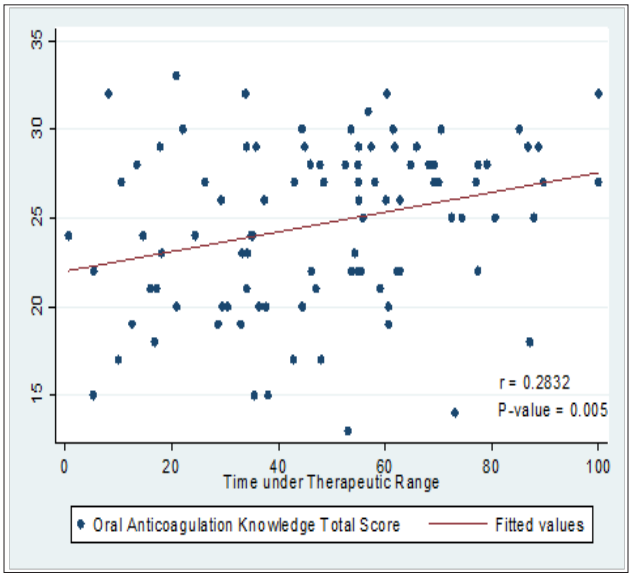

Figure 1. Scatter Plot of the Association of OAKT scores and Time in Therapeutic Range (TTR)

DISCUSSION

The patient's knowledge about anticoagulation therapy is an important factor in anticoagulation control and adherence. However, studies across the globe have shown that knowledge on anticoagulation remains in adequately low.[4–8,10,11,14,15,20–22]

In our study, adequate knowledge (AKT scores more than 70%, or 24 of 35 points) was seen in 56% of patients. Compared to neighboring Asian countries, this was higher than the proportion of adequate anticoagulation knowledge reported in Nepal (5.9%), China (9.2%), North India (17.8%), and Malaysia (44.2%).[5,6,8,14] Studies done in Singapore and Hongkong also reported low mean knowledge tool scores but not the proportion of the population studied.[4,15]

Regional differences may be accounted by the different questionnaires used, study populations and methods of recruitment. This study recruited patients from an outpatient warfarin clinic and may represent a population more adherent to warfarin therapy and INR monitoring as opposed to those with poor knowledge who would have not visited on a regular basis.

Compared to studies that used the same AKT questionnaire in Australia and Italy, mean scores were similar.[12,23] In a survey conducted via social media in Australia, mean AKT score was 25.69 (73% ± 13%) among patients taking warfarin.[12] A study in Italy also validated the AKT questionnaire showing a mean score of 23.45 (67%) ± 4.57 among 113 patients taking oral anticoagulation (92.9% taking warfarin) in two anticoagulation clinics.[23] In our study, the mean AKT score was 24.70 (71%) ± 4.7.

Questions that had a low proportion of correct responses (< 50%) were Q2, Q11, Q21, Q22 and Q27. These questions included the purpose for anticoagulation therapy, drug interactions with warfarin, target INR range, latest INR results and the interaction with Vitamin K. Most patients (86%) could identify warfarin as a "blood thinner" however only approximately half (49%) were able to correctly identify its indication as a prevention for stroke and thromboembolism. The most common misconception was that "blood thinner is for easy passage of blood through the stenosed valve or vessels of the heart."

About half of the respondents (53%) were unfamiliar with interaction of anti-inflammatory medications with warfarin and even fewer patients (21%) were able to correctly identify vitamin K and its significance to anticoagulation therapy.

Lastly, even if approximately half (49%) knew the ideal target range, only a few (15%) were aware of their latest INR reading. Paradoxically, the reason for warfarin clinic follow up was to show their latest INR result - majority of which was done during the same day. Though this was not formally investigated, the reason why patients do not look at their own results is probably because patients are dependent on warfarin clinic doctors for the interpretation of the results.

These gaps of knowledge are a recurring theme in the studies that investigate know

ledge of anticoagulation therapy. Inadequate knowledge on warfarin diet, warfarin-drug interactions, warfarin-herbal interactions, and warfarin-alcohol interactions, warfarin dosage, duration and aim of therapy; and consequences of under-dosage and over-dosage have all been reported.[4,5,20,24,7,9–12,14–16] Such deficiencies in knowledge, especially those uncovered in our study, are potential shortcomings in patient education that are often overlooked especially in high volume centers.

Conversely, our study population had a very high proportion of correct response (>90%) to questions on warfarin dosage and timing, interaction of alcohol, importance of informing other health care practitioners, surgeons or dentist prior to surgical/dental procedures, importance of INR monitoring and food interactions. Good knowledge in these areas may be inherent to a dedicated warfarin clinic and standard operating practices including the use of warfarin prescription forms that contain food interactions and date of the next INR determination and follow-up.

Many other factors that impact patient's knowledge on warfarin therapy have been demonstrated including older age,[8,12,14–16,20,22] lower educational attainment,[4,8,14,21,22] income level,[8,22] duration of warfarin therapy,[6,15,21] employment,[22] and living alone.[21] This study however showed age, sex, educational level, previous warfarin information, length of warfarin therapy and number of INR determinations in a year had no influence in good anticoagulation knowledge. Some studies similarly showed no significant associations with age, gender and indication of warfarin therapy.[5,6,21]

The impact of these factors may be varied or specific to the population being studied. In our cohort, most of the patients were young with a small proportion (3%) being over 70 years of age and majority were high school graduates; reducing the bearing of age and educational attainment on anticoagulation therapy. Majority of the patients were also rheumatic heart patients with atrial fibrillation or post mechanical valve replacement.

The mean TTR ± SD in our study is 48.96 ± 23.81 with only one third having good anticoagulation where time in therapeutic range was more than 70% in the past year. This is similar to a study done previously in our center reporting a TTR of 36.4% to 42.55%.[25] Other countries in our region also reported low measures of anticoagulation control.[4,5,15]

Our study showed that good anticoagulation control (TTR > 60) had a four-fold likelihood of having good knowledge. Furthermore, time in therapeutic range increases the odds of good knowledge while suboptimal anticoagulation negatively influences it. This finding strengthens the global evidence of a positive association between knowledge and anticoagulation control particularly in populations with poor anticoagulation control or low time under therapeutic range.[4,5,15]

Though there have been reports that knowledge was not associated with anticoagulation control,[6,9] these findings are not generalizable due to the small sample sized used, different measures of anticoagulation knowledge and anticoagulation control.

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LIMITATIONS

The major limitation of this study was that the AKT questionnaire was not validated in the Filipino language. The translated questions and wording may have led to unintended bias. Furthermore, the questionnaire was conducted as an interview solely by the primary investigator which increases the risk for social desirability bias. This study also did not explore the other factors that may contribute to anticoagulation control such as adherence and practices. Lastly, this was a single center study in a warfarin clinic which may also limit its generalizability.

CONCLUSION

Patient education and knowledge of anticoagulation therapy plays an important role in improving anticoagulation control. This was exemplified by the positive association demonstration between good anticoagulation knowledge and anticoagulation control. The gaps in knowledge that were uncovered in this study should be the basis of patient education to improve patient knowledge. It is recommended that different education strategies be investigated in order to bridge these knowledge gaps. Whether it translates to better anticoagulation control or even clinical outcome may be the subject for future research. Furthermore, validation of the Filipino version should be done in order to standardize the evaluation of anticoagulation knowledge.

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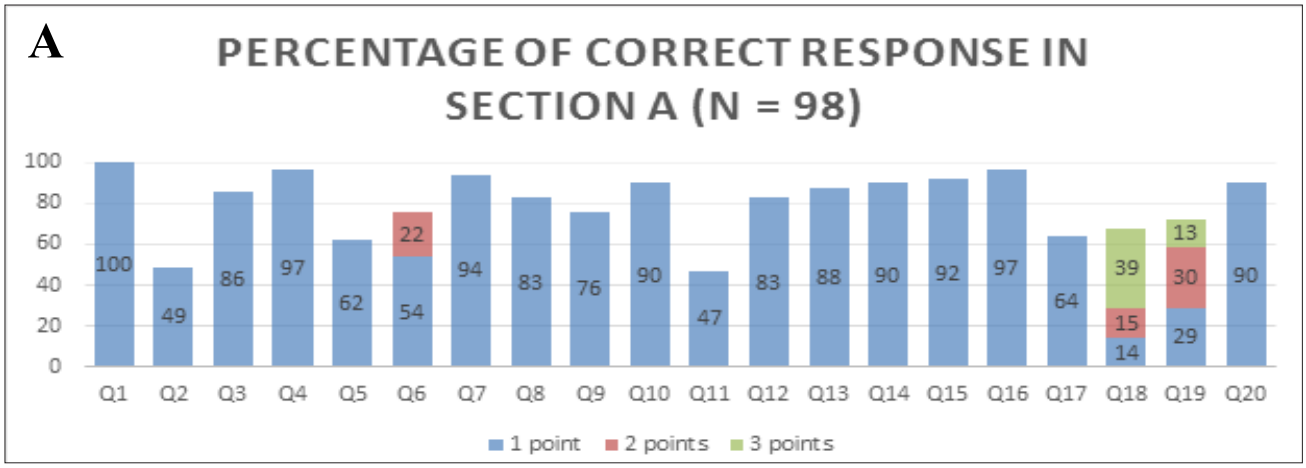
Appendix A. Tagalog Translation and Percentage of Correct Responses to Oral Anticoagulation Knowledge Tool

Question Number	Question (Filipino)	Answered correctly (%) n=98
Section A		
1.	What is the name of your anticoagulant medicine? Ano ang pangalan ng iyong gamot na pangpalabnaw ng dugo?	98 (100%)
2.	Why has your doctor prescribed you this medicine? Bakit inireseta ito ng iyong doktor?	48 (49%)
3.	How does this medicine work in your body? Paano gumagana ang gamot na ito sa iyong katawan?	84 (86%)
4	How many times a day do you need to take this medicine? Gaano kadalas mong iniinom ang gamot sa isang araw?	95 (97%)
5	For how long do you need to take this medicine (for example, 3 months, and 6 months, life-long)? Gaano katagal mong kailangan inumin ang gamot na ito? (halimbawa, 3 na buwan, 6 na buwan, isang taon, habang buhay)	61 (62%)
6	Why is it important to take this medicine exactly as your doctor has told you? Bakit mahalaga na inumin ang gamot na ito ayon sa iyong doktor?	1pt 53 (54 %) 2pts 22 (22 %)
7	Is it important to take this medicine at the same time each day? Mahalaga bang inumin ang gamot na ito sa parehong oras araw araw?	94 (96%)
8	Is it okay to double the next dose of this medicine if you miss a dose? Maari bang doblehin ang iyong gamot kung nakaligtaan mong inumin ito?	83 (85%)
9	Is it possible that skipping one dose of this medicine could worsen your condition? Kung nakaligtaan ang paginom ng gamut ng isang beses, maaari bang lumala ang iyong kondisyon?	75 (76%)
10	Is it appropriate to stop taking this medicine once you feel better? Angkop ba na itigil ang paginom ng gamot kapag maganda na ang pakiramdam mo?	88 (90%)
11	Is it safe to take anti-inflammatory medicines like ibuprofen (Advil®) while you are taking this medicine? Ligtas bang uminom ng mga anti-inflammatory na gamot tulad ng mefenamic o ibuprofen habang ininom mo ang gamot na ito?	46 (47%)
12	Is it safe to take vitamin supplements and herbal medicines with this medicine without consulting your doctor? Ligtas bang uminom ng mga herbal na gamot at bitamina kasabay sa gamot na ito nang walang pagkonsulta sa iyong doktor?	86 (88 %)
13	Is there any benefit in taking more of this medicine than your doctor has told you to take? May benepisyo ba ang labis na pag inom ng gamot higit pa sa payo ng doktor?	86 (88 %)
14	Will drinking too much alcohol increase the risk of side effects with this medicine? Makakaapekto ba ang pag-inom ng alak sa di kanaisnais na epekto ng gamot na ito?	88 (90 %)
15	Would you inform a surgeon, dentist or other health professional that you are taking this medicine before undergoing surgery or a procedure? Nais mo bang ipaalam sa isang siruhano, dentista o iba pang medikal propesyonal na iniinom mo ang gamot na ito bago sumailalim sa operasyon?	90 (92 %)
16	Is it important that all the health care practitioners you see know that you are taking this medicine? Mahalaga ba na alam ng lahat ng mga nakikita mong propesyonal sa pangangalagang pangkalusugan na iniinom mo ang gamot na ito?	95 (97 %)
17	What is the most important side effect of this medicine? Ano ang pinakamahalagang side effect ng gamot na ito?	63 (64 %)
18	Three signs of side effects that you should watch out for while taking this medicine are: Tatlong senyales ng “side effect” na dapat mong bantayan habang iniinom ang gamot na ito?	1 pt – 14 (14 %) 2 pts – 15 (15 %) 3 pts – 38 (39 %)
19	Three things you can do to reduce your risk of side effects are: Tatlong bagay na maaari mong gawin upang mabawasan ang “side effects”?	1 pt – 28 (29 %) 2 pt – 29 (30 %) 3 pt – 13 (13 %)
20	What is the best step to take if you accidentally take too much of this medicine? Ano ang pinakamahusay na hakbang gawin kung nag overdose ka sa gamot na ito?	88 (90%)

Section B		
21	What is your target INR range? Anu ang maganda resulta ng INR mo?	48 (49 %)
22	What was your last INR reading? Anu ang huling resulta ng INR mo?	15 (15 %)
23	Are regular INR tests necessary to know how well this medicine is working? Kailangn regular mag papamonitor ng INR para malaman wasto ang iyong gamut?	95 (97 %)
24	Is an INR value above your target range good for your general wellbeing? Ang mataas na INR sa target range ay mabuti sa iyong kalasugan?	81 (83 %)
25	Is it possible for INR values below your target range to be bad for your health? Ang mababa na INR sa target range ay masama sa iyong kalasugan?	80 (82 %)
26a	Is it possible for what you eat to affect your warfarin therapy? May mga pagkain ba na maaring maapektuhan ang pag-inom ng warfarin at pag-labnaw ng dugo?	97 (99 %)
26b	If you answered 'Yes' above, list THREE foods that can affect your anticoagulant therapy. Kung OO, magbigay ng tatlong pagakain na maaring maapektuhan ang pag-inom ng warfarin at pag-labnaw ng dugo?	1 pt – 10 (10 %) 2 pts – 18 (18 %) 3 pts – 65 (66 %)
27	List one vitamin that can significantly affect your anticoagulant therapy. Anu ang bitamina na maaring maapektuhan ang paglabnaw ng dugo?	21 (21%)



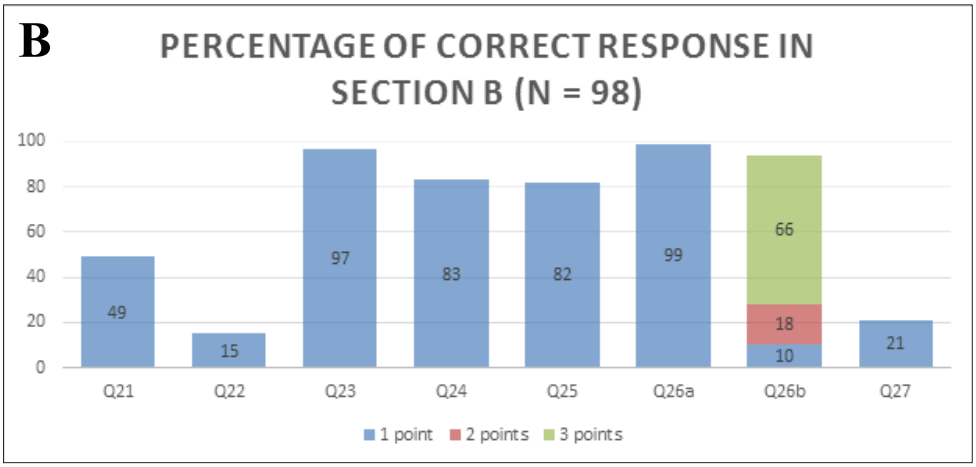


Figure 2. Percentage of correct response in section A (Fig.1a) and section B (Fig.1b) of the oral anticoagulation knowledge tool. N = 98

Association of Post-Procedural Echocardiogram with Long Term Outcomes of Patients Who Underwent Percutaneous Transvenous Mitral Commissurotomy (PTMC)

Jasper Val Ian M. Pablo, MD; Rhandy P. Panganiban, MD

Background **---** Unfavorable valve anatomy defined as Wilkins score >8 and post-PTMC mean pulmonary arterial pressure (PAP) were both independent predictors of all-cause mortality, mitral re-intervention, and the composite endpoint in a multicenter observational study from 1987 to 2011.

Method **---** This is a retrospective cohort study done in 197 patients diagnosed with rheumatic heart disease severe mitral stenosis who underwent successful PTMC. Charts were reviewed for echocardiographic parameters and clinical follow-up was done via phone call.

Result **---** Most rheumatic heart disease patients with severe mitral stenosis were female (85% female, 15% male). The mean baseline ejection fraction was 64.31 ± 6.84 % and did not change at 1 year (64.89 ± 6.90 %) and 5 years (64.59 ± 6.86 %) post PTMC. Baseline mean mitral valve area by planimetry was 0.75 ± 0.20 cm^2 and 1.53 ± 0.35 cm^2 and 1.39 ± 0.34 cm^2 at 1 and 5 years post-PTMC, respectively. The mean Wilkins score was 8 and did not change from baseline at 1 and 5 years post-PTMC. Stroke and mitral valve surgery were present in 0.69% and 1.39% of patients, 1-year post-PTMC and 10 (6.94%) patients had a stroke and 16 (11.11%) patients had mitral valve surgery at 5 years. No deaths were reported 1-year post-PTMC, but 5 (3.47%) patients died at 5 years post-PTMC.

Discussion **---** Most important independent predictors of major event-free survival include good valve score, high ejection fraction and smaller left atrial size. The presence of significant functional tricuspid regurgitation and pulmonary hypertension does not affect the long-term outcomes of patients. ***Phil Heart Center J 2022;25(1):45-51.***

Key Words: ■ rheumatic heart diesease ■ mitral stenosis ■ PTMC ■ echocardiogram ■ long-term outcomes

Acute rheumatic fever (ARF) is caused by recurrent skin or pharyngeal infection with Group A *β hemolytic Streptococcus* (GABHS) or *Streptococcus pyogenes*. Many sequelae have been described, but complications involving the valves of the heart can cause a chronic condition known as rheumatic heart disease which can lead to complications like heart failure, stroke, and death. Since the early 1900s, RF and RHD incidence and prevalence have been decreasing in developed countries but has remained a major concern in developing nations.[1]

Rheumatic fever (RF) and rheumatic heart disease (RHD) is prevalent in our country. In a study done by Lue et.al in 1979, RF and RHD were prevalent and were found to be more severe in the Philippines and other Oriental countries.[2] Left ventricular inflow obstruction secondary to mitral valve structural abnormality is termed as mitral stenosis (MS). There are many known causes of MS such as degenerative, congenital, or drugs but rheumatic fever remains to be the most common cause of MS.

With the increasing incidence of this disease, new innovations and techniques are being developed. Percutaneous transvenous mitral commissurotomy (PTMC) is a procedure used to open the mitral valve via transvenous access using a transseptal approach to enter the left atrium.[3] It is a well-established treatment of

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rheumatic MS with few reported complications. It is a class I indication in the management of patients with rheumatic mitral stenosis that is severe, without left atrial thrombus, with favorable valve morphology and with no or mild mitral regurgitation.[4] This technique is being offered more frequently and has largely replaced open commissurotomy.

In rheumatic MS patients who will undergo PTMC, and echocardiographic scoring or the Wilkins score is being used that is based on leaflet mobility, valve thickening, calcification and subvalvular thickening which predicts procedural outcome.[5] Each criterion is graded from 1 (normal) to 4 which yields a score from 4 to 16. A score of 8 or less predicts a more favorable outcome than those with a higher score. However, a score higher than 8 does not exclude a patient from undergoing PTMC. The current practice accepts a high Wilkins score in doing PTMC provided no other contraindications are present.[6]

This study will try to associate the 5-year outcome of PTMC by clinical and echocardiographic parameters.

METHODS

This study was approved for implementation by the Institutional Ethics and Review Board with compliance with the ethical principles stated in the Declaration of Helsinki, International, and local guidelines. As this was an observational, retrospective, non-intervention study, informed consent procedures were waived. This is a retrospective cohort study.conducted from April 2017 to December2019.

Inclusion Criteria; All patients aged 19 years old and above, with severe rheumatic MS who had successful PTMC, defined as MVA of > 1.5 cm^2 or doubling of MVA without MR 2+, between 2009 to 2014, who had follow-up for more than 5 years and at least two 2-dimensional echocardiograms done within the follow-up period.

Exclusion Criteria;

- Patients without baseline 2d echo at the institution.
- Patients who developed complications during PTMC requiring immediate mitral valve surgery.
- Patients without post-procedural 2d echo.

Study Maneuver; A chart record of patients admitted from 2009 to 2014 who had successful PTMC because of severe MS were reviewed. Successful PTMC was defined as post-procedural valve area $\geq$ 1.5 cm^2 and regurgitation of moderate or less, without in-hospital major adverse cardiacand cerebrovascular events. The echocardiographic record pre-PTMC was reviewed. Pre-procedural Wilkins score, MVA by planimetry, sPAP and MR quantification were recorded. An echocardiogram done as either intra-operative echocardiogram or immediately post-procedural echocardiogram were also reviewed and echocardiogram parameters being assessed were recorded.

Clinical follow-up data were collected using outpatient clinic charts. Primary care physicians and referring cardiologists were contacted and medical records were reviewed to obtain additional information. Surgical notes were obtained on all patients who underwent surgery after PTMC. Primary endpoints were noted on patients' records. A telephone follow-up was conducted using an IERB approved script to follow up on patients' status who were not able to follow up at the out-patient department and were also recorded as part of the composite outcomes.

Definition of Outcomes; Three primary endpoints were defined: (1) stroke (ischemic or bleed); (2) CV mortality; and (3) post-PTMC mitral re-intervention (either PTMC or surgery). PH persistence after PMV was considered a secondary endpoint and was defined by a systolic PAP (sPAP) >30 mm Hg in the post-PTMC hemodynamic evaluation.

*Sample Size Computation***:** Based on a study by Jorge, et.al., the all-cause mortality rate

among patients who underwent PTMC is 21%. Using the all-cause mortality rate of 21% among patients who underwent PTMC, estimated at 15% at 95% CI, then this study had 114 representative sample size.

Statistical Analysis; Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, a median and interquartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Odds ratio and corresponding 95% confidence intervals from binary logistic regression were computed to determine significant predictors of outcome at 1 year and 5 years. Missing variables were neither replaced nor estimated. Null hypotheses were rejected at 0.05α-level of significance. STATA 13.1 was used for data analysis.

RESULTS

The records of 197 patients who underwent PTMC were reviewed. Fifty-three potential participants were excluded in the study due to incomplete data such as the unavailability of post-PTMC 2D echo results.

The demographic profile of patients with rheumatic heart disease and severe mitral stenosis who underwent successful PTMC are shown in Table 1. There were 122 (84.72%) females and 22 (15.28%) males showing a female preponderance. The mean age was 38.86 (SD ± 10.66).

Other parameters such as echocardiographic measurements, Wilkins score, rhythm, and functional classification of patients are shown in Table 2. Highest Wilkins score recorded was 10. Mean baseline ejection fraction was 64.31 ± 6.84% and did not change at 1 year, 64.89 ± 6.90% and 5 years, 64.59 ± 6.86% post-PTMC. Mean left atrial size at baseline was 4.71 ± 0.76 cm and has no significant change at 1 year, 4.48 ± 0.86 cm and 5 years, 4.44 ± 0.92 cm post-PTMC. One hundred twenty-nine patients had mitral valve area of <1 cm^2 by planimetry. At 1-year post,PTMC, 137 patients (95.14%) had a mitral valve area of >1 cm^2 by planimetry. After 5 years post-PTMC, 133 patients (93.01%) had a mitral valve area of >1 cm^2 by planimetry. Baseline means mitral valve area by planimetry was 0.75 + 0.20 cm^2. At 1 year post-PTMC, the mean mitral valve area was 1.53 ± 0.35 cm^2 and the mean mitral valve area at 5 years post-PTMC was 1.39 ± 0.34cm^2 or a decrease in mitral valve area by 0.02 cm^2/year.

The baseline means the valve gradient was 14.63 ± 5.51 mmHg. At 1 year and 5 years post-PTMC, the mean valve gradient decreased to 6.53 ± 3.22 mmHg and 6.46 ± 3.22 mmHg, respectively.

One hundred ten (110) patients (76.39%) had mild tricuspid regurgitation. Severe tricuspid regurgitation was noted in 30 patients (20.83%) at baseline and decreased to 18 patients (12.50%) and 19 patients (13.29%) after 1 year and 5 years post-PTMC, respectively. Most of the patients, 55 (38.19%), had mild pulmonary hypertension and 41 patients (28.47%) had severe pulmonary hypertension pre-PTMC. At 1 year and 5-years post-PTMC, only 6 (4.17%) and 5 (3.50%) patients were noted to have severe pulmonary hypertension.

The mean valve score using the Wilkins scoring system was 8 at baseline and 1 year and 5 years post-PTMC. Twenty-nine patients (20.14%) had atrial fibrillation at baseline rhythm and 115 patients (79.86%) were at sinus rhythm. However, 1 year and 5 years post-PTMC, there were 40 (27.78%) and 48 (33.57%) patients with atrial fibrillation, respectively. Six (4.17%) patients had a previous history of PTMC.

The percentage of patients in functional class I increased while those with functional class II decreased as shown in Table 2.

As shown in Table 3, 1 (0.69%) patients had a stroke and 2 (1.39%) patients had mitral valve surgery at 1-year post-PTMC. At 5 years post-PTMC, 10 (6.94%) patients had a stroke and 16 (11.11%) patients had mitral valve

surgery. No deaths were reported 1-year post-PTMC, but 5 (3.47%) patients died at 5 years post-PTMC.

Composite outcomes at 1 year after PTMC (Table 4) were present in 3 patients and at 5 years post-PTMC (Table 5), 31 had composite outcomes of stroke, mitral valve surgery or death.

Table 1. Demographic profile of the patients

n = 144	Frequency (%); Mean ± SD
Age	38.86 ± 10.66
Sex	
Male	22 (15.28)
Female	122 (84.72)
Civil status	
Single	52 (36.11)
Married	92 (63.89)
Category of patient	
Service	112 (77.78)
Private	32 (22.22)
Years of follow up	6.48 ± 2.0

Table 2. Other parameters

	Baseline n=144	Year 1 n=144	**Year 5 n=144**
	Frequency (%); Mean ± SD; Median (Range)		
EF (Simpsons; %)	64.31 ± 6.84	64.89 ± 6.90	64.59 ± 6.86
LA size (Mm; cm)	4.71 ± 0.76	4.48 ± 0.86	4.44 ± 0.92
MVA PLN >1 (cm^2)	15 (10.42)	137 (95.14)	133 (93.01)
Mean MVA(cm^2)	0.75 ± 0.20	1.53 ± 0.35	1.39 ± 0.34
MVG (mmHg)	14.63 ± 5.51	6.53 ± 3.22	6.46 ± 3.22
TR			
None	4 (2.78)	9 (6.25)	6 (4.20)
Mild	110 (76.39)	117 (81.25)	118(82.52)
Severe	30 (20.83)	18 (12.50)	19 (13.29)
PH			
None	48 (33.33)	88 (61.11)	94 (65.73)
Mild	55 (38.19)	50 (34.72)	44 (30.77)
Severe	41 (28.47)	6 (4.17)	5 (3.50)
Wilkins	8 (6 to12)	8 (5 to 11)	8 (0 to 10)
Rhythm			
AF	29 (20.14)	40 (27.78)	48 (33.57)
SR	115 (79.86)	104 (72.22)	95 (66.43)
Functional class			
Class I	68 (47.22)	117 (81.82)	114 (79.17)
Class II	76 (52.78)	25 (17.48)	28 (19.44)
Class III	0	1 (0.70)	2 (1.39)

Table 3. Incidence of outcomes Post-PTMC

	Year 1 n = 144	Year 5 n = 144
	Frequency (%)	
Stroke	1 (0.69)	10 (6.94)
Mitral valve surgery	2 (1.39)	16 (11.11)
Death	0	5 (3.47)

Table 4. Association of Baseline Parameters with Composite outcome Post-PTMC at 1 year.

Baseline parameters	Present (n=3)	Absent (n=141)	Crude odds ratio (95% CI)	P-value
	Frequency (%); Mean ± SD			
EF (Simpsons; %)	55.67 ± 13.01	64.49 ± 6.61	0.85 (0.73 to 0.99)	0.040
LA size (Mm; cm)	6.23 ± 1.59	4.68 ± 0.71	7.5 (1.68 to 33.51)	0.008
MVA PLN >1(cm2)	1 (33.33)	14 (9.93)	4.54 (0.39 to 53.25)	0.229
MVG (mmHg)	10.67 ± 2.52	14.72 ± 5.53	0.84 (0.64 to 1.1)	0.204
TR				
None	0	4 (2.84)	-	-
Mild	1 (33.33)	109 (77.30)	(reference)	-
Severe	2 (66.67)	28 (19.86)	7.79 (0.68 to 88.98)	0.099
PH				
None	1 (33.33)	47 (33.33)	(reference)	-
Mild	1 (33.33)	54 (38.30)	0.87 (0.05 to 14.3)	0.923
Severe	1 (33.33)	40 (28.37)	1.18 (0.07 to 19.39)	0.910
Wilkins score	9 ± 1	8.26 ± 1	1.85 (0.72 to 4.74)	0.202
Functional class				
Class I	1 (33.33)	67 (47.52)	(reference)	-
Class II	2 (66.67)	74 (52.48)	1.81 (0.16 to 20.43)	0.631

Table 5. Association of Baseline Parameters with Composite outcome Post-PTMC at 5 year.

Baseline parameters	Present (n=29)	Absent (n=115)	Crude odds ratio (95% CI)	P-value
	Frequency (%)			
EF (Simpsons; %)	63.52 ± 5.43	64.50 ± 7.16	0.98 (0.92 to 1.04)	0.487
LA size (Mm; cm)	4.84 ± 0.76	4.68 ± 0.76	1.31 (0.78 to 2.19)	0.306
MVA PLN >1(cm2)	4 (13.79)	11 (9.57)	1.51 (0.44 to 5.15)	0.508
MVG (mmHg)	14.39 ± 4.86	14.69 ± 5.67	0.99 (0.92 to 1.07)	0.791
TR				
None	0	4 (3.48)	-	-
Mild	22 (75.86)	88 (76.52)	(reference)	-
Severe	7 (24.14)	23 (20)	1.22 (0.46 to 3.20)	0.690
PH				
None	10 (34.48)	38 (33.04)	(reference)	-
Mild	13 (44.83)	42 (36.52)	1.18 (0.46 to 3)	0.733
Severe	6 (20.69)	35 (30.43)	0.65 (0.21 to 1.98)	0.450
Wilkins score	8.76 ± 1.12	8.15 ± 0.92	1.84 (1.21 to 2.80)	**0.005**
Functional class				
Class I	10 (34.48)	58 (50.43)	(reference)	-
Class II	19 (65.52)	57 (49.57)	1.93 (0.3 to 4.52)	0.128

DISCUSSION

This study implicates that rheumatic patients with severe mitral stenosis have good 5-year outcomes given they have good valve score and left ventricular systolic function.

Percutaneous commissurotomy techniques have developed significantly since the early attempts were pioneered at our institution in 1989. To date, PTMC for severe mitral stenosis is considered the method of choice in this group of patients for several reasons. First, PTMC is non-surgical with comparable results to surgical intervention less the risks associated with surgery. In several randomized trials, PTMC and surgical commissurotomy are comparable with similar restenosis rates.[11]

In several studies, the overall success rate was 95 % and the "hospital" (30-day) mortality rate was only 4.5%.[12]

This study involves patients with severe mitral stenosis caused by rheumatic heart disease that underwent PTMC. The majority were female patients, as what was reported in most journals, with limited symptoms in functional class II with good valve score. This study provides information regarding long term outcomes of PTMC in our institution.

Our study demonstrates that PTMC for MS was successfully completed in 100% of patients. The event-free survival was 79.86% after 5 years in the 144 patients that completed follow-up. Most of the patients were functionally improved at baseline and on follow-up.

In several studies, the best periprocedural predictor of the mitral opening was Wilkins Score, but it is the post-procedural result (mitral valve area and gradient) that is the most important independent predictor of major event-free survival. Other predictors of major adverse cardiac events were atrial fibrillation, Pulmonary Artery Wedge Pressure (PAWP) greater than 18 mmHg and moderate to severe tricuspid insufficiency.[13]

This study involves PTMC in a population of mostly middle-aged women with a low Wilkins Score. This explains the favorable results, with a low incidence of complications. Echocardiographic and clinical follow-up data were analyzed in 144 patients that underwent PTMC. For every percent increase in baseline EF, the odds of having outcome at 1 year decreases by 15% (Crude OR 95% CI = 0.85 (0.73 to 0.99); p = 0.040) and for every unit increase in baseline LA size, the odds of having outcome at 1 year also increases by 7.5 times (Crude OR 95% CI = 7.5 (1.68 to 33.51); p = 0.008). For every score increase in baseline Wilkins score, the odds of having outcome at

1-year increases by 84% (Crude OR 95% CI =1.84 (1.21 to 2.80); p = 0.005). The mitral valve area, mitral valve gradient, presence of tricuspid regurgitation, presence of pulmonary hypertension and the pre-operative functional class of the patient did not predict long-term outcomes. Mitral valve area and mitral valve gradient may not be predictors of long-term outcomes for PTMC but rather the morphology of the valve causing the stenosis. Valve morphologyis an independent predictor of successful PTMC which then predicts successful long-term outcomes. This is in contrast to several studies concluding that the mitral valve area and gradient pre-PTMC influences the outcomes after PTMC. Still, mitral valve anatomy predicts successful mitral valve opening after PTMC. The presence of pulmonary hypertension and significant tricuspid regurgitation did not predict outcomes mainly because significant tricuspid regurgitation resolved upon resolution of pulmonary hypertension after PTMC, mainly because of the reduction in LA pressure after the procedure.

The long - term event - free survival after PTMC in several studies was between 75% and 97%.[14] In our study, the event-free survival was 79.86 % at 5 years.

Our data showed that the 5-year results of PTMC are good in selected subgroups of patients. These findings of favorable results support the previous recommendation that PTMC should be the procedure of choice in selected patients in centers with experience and skill in performing this procedure.

The limitation of the study, however, includes physicians' bias in reading the echocardiogram. A multi-reader review of the echocardiogram to assess Wilkin's score was not done because of the unavailability of the clips. Another limitation of this study was the exclusion of metabolic parameters (e.g. nutritional status, frailty score) that might affect outcomes after the procedure.

CONCLUSION

PTMC remains a safe and effective procedure for patients with rheumatic mitral stenosis. This study confirms the long-term efficacy of PTMC in a large population comprising a variety of patient subsets. The most important independent predictors of major event-free survival include good valve score, high ejection fraction and smaller left atrial size. Also, the presence of significant functional tricuspid regurgitation and pulmonary hypertension does not affect long-term outcomes of patients, thus, the presence of these lesions must not affect the decision of the physician to subject patients to undergo PTMC without other contraindications.

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Utility of the Pulmonary Artery Pulsatility Index in the Prognostication of Post-Valvular Surgery Outcomes of Patients with Combined and/or Multiple Valvular Heart Disease at a Tertiary Hospital

Emily Mae L. Yap, MD; Ronaldo Estacio, MD

Background **---** Studies on combined or multiple valve diseases are limited precluding the availability of evidence-based guidelines. Accurate measurement of pressure gradients is pivotal in assessing the hemodynamic burden of these lesions. The Pulmonary Artery Pulsatility Index (PAPi) is calculated by dividing the difference of the pulmonary artery systolic and diastolic pressures with the right atrial pressure.

Method **---** A retrospective analysis was done on all patients with combined or multiple valve disease who underwent right heart catheterization prior to valve surgery at a tertiary hospital from January 1, 2009 to December 31, 2018. Binary logistic regression was used to determine if the PAPi can predict major adverse events or in- hospital mortality.

Result **---** There were 65 patients in our cohort with a mean age of 44.52 years with a male:female ratio of 1.2. Rheumatic heart disease was the most common valve pathology (75%). Multi-valve involvement predominated (74%). Mitral valve replacement with tricuspid valve annuloplasty was the most common surgical procedure done (45%). Prolonged hospitalization (43%), right ventricular dysfunction (40%) and cardiogenic shock (23%) were the most common major adverse events (MAE). The mean PAPi was 2.09 +/- 1.08. On multivariate analysis, lower PAPi levels were independently associated with higher risk of developing MAE (OR, 0.50, 95% CI, 0.25-0.99, p= 0.048) and/or in-hospital mortality (OR, 0.21, 95% CI, 0.07-0.65, p=0.007).

Conclusion **---** The PAPi is a strong predictor of MAE and/or in-hospital mortality. Patients who had lower levels were at higher risk of MAE and/or in-hospital mortality. Early recognition of these subset of patients may improve clinical outcomes. ***Phil Heart Center J 2022;25(1):52-59.***

Key Words: ■ PAPi ■ valvular heart disease ■ surgery

Studies on combined or multiple valve diseases are limited precluding the availability of evidence-based guidelines and recommendations.[1] Stenosis and regurgitation occurring on the same valve and/or involvement of multiple valves may be seen in patients with rheumatic heart disease, congenital heart disease and less often, in degenerative valve disease.[1-2] In the Euro Heart Survey on valvular heart disease, 20.2% of the 5,001 patients had native multi-valvular involvement.[3] Measurement of the pressure gradients using right and/or left heart catheterization then becomes crucial in this setting to assess the hemodynamic burden of these lesions which will guide the clinician and the surgeon in the approach to the definitive and supportive management of combined or multiple valve disease which carry a substantially higher risk of morbidity and mortality compared to those with isolated or single valve involvement.

Right and/or left heart catheterization, commonly referred to as "hemodynamic studies" or "HS," are performed in the cardiac catheterization laboratory to obtain and study pressures in the cardiac chambers, calculate vascular resistance in both the pulmonary and systemic circulation, and measure cardiac output.[4] Hemodynamic indices derived from these procedures

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have been used as predictors of outcome in various clinical settings. In particular, the transpulmonary pressure gradient (TPG), diastolic pressure gradient (DPG) and pulmonary artery pulsatility index (PAPi) are novel hemodynamic indices that can be calculated with the pressures recorded with right heart catheterization alone.

The TPG is the difference between the mean pulmonary arterial pressure (MPAP) and the pulmonary capillary wedge pressure (PCWP) or the left atrial pressure (LAP). has been recommended for the detection of intrinsic pulmonary vascular disease in patients with left ventricular (LV) dysfunction.[5] Since this index iseasily affected by changes in heart rate, stroke volume and left atrial pressure, the DPG was subsequently proposed as a more superior index, being less sensitive to changes in loading conditions. The DPG is the difference between the pulmonary artery diastolic pressure (PADP) and mean pulmonary capillary wedge pressure (PCWP).[6] It has been well-studied in patients with pulmonary hypertension due to left-sided heart disease brought about by an increase in the left atrial pressure consequent to an increase in pulmonary vascular resistance.[6] In this setting, worse median survival (78 months) were reported among those with a TPG of more than 12mmHg and a DPG of more than 7mmHg than those who had lower values which had a better median survival (101 months).

The pulmonary artery pulsatility index (PAPi) is the difference in the pulmonary artery systolic pressure (PASP) and the pulmonary artery diastolic pressure (PADP) which represent right ventricular contractility and left atrial filling pressure respectively divided by the right atrial pressure which reflects right ventricular preload.[7-9] It is a relatively new hemodynamic index that has been first utilized in identifying patients with right ventricular (RV) dysfunction during an acute inferior wall myocardial infarction[7] and more recently, among patients with advanced heart failure.[8] This index has also been used to predict the need for mechanical circulatory support and to stratify patients who are at high risk for in-hospital mortality.[7]

The prognostic impact of the hemodynamic data derived from right and/or left heart catheterization prior to valve surgery is still an area for active investigation. Complications following valve surgery include arrhythmias, acute heart failure, low cardiac output syndrome, acute kidney injury, metabolic, pulmonary and embolic complications which contribute to prolonged hospitalization and increase morbidity and mortality.

SIGNIFICANCE OF THE STUDY

There have been no published studies in the predictive values of the DPG, TPG and PAPi in predicting major adverse events and in-hospital mortality among post-valve surgery patients. This has prompted the investigators to study the potential utility of these novel hemodynamic indices to identify these possible complications at the earliest possible time with the goal of improving clinical outcomes post-surgery in this subset of patients. The authors aim to be the first one to provide the most comprehensive data and to study the prognostic value of these indices among patients with combined or multiple valve disease.

OBJECTIVES

The General Objective of this study is to determine the utility of the TPG, DPG and PAPi obtained in the pre-operative setting in predicting in-hospital mortality in patients with combined and/ or multivalve disease who underwent valve surgery at the specialty centre from January 1, 2009 to December 31, 2018. while its Specific Objectives are;

1. To describe the clinical profile of patients with combined and/or multivalve disease who underwent hemodynamic studies prior to valve surgery
2. To describe the hemodynamic findings prior to valve surgery
3. To determine the mean TPG, DPG and PAPi prior to valve surgery

4. To determine the proportion of patients who developed major adverse events
5. To compare the mean TPG, DPG and PAPi between patients with and without major adverse events
6. To determine if the TPG, DPG and PAPi can predict the development of major adverse events and/or in-hospital mortality
7. To determine the sensitivity and specificity values of the TPG, DPG and PAPi in predicting major adverse events and/or in-hospital mortality

METHODS

This was a retrospective study done at specialty centre. Institutional Ethics Review Board approval was secured prior to study initiation. The medical records of patients aged > 19 years old with combined and/or multivalve diseases who underwent right heart catheterization (RHC) within 180 days prior to valve surgery from January 1, 2009 to December 2018 were included. Exclusion criteria included those who did not undergo RHC, have non-valvular heart disease or concomitant non-valvular cardiac surgery were excluded. There were a total of 69 patients who met the inclusion crtieria. Four of these patients were excluded in the final analysis due to missing hemodynamic data.

Demographic data were collected. Preoperative echocardiography [left ventricular ejection fraction (LVEF), tricuspid annular systolic plane excursion (TAPSE) and right ventricular fractional area change (RVFAC)] and right heart catheterization [right atrial pressure (RAP), right ventricular pressure (RVP), systolic pulmonary artery pressure (SPAP), diastolic pulmonary artery pressure (DPAP), mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (PCWP), pulmonary vascular resistance (PVR) and cardiac output (CO)] findings were recorded. The following were then computed:

1. Transpulmonary gradient (TPG)
   = MPAP - PCWP
2. Diastolic pulmonary gradient (DPG)
   = DPAP - PCWP
3. Pulmonary artery pulsatility index (PAPi)
   = PASP - PADP / RAP

The development of major adverse events and/or in-hospital mortality were the outcomes analyzed in our cohort. Major adverse events were defined as the development of right ventricular dysfunction (tricuspid annular plane systolic excursion of <1.7 cm and/or a right ventricular fractional area change < 35%)[10], cardiogenic shock (frank or relative hypotension, defined as a systolic blood pressure <90mm Hg, or a reduction in mean arterial pressure (MAP) of 30mm Hg; or a cardiac index of <1.8L/min/m^2 without mechanical or pharmacologic support, or <2.2L/min/m^2 with support; or an elevated end-diastolic pressures on the right of >10-15mmHg, and/or left of >18mmHg)[11], prolonged ICU stay (>3 days)[12], prolonged mechanical ventilation (>24 hours)[13], prolonged hospitalization (>7 days)[14] and/or acute kidney injury (increase in serum creatinine (SCr) by >0.3mg/dl within 48 hours, or an increase in SCr by 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days).[15]

All data were encoded in password-protected Microsoft Excel spreadsheets. A code number was assigned to each patient. To maintain anonymity, a separate spreadsheet that linked the study code to the patient's name was made with only the primary investigator having access to this file.

A minimum of 51 patients were required for this study based on the 88.9% sensitivity of PAPi for predicting in-hospital mortality among patients with acute inferior myocardial infarction[7] since there have been no prior published studies on the use of the TPG, DPG and PAPi in the setting of valvular heart disease. The desired width of confidence interval was 10%. The level of significance was set at 5%.

Categorical variables were described using frequency and percentages. Continuous variables were described using mean and standard

deviation (SD), and median and interquartile range (IQR) if normally distributed and non-normally distributed respectively. Univariate binary logistic regression analysis was used to determine if the TPG, DPG or PAPI can independently predict major adverse events and/ or in-hospital mortality. Multivariate binary logistic regression was used to further determine if each of the index continue to be significant after adjusting for the other indices.

Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), positive likelihood ratio, negative likelihood ratio and accuracy was used to determine the diagnostic accuracy and cut-off values of TPG, DPG and PAPi in predicting major adverse events and in-hospital mortality. The receiver operating characteristic (ROC) curve of the three indices was plotted to determine its discriminatory ability in predicting major adverse events and in-hospital mortality. Chi-square test was used to compare the three indices. Missing variables were neither be replaced nor estimated. STATA v13.1 was used for data analysis.

RESULTS

Baseline characteristics of patients included in this study are shown in Table 1. The mean age of our patients was 44.52 $\pm$ 11.58 years with a male to female ratio of 1.2. Rheumatic heart disease was the most common valve pathology. Seventy-four percent of the patients had multi-valve involvement. The rest of the patients had combined valve diseases. Mitral valve replacement with tricuspid valve annuloplasty was the most common surgical procedure done (44.62%, 29) followed by mitral and aortic valve replacement with tricuspid valve annuloplasty (26.15%, 17). The mean left ventricular ejection fraction was 52.62 $\pm$ 12.74%. The mean right ventricular fractional area change was 38.6 $\pm$ 9.

The pre-operative hemodynamic findings of patients with combined and/or multiple valve diseases were reviewed. Compared to the post-valvular surgery patients who expired during the course of their admission, patients who were subsequently discharged improved were observed to have higher diastolic blood pressures (72.98 $\pm$ 15.94 vs 63.67 + 2 3 . 2 4 , p=0.010), lower mean RA pressures (14.38 $\pm$ 6.87 vs 25 + 10.85, p<0.001), lower RV diastolic pressures (12.55 $\pm$ 8.07 vs 19.83 $\pm$ 6.59, p=0.005) and lower LVEDP levels (15.45 $\pm$ 5.63 vs 19.92 $\pm$ 6.46 p=0.019). Patients who had higher pre-operative PAPi were also observed among those who underwent surgery and were discharged improved. Significantly lower PAPi levels were observed among those who expired.

The predictive value of the TPG, DPG and PAPi in determining (1) major adverse events and (2) in-hospital mortality among patients with combined and/or multiple valve disease prior to valve surgery were determined. Major adverse events are shown in Table 3. A higher PAPi level was independently associated with a reduced risk of major adverse events (Odds Ratio, 0.50; 95% Confidence Interval, 0.25-0.99, p=0.048). As shown in Table 4, for every unit increase in PAPi, the odds of having major adverse events decrease by 50% after adjusting for TPG and DPG.

A higher PAPi level was associated with lower risk of in-hospital mortality on both univariate (Odds Ratio, 0.27; 95% Confidence Interval, 0.10 to 0.72) and multivariate analysis (Odds ratio, 0.21; 95% Confidence Interval, 0.07 to 0.65, p=0.007) as shown in Table 5.

For every unit increase in PAPi, the odds of in-hospital mortality decrease by 73%. After adjusting for TPG and DPG, the odds of in-hospital mortality decrease by 79% for every unit increase in PAPi.

Table 1. Baseline characteristics of patients with combined and/or multiple valve disease who underwent valve surgery from January 1, 2009 to December 31, 2018

	Alive (n=53)	Expired (n=12)	Total (n=65)	P-value
	Frequency (%); Mean ± SD			
Age	44.08 ± 11.64	46.5 ± 11.57	44.52 ± 11.58	0.517
Sex				0.359
Male	27(50.94)	8 (66.67)	35(53.85)	
Female	26(49.06)	4 (33.33)	30(46.15)	
Valvular heart disease				0.419
Rheumatic	38(71.70)	11(91.67)	49(75.38)	
Degenerative	7 (13.21)	0	7 (10.77)	
Congenital	8 (15.09)	1 (8.33)	9 (13.84)	
Combined	14(26.42)	2 (16.67)	48(73.85)	0.714
Multivalve	38(71.70)	10(83.33)	48(73.85)	0.494
Operation				0.548
MVR and TVA	25 (47.17)	4 (33.33)	29 (44.62)	
MAVR and TVA	13 (24.53)	4 (33.33)	17 (26.15)	
MVR	7 (13.21)	1 (8.33)	8 (12.31)	
MAVR	5 (9.43)	3 (25)	8 (12.31)	
AVR	3 (5.66)	0	3 (4.62)	
LV and RV systolic function				
LVEF (Simpson's method) (%)	53.83 ± 13.37	47.25 ± 7.77	52.62 ± 12.74	0.107
RVFAC (%)	38.42 ± 9.01	39.42 ± 12.72	38.6 ± 9.69	0.749
TAPSE (%)	2.01 ± 0.57	1.75 ± 0.51	1.96 ± 0.57	0.152

MVR - Mitral valve replacement,
TVA - Tricuspid valve annuloplasty,
MAVR - Mitral and aortic valve replacement,
AVR - Aortic valve replacement,
LV - Left ventricle,
RV - Right ventricle,
LVEF - Left ventricular ejection fraction,
RVFAC - Right ventricular fractional area change,
TAPSE – Tricuspid annular plane systolic excursion

Table 2. Hemodynamic measurements of patients with combined and/or multiple valve disease prior to valve surgery from January 1, 2009 to December 31, 2018

	Alive (n=53)	Expired (n=12)	Total (n=65)	P-value
	Mean ± SD			
Systolic blood pressure, mm Hg	122.08 ± 22.99	124.42 ± 27.35	122.51 ± 23.64	0.759
Diastolic blood pressure, mm Hg	72.98 ± 15.94	63.67 ± 23.24	71.26 ± 17.69	0.010
Mean arterial pressure, mm Hg	91.42 ± 16.01	92.83 ± 24.36	91.68 ± 17.62	0.804
RA mean, mm Hg	14.38 ± 6.87	25 ± 10.85	16.34 ± 8.71	<0.001
RV systolic, mm Hg	57.43 ± 26.52	64.58 ± 21.43	58.75 ± 25.66	0.388
RV diastolic, mm Hg	12.55 ± 8.07	19.83 ± 6.59	13.89 ± 8.27	0.005
PA systolic, mm Hg	60.26 ± 25.02	67.17 ± 18.86	61.54 ± 24.02	0.373
PA diastolic, mm Hg	30.66 ± 16.36	37.83 ± 12.98	31.98 ± 15.94	0.161
LVEDP, mm Hg	15.45 ± 5.63	19.92 ± 6.46	16.28 ± 6	0.019
MPAP, mm Hg	41.26 ± 18.36	50.25 ± 13.54	42.92 + 17.82	0.116
SPAP, mm Hg	57.16 ± 22.88	53.1 ± 20.96	56.49 ± 22.46	0.606
PCWP, mm Hg	21.39± 11.18	25.64 ± 7.37	22.24± 10.61	0.238
Transpulmonary gradient	19.45 ± 10.96	24.09 ± 10.79	20.38 ± 10.79	0.206
Diastolic pulmonary gradient	10.66 ± 8.68	14.45 + 7.72	11.42 ± 8.57	0.192
Pulmonary artery pulsatility index	2.27± 1.08	1.32 ± 0.69	2.09± 1.08	0.005

RA - Right atrium,
RV - Right ventricle,
PA - Pulmonary artery,
LVEDP - Left ventricular end-diastolic pressure,
PCWP - Pulmonary capillary wedge pressure,
PVR - Pulmonary vascular resistance,
SVR - Systemic vascular resistance,
CO - Cardiac output

Table 3. . Major adverse events in patients with combined and/or multiple valve disease who underwent valvular surgery from January 1, 2009 to December 31, 2018

	Alive (n=53)	Expired (n=12)	Total (n=65)	P-value
	Frequency (%)			
Right ventricular dysfunction	15(28.3)	11 (91.7)	26 (40)	<0.001
Cardiogenic shock	11 (20.7)	4 (33.3)	15 (23.1)	0.449
Acute kidney injury	2(3.8)	5 (41.7)	7 (10.8)	0.002
Prolonged ICU stay	5(9.4)	8 (66.7)	13 (20)	<0.001
Prolonged mechanical ventrilation	4(7.5)	8 (66.7)	28 (43.1)	<0.001
Prolonged hospitalization	20(37.7)	8 (66.7)	12 (18.5)	0.106

Table 4. Predictors of major adverse events among patients with combined and/or multiple valve disease prior to valve surgery from January 1, 2009 to December 31, 2018

	With MAE	Without MAE	Unadjusted		Adjusted	
	Mean ± SD		Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
TPG	20.53 ± 11.08	19.83 ± 10.14	1.006 (0.95 – 1.07)	0.841	1.04 (0.94 – 1.14)	0.476
DPG	11.79 ± 9.24	10.08 ± 5.68	1.03 (0.95 – 1.11)	0.540	0.98 (0.87 – 1.11)	0.748
PAPi	1.97 ± 1.15	2.44 ± 0.77	0.67 (0.40 – 1.12)	0.130	0.50 (0.25 – 0.99)	0.048

TPG - Transpulmonary gradient,
DPG - Diastolic pulmonary gradient,
PAPi - Pulmonary Artery Pulsatility Index

Table 5. Predictors of in-hospital mortality among patients with combined and/or multiple valve disease prior to valve surgery from January 1, 2009 to December 31, 2018

	Alive	Expired	Unadjusted		Adjusted	
	Mean ± SD		Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
TPG	19.45 ± 10.96	24.09 ± 9.67	1.04 (0.98 – 1.11)	0.206	1.11 (0.99 – 1.25)	0.085
DPG	10.66 ± 8.68	14.45 ± 7.72	1.05 (0.97 – 1.13)	0.196	0.96 (0.83 – 1.10)	0.521
PAPi	2.27 ± 1.08	1.32 ± 0.69	0.27 (0.10 – 0.72)	0.009	0.21 (0.07 – 0.65)	0.007

TPG - Transpulmonary gradient,
DPG - Diastolic pulmonary gradient,
PAPi - Pulmonary Artery Pulsatility Index

DISCUSSION

This is the first study to evaluate the prognostic utility of the pre-operative TPG, DPG and PAPi among patients with combined and/or multiple valvular heart diseases who underwent valvular surgery. These hemodynamic indices have not yet been previously studied on these subset of patients.

Whilst the TPG and DPG did not significantly vary among those were discharged improved or expired and those with and without major adverse events, the PAPi showed significantly higher values among (1) patients who were discharged improved after valve surgery compared to those who expired (2.27 $\pm$ 1.08 vs 1.32 $\pm$ 0.69, p=0.005), and (2) patients

who did not have any major adverse events compared to those who did (2.44 ± 0.77 vs 1.97 ± 1.15, p=0.048). Additionally, the PAPi level was an independent predictor of major adverse events or in-hospital mortality in our cohort with higher pre-operative PAPi levels seen among those who had lower risks of major adverse events and/or in-hospital mortality.

Similar findings have been shown in other studies but with a different subset of patients. The PAPi has been well-studied in patients with acute inferior myocardial infarction.[7] A significantly lower PAPi was observed in patients with suspected right ventricular dysfunction compared to controls without coronary artery disease and acute coronary syndrome (1.11 ± 0.57 vs 4.32 ± 3.04 vs. 5.52 ± 4.40 vs., respectively, p< 0.001).[7] In the same study, the PAPi demonstrated the highest sensitivity (88.9%) and specificity (98.3%) for predicting in-hospital mortality and/or requirement of a percutaneous RV support device.[7] Patients with a PAPI < 0.9 showed 100% sensitivity and 98.3% specificity in predicting in-hospital mortality and/or a requirement for a percutaneous right ventricular support device.[7]

The PAPi was also found to be an independent predictor of right ventricular failure among patients with left ventricular assist devices.[8] More recently described among those with symptomatic advanced heart failure (New York Heart Association Class IV) with a reduced left ventricular ejection fraction of 30% or less despite optimal medical treatment was the association of the PAPi with measures of left ventricular function, such as ejection fracton, cardiac index and pulmonary capillary wedge pressure, in addition to its correlation with clinical, hemodynamic and echocardiographic findings of right ventricular failure.[9] Moreover, the PAPi was an independent predictor of adverse clinical events, notably rehospitalization or mortality at 6 months, in this subset of patients.[9]

Finally, compared to the post-valvular surgery patients who were discharged improved, patients who expired were observed to have higher mean RA pressures (25 ± 10.85 vs 14.38 ± 6.87, p<0.001), lower diastolic blood pressures (63.67 + 23.24 vs 72.98 + 15.94, p=0.010) and higher LVEDP levels (19.92 ± 6.46 vs 15.45 + 5.63, p=0.019) which are significant findings seen in patients with heart failure.[9]

The main limitations of our study include its retrospective nature which precludes ascertainment of the completeness of the data, its single-center design which may limit generalisability and and the relatively small sample size which has reduced its power, possibly explaining why a good discriminatory ability of either of the three hemodynamic indices could not be obtained.

The authors recommend a study comparing the pre-operative and immediate post-operative PAPi score to determine the level of risk using the Cox proportion hazards model. A prospec tive study with a larger sample size will obviate the limitations of this study and can substantially improve its statistical power.

CONCLUSION

The PAPi is a strong predictor of major adverse events and/or in-hospital mortality. Patients with lower PAPi levels were at higher risk of major adverse events and/or in-hospital mortality. Early recognition of these subset of patients may improve clinical outcomes.

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DISCLOSURES

The authors of this study declare no conflicts of interest.

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Association of Post-Procedural Tricuspid Regurgitation with Long Term Outcomes among Patients who Underwent Percutaneous Transvenous Mitral Commissurotomy

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Background **---** Percutaneous transvenous mitral commissurotomy or PTMC is considered as the first-line treatment for symptomatic mitral stenosis (MS) because it provides immediate hemodynamic changes which leads to symptomatic relief and improvement in functional capacity. However, it has been observed that despite intervention, a concomitant moderate or severe tricuspid regurgitation (TR) may persist not related to a drop in left atrial and pulmonary artery pressure. The objective of this study is to determine the association of the persistence of TR post-procedure with long term outcomes of patients with moderate to severe tricuspid regurgitation who underwent PTMC.

Method **---** The study is a retrospective cohort design over a 5-year period (January 2005 to December 2010) of cases of PTMC done here in the Philippine Heart Center. This study analyzed long-term outcomes in terms of functional impairment, death, right-sided heart failure, hospitalization frequency, valve surgery and death among patients with persistent post-procedural tricuspid regurgitation.

Result **---** Fifty-three patient have been collected for preliminary analysis. Seventy-one (71%) of the population are female with a mean age of 37.8 + 10 years old. Persistent TR comprised two-thirds of the patient who underwent PTMC, 30% having a moderate TR and almost 34% as having severe TR. Twenty-three (23%) of the successful PTMC patients with persistent TR had hospitalization due heart failure while 11% developed right-sided heart failure. Logistic regression analysis of the available data shows a statistical trend between the persistence of TR and long-term outcomes (p = 0.081).

Conclusion **---** Based on the preliminary data analyzed, this study shows that persistence of post-procedural tricuspid regurgitation even after a successful PTMC produce worsening functional capacity and worse outcomes. ***Phil Heart Center J 2022;25(1):60-64.***

Key Words: ■ PTMC ■ Mitral Stenosis ■ Tricuspid Regurgitation

Mitral stenosis, which is predominantly due to rheumatic fever is characterized by obstruction of blood flow into the left ventricle due to structural abnormally of the mitral valve. It is a very disabling disease which causes shortness of breath, easy fatigability and if left untreated may lead to pulmonary edema, stroke, embolism, pulmonary hypertension and death.[1] As part of its natural history, severe mitral stenosis may lead to pulmonary hypertension brought about by the passive backward transmission of left atrial pressure which eventually leads to right ventricular overload. This in turn leads to dilation of the tricuspid valve annulus and eventual formation of a functional tricuspid regurgitation.[2] One-third of patients with mitral stenosis have at least moderate tricuspid regurgitation.[3]

Tricuspid regurgitation complicates survival and quality of life of patients with mitral stenosis, even among those who undergo any form of mitral valve intervention, such as PTMC. It has been proposed that tricuspid regurgitation can be reversed once left atrial pressure is relieved, however some studies,[4,5] show conflicting results, stating that as much as 23-37% have clinically significant tricuspid regurgitation years after intervention with even higher rates among those with rheumatic type

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of valvular disease.[6] Patients with moderate to severe mitral stenosis with symptoms in the presence of good pliable valve anatomy, absence of left atrial thrombus, and at most a mild mitral regurgitation all have a Class I indication to undergo percutaneous transvenous mitral commissurotomy which was only introduced in the Philippines in 1989.[1,7]

In the local setting, the most recent data available is from the study of Ang et al which showed a 52% event-free survival rate after 5 years for patients with significant tricuspid regurgitation post-PTMC.[8] In light of this information, it is of interest for the proponents of this study to investigate the association of the development of post-PTMC tricuspid regurgitation with specific outcome measures (death, hospitalization, heart failure, worsening functional capacity, valve surgery) to determine the continued utility of this procedure for this subset of patients.

As such, this study aims to update the current body of knowledge regarding the association of post-PTMC tricuspid regurgitation and long term clinical and echocardiographic outcomes.

METHODS

The conduction of this study has been approved after presentation of the protocol to the institutional The conduction of this study has been approved after presentation of the protocol to the institutional review board of the Philippine Heart Center in compliance with the ethical principles set by the Declaration of Helsinki. Informed consent was waived by the investigator due to the difficulty of obtaining individual authorization since the last contact with research subjects since patients are already discharged. However, anonymity was maintained, and that all data were encoded using a password-protected Excel spreadsheet. A code number was assigned for each patient and another separate password-protected spreadsheet that lines the study code to the patient's name. Only the primary investigator has access to this file.

The study design is a retrospective cohort, which included all patients 19 years old until 60 years old at the time of review, echocardiographic evidence at least a moderate tricuspid regurgitation by 2D echocardiography, Functional class II-III who underwent PTMC in the Philippine Heart Center between January 2005 to December 2010 and had followed-up for at least 5 years. Patients with multilesional rheumatic heart disease (RHD) (defined as any RHD with stenotic lesions aside from mitral stenosis), RHD with primary tricuspid stenosis, with significant pulmonary disease, with concomitant congenital heart disease including Lutembacher's syndrome were excluded from this study. (see Figure 1.)

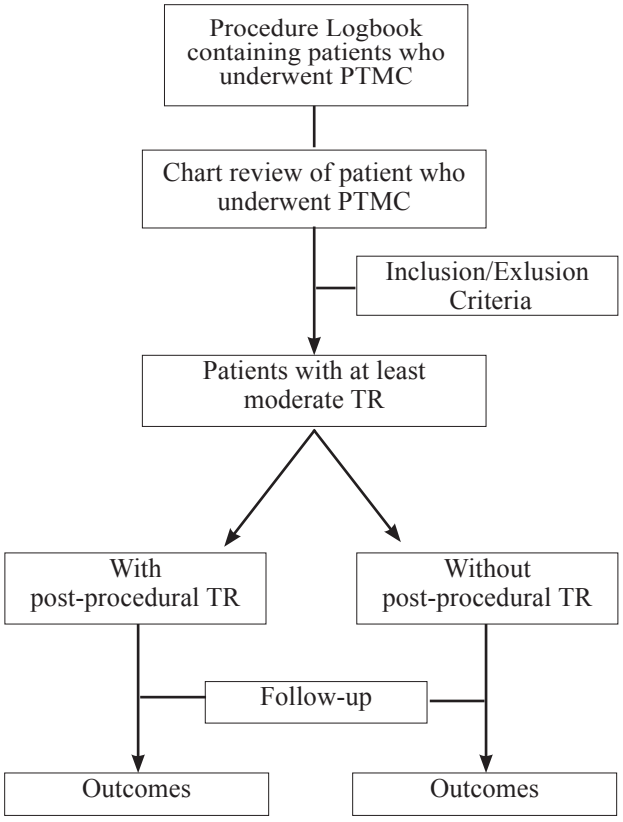

Figure 1. Flowchart of the methodology

Patient data records were retrieved from medical records section as well as the MedTrak® online records. Outcomes obtained and analyzed included echocardiographic Doppler presence of TR and severity, patient's functional capacity expressed in New York Heart Association classification, and morbidity and mortality – death, hospitalization, subsequent valve surgery.

Echocardiographic data of the patients before and after valve intervention were evaluated including the Wilkin's score of the mitral valve pathology, the mitral valve area – both planimetry measurements and by pressure half-time determination, mitral regurgitation presence and pulmonary arterial pressure.

Statistical Analysis:

Descriptive statistics was used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables and mean and SD for normally distributed continuous variable such as age. Fisher's exact test was used to determine the difference of the percentage from Prior PTMC to Post PTMC. Missing variables was neither replaced nor estimated. Null hypotheses were rejected at 0.05 α-level of significance. STATA 13.1 was used for data analysis.

A minimum of 55 patients were required for this study based on 9.381 hazard ratio of patients with pre-procedural TR to develop TR recurrence [5], 5% level of significance and 95% power.

RESULT

The invasive laboratory registry reviewed showed 308 patients who underwent PTMC between 2005 to 2010. Only 53 patients fulfilled the inclusion criteria. The remainder had insufficient data or incomplete follow-up.

Baseline characteristics of the patient are shown in Table 1. Of the 21 patients analyzed, 29% are male while the remaining 71% are female. The mean age of the patients are 38 years old. Around 19 percent have a Class II NYHA functional class while the rest are Class III. Fifty-three percent (53%) of these patients have long-standing atrial fibrillation.

Echocardiographic assessment of before and after PTMC are shown in Table 2. 78% of the patients have a Wilkin's score of 6 to 8 and only 21% attain high valve scores (Wilkin's >8). Ninety percent (90%) to 95% have a valve area of <1.0 cm^2. Persistent TR comprised two-thirds of the patient who underwent PTMC, 30% having a moderate TR and almost 34% as having severe TR. Majority of post-PTMC patients had a normal pulmonary pressure to mild pulmonary hypertension. Around 51% of patients had a NYHA classification of II to III with the remaining percentage as having a class I functional classification, and only one patient having dyspnea at rest.

Based on follow-up data as shown on Table 3, twenty-three (23%) had hospitalization due heart failure while 11% developed right-sided heart failure. Five patients had subsequent valve surgery – including both mitral and tricuspid valve surgery. Only two patients were reported to have died due to cardiac causes.

Table 1. Demographic and clinical profile of the patient (n=53)

	Frequency (%); Mean + SD
Age	37.77 + 10.04
Sex	
Male	10 (18.87)
Female	43 (81.13)
BMI	
< 18.5	7 (13.46)
18.5 to 24.9	38 (73.08)
>25	7 (13.46)
Functional class	
Class I	1 (1.89)
Class II	42 (79.25)
Class III	10 (18.87)
Class IV	0
Comorbidities	
Hypertension	1 (1.89)
Diabetes mellitus	0
AF	28 (52.83)
COPD	3 (5.66)
Previous stroke	2 (3.77)
CAD	0
CKD	0
Liver disease	1 (1.89)

Table 2. PTMC results (n=53)

	Prior PTMC	Post PTMC	P-value
	Frequency (%)		
Wilkins score			-
< 5	0	-	
6 to 8	36 (78.26)	-	
9 or 10	10 (21.74)	-	
MVA Planimetry			<0.001
< 1.0 cm	49 (96.08)	6 (12)	
1.0 to 1.5cm	2 (3.92)	23 (46)	
> 1.5cm	0	21 (42)	
MVA PHT			<0.001
< 1.0 cm	47 (90.38)	6 (11.54)	
1.0 to 1.5cm	5 (9.62)	22 (43.31)	
> 1.5cm	0	24 (46.15)	
MVG			<0.001
< 5	0	11 (20.75)	
5 to 10	5 (10.64)	29 (54.72)	
> 10	42 (89.36)	13 (24.53)	
MR			<0.001
None or trivial	27 (50.94)	15 (28.30)	
Mild	25 (47.17)	19 (35.85)	
Moderate	1 (1.89)	15 (28.30)	
Severe	0	4 (7.55)	
TR			<0.001
None or trivial	0	3 (5.66)	
Mild	0	16 (30.19)	
Moderate	22 (41.51)	16 (30.19)	
Severe	31 (58.49)	18 (33.96)	
Pulmo pressure			<0.001
Normal	0	21 (39.62)	
Mild	9 (17.31)	20 (37.74)	
Moderate	21 (40.38)	7 (13.21)	
Severe	22 (42.31)	5 (9.43)	
Functional class			<0.001
Class I	0	25 (47.17)	
Class II	41 (77.36)	13 (24.53)	
Class III	12 (22.64)	14 (26.42)	
Class IV	0	1 (1.89)	

Table 3. Follow up status (n=53)

	Frequency (%)
Cardiac death	2 (3.77)
Right side HF	6 (11.32)
Hospitalized due to HF	12 (22.64)
Valve surgery	5 (9.43)
Stroke	1 (1.89)

Table 4. Tabulation of Persistent TR to the outcome

	Total (n=53)	With outcome (n=16)	Without outcome (n=37)	P-value
	Frequency (%)			
With persistent TR	25 (47.17)	13 (81.25)	12 (32.43)	0.001
Without persistent TR	28 (52.83)	3 (18.75)	25 (67.57)	

Table 5. Association of Persistent TR to the outcome

	Crude odds ratio	95% CI	P-value
With persistent TR	9.0278	2.1568 to 37.7885	0.003
Without persistent TR	(reference)	-	-

DISCUSSION

This study involved retrospectively patients who had successful PTMC in a population majority of which were 37.8 + 10 years old females with symptomatic severe mitral stenosis with functional limitation, mostly NYHA class II with mostly acceptable valve scores (Wilkin's 6 to 8). Based on the preliminary result of this study, there is a trend of worse outcomes among patients with persistent tricuspid regurgitation.

It was believed then that patients with significant tricuspid regurgitation in patients who underwent mitral stenosis PTMC does not need further tricuspid valve intervention.[3] Symptom relief and improved functional capacity is the general goal of PTMC as evidenced by the change in valve size and drop in mitral valve gradient. However, concomitant significant tricuspid regurgitation with mitral stenosis is a common problem physicians and cardiologist

face even after successful PTMC. This study showed similar results to the papers by Song and Hannoush which showed that TR did not improve in 46% to 85% of the patients with moderate or severe TR even after successful mitral balloon valvulotomy, respectively.[11,12] Sagie et al determined that around 16% of patients with persistent TR die in 1-year after successful PTMC.[13]

The initial thought amongst clinicians the reversibility of TR in MS patients was based on tricuspid annular dilatation or right ventricular dilatation due to the pulmonary venous hypertension brought about by the increased left atrial pressure produced by the mitral stenosis. This was coined the term "functional" TR. However, in rheumatic mitral stenosis, TR can also be due to an organic tricuspid valve disease which may not be overtly evident of standard 2D-echocardiography.

The current practice done in this institution on the management of severe MS with concomitant moderate to severe TR should be reevaluated. This is study is consistent with the current 2017 ESC/EACT guidelines on valvular heart disease indicates that patients with severe TR should be discouraged from PTMC as this is an unfavorable characteristic. Only the absence of significant TR is recommended for PTMC whether the patient is symptomatic or asymptomatic.[14]

Limitations of the Study:

The study population was rather modest. The study was also conducted in a retrospective manner. A prospective design could further elaborate more accurately the different outcomes as identified by this study. Further limitations in the study also include the subjective nature of assessment of functional capacity. NYHA classification assessment is known for its inter-observer variability which may be emphasized greatly given the retrospective nature of this study.

CONCLUSION

Based on the results of this study, it shows that persistence of post-procedural tricuspid regurgitation even after a successful PTMC produce worsening functional capacity and worse outcomes. Perhaps this study will change the way we manage severe MS patients with significant TR.

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The Spectrum of Rheumatic Valvular Heart Disease in a Cardiovascular Center in the Philippines Spanning 40 Years (1977-2016)

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Background **---** High incidence of rheumatic heart disease patients are still reported in underdeveloped nations with a declining rate of cases in industrialized countries. In a retrospective study, we described the socioeconomic, demographic, clinical pattern, and histopathologic findings of patients with rheumatic valvular disease in the Philippine Heart Center from 1977 to 2016.

Methods **---** This registry enrolled all patients with rheumatic heart disease from the Philippine Heart Center who underwent valvular replacement surgery, repair, and redo, and in whom clinical history and histopathologic data were concordant. Medical charts and/or HIS records were reviewed. Socioeconomic status, geographic location, age at presentation, gender, clinical history, and surgical pathologic data were recorded.

Results **---** The study group of 4,455 patients consists of predominantly female (54%), with interquartile mean age of 16 (pediatric) and interquartile mean age of 31 (adult). Patients from low-income households are mostly affected (51.20%). The most number of patients diagnosed with rheumatic heart disease were from Region III (21.80%). Associated comorbidities include pulmonary hypertension (15.98%), congestive heart failure (11.31%), and cerebrovascular accident (2.96%). The mitral valve is mostly involved (53.74%). Most severe surgical pathologic findings of combined gross calcification, leaflet or cuspal thickening, and commissural fusion are observed in 82% of patients.

Conclusion and Recommendation **---** The spectrum of rheumatic heart disease comprises low socioeconomic status from dense populated regions, female sex, and early adult age at presentation usually at the height of the severity of the disease. Associated clinical characteristics most commonly include pulmonary hypertension, congestive heart failure, and cerebrovascular accident. Mitral valve is the most implicated in chronicity, severity, and rheumatic activity. The efficiency of standardized medical practice procedures in the Philippines as to where ARF and RHD is concerned, is still up for review. New and updated screening tools for detection should be explored, and preventive practices from developed countries with declining incidences should be modelled upon. Early detection of symptomatology at the onset of disease, community education, and screening tests are instrumental for appropriate antibiotic coverage to thwart development of new ARF cases and to cull the rise of RHD. ***Phil Heart Center J 2022;25(1):65-72.***

Key Words: ■ rheumatic heart disease ■ acute rheumatic fever ■ pulmonary hypertension ■ congestive heart failure ■ infective endocarditis ■ valve surgery

There are about 20 million incidences of rheumatic fever in developing countries annually, with a progression to advanced rheumatic heart disease (RHD) later in adulthood. An average of 30 to 45% patients with acute rheumatic fever (ARF) develop RHD. A high incidence of both ARF and RHD persists in tropical areas, involving mainly the pediatric population presenting with the first episode as carditis.[1] More than 4 million new cases are diagnosed and about 2 million deaths have been attributed to RHD.[2]

ARF is a systemic, autoimmune disease which occurs as a delayed consequence to Group A Beta-hemolytic Streptococcal (GAB HS) pharyngitis. A cross-reaction occurs due to molecular mimicry of the M-protein found on GABHS cell wall and cardiac tissue.[3] Virulent GABHS strains and genetic susceptibility linked

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to Human Leukocyte Antigen (HLA) alleles contribute to ARF and consequently Chronic Rheumatic Heart Disease (CRHD).[4] CRHD leads to irreversible valvular damage leading to cardiac dysfunction.[5] Other cardiac lesions include murmurs, hypertrophy and dilation, arrhythmias, and eventual heart failure.[1] Arrhythmias, in particular atrial fibrillation, may also arise, in addition to thromboembolic complications, and infective endocarditis. The cycle of deforming fibrosis yields hmodynamic changes, which further adds to the deformity. CHRD not only involves the valves but also variably affects the pericardium, endocardium, and in some cases the myocardium, severely resulting in cardiac dilation and progressive heart failure.[6]

Manifestations of valvular disease depend on which cardiac valve sare involved, the most common of which is the mitral valve.[1] The most common pure valvular lesion is mitral regurgitation. Combination of mitral regurgitation, mitral stenosis and aortic regurgitation is seen among multivalvular cases.[2] Mitral stenosis commonly arises from post inflammatory scarring of RHD. Microscopically, the valve discloses fibrosis, calcification, neovascularization, lymphoplasmacytic infiltration, and osseous metaplasia. The surface of the valve, principally at the line of closure, may be covered with fibrin. Aschoff nodules are more often observed in surgically removed atrial appendages and also seen in papillary muscles.[7]

An extensive review of cases from underdeveloped nations described characteristics, complications, and interventions in rheumatic heart disease. This report showed that RHD patients from countries with low to middle income falls under the median age of 28 years, of which 66.2% involves females, and 75.3% are largely unemployed.[8]

In this study, we describe the socioeconomic, demographic, clinical pattern, and histopathologic findings of patients with rheumatic valvular heart disease in the Philippine Heart Center spanning 40 years. To the authors' knowledge, no similar study of this magnitude has been conducted in the Philippines to date.

METHODS

Study Group;

This is a retrospective cross-sectional study involving archival cases from institutional and surgical pathology files from the Philippine Heart Center - Division of Laboratory Medicine from patients with rheumatic heart disease who underwent valvular replacement surgery, repair, and redo, and in whom clinical history and histopathologic data were concordant, done from January 1977 to December 2016. Excluded from the study groups were cases of valve tissues diagnosed as "chronic nonspecific valvulitis" and those with incomplete or unavailable data from patient medical charts and hospital information system (MedTrak).

Clinical Data;

For the period of January 1977 to December 2001, the cardiovascular register at the Philippine Heart Center - Division of Laboratory Medicine was reviewed. For the period of January 2002 to December 2016, the surgical pathology logbook of the Philippine Heart Center - Division of Laboratory Medicine was reviewed. Medical charts and/or HIS records (MedTrak) were reviewed retrospectively and the following data were recorded: socioeconomic status, geographic location, age at presentation, gender, and clinical history.

Histopathologic Data;

Severity of valvular lesions were categorized based on pathophysiologic progression seen by gross anatomic findings[9] as presence of (a) leaflet thickening, (b)leaflet thickening and commissural fusion, and (c)leaflet thickening, commissural fusion, and calcification. Histologic evaluation for activity or chronicity was defined according to presence of (1)lymphocytic infiltration, (2)neutrophilic infiltration, (3) Aschoff body, (4)vegetation, (5)fibrosis, and (6)neovascularization or vascular proliferation.

Statistical Analysis;

Descriptive statistics was used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion was used for nominal variables, and mean and SD for interval/ratio variables. Chi-square analysis was

used to determine the difference between patients with low and upper/middle income class in terms of NYHA status and medical history. Missing variables were neither replaced nor estimated. STATA 13.1 was used for data analysis.

RESULTS

Overview;

A total of 5,451 patients underwent valvular replacement surgery due to rheumatic valvular disease at the Philippine Heart Center from January 1, 1977 to December 31, 2016. However, only a total number of 4,455 existing or available medical records and surgical reports were reviewed. Nine-hundred ninety-six (996) were not included in the study due to incomplete and/or missing charts.

Demographics and Surgery;

The study group included a total of 4,455 cases, 2,049 (46%) of which were male and 2,406 (54%) were female, with an interquartile mean age of 16 in the pediatric age group and an interquartile mean age of 31 in the adult age group (*Table 1*). Surgical indications were aortic valve replacement surgery in 751 cases (16.88%), mitral valve replacement surgery in 2,349 cases (53.74%), mitral and aortic valve replacement surgery in 1,227 cases (27.54%), pulmonic valve replacement in 4 cases (0.09%), and mitral, aortic and tricuspid valve replacement surgery in the remaining 28 cases (0.63%). Mitral valve repair involved 33 cases (0.74%), and aortic valve repair in 2 cases (0.04%). Redo valve surgery of the mitral valve involved 22 patients (0.49%) (*Table 3*).

Clinical Characteristics;

A trial fibrillation was recorded in 1,371 (30.71%) of patients based on electrocardiogram results performed before the surgical procedure (*Table 3*). Differences in clinical manifestations were found between the two income groups. NYHA III-IV, pulmonary hypertension, cerebrovascular accident, and congestive heart failure, were observed more often in patients from low income households (55.97%, 57.16%, 50.75%, and 52.08%, respectively) in comparison to those from middle-upper income households (44.02%, 42.69%, 49.24%, and 47.91%, respectively) (*Table 4*).

Geographic Location and Income Class;

Overall, the most number of patients diagnosed with rheumatic heart disease were from Region III (21.80%), followed by the National Capital Region (19.82%), Region IVA (14.79%), Region I (9%), and Region VI (7.41%) (*Table 2*). Low income patients comprise 53% from Region III, 57% from the National Capital Region, 54% from Region IVA, 42% from Region I, and 51% from Region VI.

Surgical Pathologic Findings;

Preoperatively, about 112 patients (2.51%) were diagnosed with acute rheumatic fever based upon Jones criteria. ARF was reported more frequently in low income households (56.25%), compared to middle-upper households (43.75%). The apparent clinical manifestations were used to indicate possible rheumatic activity. Histopathologic results showed neutrophilic infiltration seen in 110 (3%) involving mitral valves, 71 (3.58%) involving aortic valves, and 2 (8%) involving tricuspid valves, as well as presence of Aschoff bodies involving 5 (0.13%) of mitral valves, 4 (0.20%) of aortic valves, and 1 (4%) of tricuspid valves (*Table 6*). Gross features of infective endocarditis were recorded in 3% of patients and comprised 60% from low income households. Chronicity and severity findings were evident by gross calcification, leaflet or cuspal thickening, and commissural fusion in 82.06% of patients (*Table 5*). These are seen in patients as early as 25 years. However, pliable leaflets were observed in patients less than this age.

Table 1. Characteristics of the Study Group

	Total N=4,455
	Frequency (%); Median (Range)
Age	
Pediatric mean (SD)	16
Range	(13-18)
Adult mean (SD)	31
Range	(25-41)
Gender	
Male	2,049 (45.99%)
Female	2,406 (54.00%)

Table 2. Geographic Distribution and Socioeconomic Status of the Study Group

	Total N=4,455
	Frequency (%);
Region of Distribution	
I	401 (9%)
II	130 (2.92%)
III	971 (21.80%)
IVA	659 (14.79%)
IVB	137 (3.08%)
V	283 (6.35%)
VI	330 (7.41%)
VII	82 (1.84%)
VIII	103 (2.31%)
IX	32 (0.72%)
X	77 (1.73%)
XI	131 (2.94%)
XII	42 (0.94%)
XIII	25 (0.56%)
National Capital Region	883 (19.82%)
Cordillera Administrative Region	72 (1.62%)
Autonomous Region of Muslim Mindanao	34 (0.76%)
Micronesia	33 (0.64%)
Others	1 (0.02%)
Socioeconomic Class	
Low Income	2,281 (51.20%)
Upper/Middle Income	2,153 (48.33%)

Numeral numbers I-XIII pertains to the different regions comprising the Philippine archipelago.

Table 3. Geographic Distribution and Socioeconomic Status of the Study Group

	Total N=4,455
	Frequency (%);
New York Heart Association Functional class III & IV	452 (10.15%)
Medical History/Risk Factors	
Acute rheumatic fever	112 (2.51%)
Congestive heart failure	503 (11.31%)
Pulmonary hypertension	712 (15.98%)
Cerebrovascular accident	132 (2.96%)
Infective endocarditis	133 (2.99%)
Major bleeding	27 (0.61%)
Peripheral embolism	72 (1.62%)
Atrial fibrillation	1,371 (30.77%)
Native Valve Surgery	
AVR	751 (16.88)
MVR	2,394 (53.74)
PVR	4 (0.09)
MAVR	1,227 (27.54)
MAVR + TVR	28 (0.63%)
Repair Surgery	
Aortic valve	2 (0.04%)
Mitral valve	33 (0.74%)
Redo Valve Surgery	22 (0.49%)

AVR indicates aortic valve replacement; MVR, mitral valve replacement, TVR, tricuspid valve replacement;

Table 4. Clinical Characteristics and Income Class of the Study Group.

Clinical Characteristics	Low Income Households	Middle-Upper Households	P-value
	Frequency (%);	Frequency (%);	
New York Heart Association Functional class III & IV	253 (55.97%)	199 (44.02%)	<0.001
Medical History/Risk Factors			
Acute rheumatic fever	63 (56.25%)	49 (43.75%)	0.338
Congestive heart failure	262 (52.08%)	241 (47.91%)	0.776
Pulmonary hypertension	407 (57.16%)	305 (42.69%)	0.001
Cerebrovascular accident	67 (50.75%)	65 (49.24%)	0.930
Infective endocarditis	81 (60.90%)	52 (39.09%)	0.028
Major bleeding	17 (62.96%)	11 (40.74%)	0.349
Peripheral embolism	28 (38.88%)	44 (61.11%)	0.033
Atrial fibrillation	773 (56.38%)	598 (43.61%)	<0.001

Table 5. Grossevaluation for severity ofvalvular lesion.

Features	Frequency in AV (%) N= 1,981	Frequency in MV (%) N= 3,665	Frequency in TV (%) N= 25	Frequency in PV (%) N= 4
Leaflet/cuspal thickening	337 (17%)	548 (14.95%)	**7 (28%)**	**1 (20%)**
Leaflet/cuspal thickening/ commissural fusion	362 (18.27%)	759 (20.70%)	5 (20%)	0
Leaflet/cuspal thickening/ commissural fusion/calcification	1,281 (64.6%)	2,358 (64.3%)	13 (52%)	4 (80%)

AVR indicates aortic valve replacement; MVR, mitral valve replacement, TVR, tricuspid valve replacement;

Table 6. Histologic evaluation for activity/chronicity of valvular lesion.

Features	Frequency in AV (%) N= 1,981	Frequency in MV (%) N= 3,665	Frequency in TV (%) N= 25	Frequency in PV (%) N= 4
Lymphocytic infiltration	1,374 (69.35%)	2,641 (72.06%)	**15 (60%)**	**4 (100%)**
Neutrophilic infiltration	71 (3.58%)	110 (3%)	2 (8%)	0 (0%)
Aschoff body	4 (0.20%)	5 (0.13%)	1 (4%)	0 (0%)
Vegetation	55 (2.77%)	78 (2.12%)	1 (4%)	0 (0%)
Fibrosis	1,981 (100%)	3,665 (100%)	25 (100%)	4 (100%)
Neovascularization/vascular proliferation	1,981 (100%)	3,665 (100%)	25 (100%)	4 (100%)

DISCUSSION

The data presented in this study represents the spectrum of rheumatic valvular disease in the Philippine Heart Center from 1977 to 2016. It can be surmised that the pattern of prevalence and incidence reported throughout four decades as presented shows that there still exists a significant number of cases of ARF and RHD in the Philippines. The World Health Organizationin 2017 reported a staggering 2,821 or 0.46% involving RHD cases. The mortality rate is 3 per 100,000 population (age adjusted). This data ranks the country as the 75th in the world.[10] The Philippine Heart Center, which comprises only a portion of the country as a whole, as to where these cases are concerned, still stands as a fair representation of the status of the disease. Seckeler et al. attributes this continuing problem to nonstandardized practice patterns for ARF diagnosis, varying across nations.[11] This is true in countries with limited health resources such as ours.

In Africa, for example, only half of patients-diagnosed with ARF is backed up by laboratory evidence of an elevated or increased ASO titer. Poor diagnostic practices have also been described in other underdeveloped regions, in particular the Western Pacific and South-east Asia.[11] In South Africa, the overall crude incidence of symptomatic RHD is recorded at 24.7 per 100,000, while the prevalence of asymptomatic RHD diagnosed using echo-cardiography in school children was 20.2 cases per 1000.[12] Echocardiography screening studies among asymptomatic schoolchildren in sub-Saharan Africa showed a very high prevalence rate of 30.4 per 1000 in Mozambique in 2007. The same high prevalence rate of 15 per 1000 in a cohort study in Ugandan schoolchildren was reported in 2012. RHD was the most common heart condition in Cameroon affecting 62.1% in patients aged 10 - 19 years, while RHD was present in 22.4% of pediatric studies done in Malawi.[13]

Children and young adults are still affected by RHD in the Indian subcontinent with prevalence rates of 4.54 to 6 per 1000, some studies with estimates as high as 51 per 1000. However, recent large population school surveys conducted

show a decrease in the prevalence of RHD varying from 0.5 to 0.68 per 1000.[14]

Children and young adults are still affected by RHD in the Indian subcontinent with prevalence rates of 4.54 to 6 per 1000, some studies with estimates as high as 51 per 1000. However, recent large population school surveys conducted show a decrease in the prevalence of RHD varying from 0.5 to 0.68 per 1000.[14]

High prevalence rates are attributed by poor socioeconomic status, dense populated regions, inaccessible healthcare facilities and services, and unavailability of penicillin for prophylaxis.[13] The majority of cases seen from this research are from the National Capital Region (19.82%) previously mentioned, the REMEDY study, and Region III (21.80%) comprising 57% and 53% of patients coming from low income households, respectively. These regions are also the most accessible to the institution. As which described characteristics, complications, and interventions in rheumatic heart disease involving African nations, India, and Yemen, reported that RHD patients from countries with low to middle income falls under the median age of 28 years, of which 66.2% involves females, and 75.3% are largely unemployed.[8] RHD patients in this present study falls under the median age of 38 years, and are usually diagnosed at the height of the severity of the disease, thus the age of presentation. Filipino patients are not keen on health care preventive practices, with high cost of health care access a major reason.[15] Disease progression from streptoccocal infection to RHD is not monitored, and clinical symptomatology at the onset of illness cause no major concern to most parents of infected children. Standardized practices are likewise not in place, and screening diagnostic procedures in the pediatric population are yet to be implemented.[15]

In developed countries such as the United States and western Europe, the incidence of ARF particularly showed a significant decline in the last century, the decrease more pronounced during the 1970s, with cases recorded in Chicago and Baltimore. The 1980s showed a resurgence in some US states, which temporarily halted the decline. Recently, very few cases of ARF have been documented in the US, the most number limited to Utah. The significant decline in the early 20th century may be ascribed to better living conditions, decreased over crowding, better nutrition, easy access to health services, and availability of treatment.[16]

Reports of new cases and readmissions were not included here, however, review of a study from 1992 to 1999 from the Philippine Heart Center recorded a significant decline. The 8-year review of in-patients showed 5,513 (4.7%) admitted cases, and a total of 2,953 (3.4%) new cases. Inpatient outcome of new RHD cases showed a 14.3% mortality rate predominantly among females (57%), but with a 96.2% recovery rate among those later discharged.[17] In a 6-year review of outpatient cases from 1994 to 1999 also done in the same institution, 6,417 were diagnosed with RHD alone. Of these, 60% were female and 40% were male, of which ages fall in early adulthood (21 - 40 years old). The present study still shows female preponderance (54%) in comparison to males (45%) with a pediatric range of 13-18 years old and adult range of 25 - 41. Outpatient and nonsurgical cases, however, were not reviewed or involved in this study.

In comparison to Japan, ARF is the most common cause of RHD particularly in the 5 to 30 age group with a declining annual mortality as reported by the Ministry of Health Welfare, between years 1960 and 1981. A survey conducted from pediatric clinics of 20 major hospitals done between 1952 and 1980 described the annual incidence of ARF among school-children to be steadily declining. The prevalence rate decreased from 4.6 per 1000 population in 1958 to 0.14 per 1000 population in 1981. Due to the improvement of socioeconomic conditions, and proper antibiotic use to control GABHS, these factors may have majorly contributed to the decline in first and recurrent attacks of ARF in the country.[18]

Majority of the cases reported shows mitral valve involvement. Mitral valve replacement surgery is performed in 54% of cases and mitral valve repair is done in 33% of cases. A previous study done from 1994 to 1999 in the same institution also showed a total of 63% who

underwent mitral valve replacement.[17] Another review done from 1991 to 1998 described 80% of RHD cases who underwent mitral valve replacement procedure, from a total number of 89 cases with 69 females and 27 males.[19]

A review of mitral valve surgery in this same institution from 1975 to 1995 states that major postoperative complications included ischemic heart disease, and pulmonary hypertension.[20] In a study conducted in underdeveloped countries, majority of RHD patients suffered from moderate-to-severe valvular heart disease with associated pulmonary hypertension and about a fourth of the subjects presented with left ventricular dysfunction.[8] In a similar manner, this study includes pulmonary hypertension, congestive heart failure, and cerebrovascular accident as the most frequently associated comorbidities.

A report on postmortem distribution of acquired heart disease in this same institution from 1975 to 1984 showed a total number of 411 RHD cases. During this period, the registry of RHD cases mostly include advanced stages of chronic rheumatic valvular deformity, the mitral valve being the most frequent at 58% with gross findings of predominantly commissural fusion (35%), cuspal fibrosis (6%), and rare predominant chordal thickening.[21] Combined gross calcification, leaflet or cuspal thickening, and commissural fusion are still seen in the majority of our cases reviewed, which involves 82.06% of patients.

Gross examination usually constitutes the entire pathologic inspection of cardiac valves. However, a more precise analysis is accomplished with histologic examination.[22] The main pathological process in CRHD is cuspal and chordal thickening. An associated mononuclear cell infiltration resulting to fibrohistiocytic (Aschoff) cells may be observed, the presence of which may indicate a recent bout or ARF.[1] Our present study only showed 0.13% of Aschoff nodules found mostly in 5 cases involving mitral valves. Morphologic review done by Roberts et. al. states the aortic valve as most commonly affected by infective endocarditis.[23] This is in contrast to the present study, with the mitral valve affected in 82% of cases.

About 2.51% patients were diagnosed with acute rheumatic fever based upon Jones criteria, and comprised patients from low income households (56.25%). Numerous disagreements of histopathologic findings from clinical symptomatology or diagnostic evidence to signify activity are usually reported.[24] However, the present study recorded agreement of clinical characteristics with confirmatory histopathologic results, findings of which include neutrophilic infiltration and presence of Aschoff bodies.

CONCLUSIONS AND RECOMMENDATIONS

The number of cases of RHD in the Philippines seems to be significant. The spectrum of rheumatic heart disease comprises low socioeconomic status from dense populated regions, female sex, and early adult age at presentation usually at the height of the severity of the disease. Associated clinical characteristics most commonly include pulmonary hypertension, congestive heart failure, and cerebrovascular accident. Mitral valve is the most implicated in chronicity, severity, and rheumatic activity.

The efficiency of standardized medical practice procedures in the Philippines as to where ARF and RHD is concerned, is still up for review. New and updated screening tools for detection should be explored, and preventive practices from developed countries with declining incidences should be modelled upon. Early detection of symptomatology at the onset of disease, community education, and screening tests are instrumental for appropriate antibiotic coverage to thwart development of new ARF cases and to cull the rise of RHD.

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Neurovascular Interventional Imaging in the Preoperative Evaluation of Craniopagus Twins

Lyzyl Anne S. Quinio, MD;

Background **---** Craniopagus twinning is an extremely rare congenital malformation which usually involves complex vascular connections and can lead to poor surgical outcomes. Preoperative planning and surgical separation of craniopagus are challenging tasks to physicians. Newer neurosurgical and endovascular techniques with the aid of recent advances in medical imaging (computed tomography, magnetic resonance imaging and digital subtraction angiography) have contributed to very few reported successful cases of separation.

Case **---** We present a case of 9 month old craniopagus twins for preoperative evaluation. A four-vessel angiography demonstrated a shared superior sagittal sinus.

Conclusion **---** For cases of craniopagus, accurate anatomic imaging, a comprehensive planning and preparation, neuroendovascular techniques and multidisciplinary approach are of utmost importance to achieve a successful separation. ***Phil Heart Center J 2022;25(1):73-80.***

Key Words: ■ craniopagus ■ conjoined twins■ interventional imaging

Craniopagus is an extremely rare type of conjoined twins fused at the skull. It occurs in about 2-6% of conjoined twins, approximately 0.6 per million births with a female preponderance.[1] About 40-60 % of conjoined twins were stillborn and approximately 35% of conjoined twins die within the perinatal period.[2] Hence, in these cases, prenatal imaging plays a significant role in parental counseling and preparation for post-natal management. Medical imaging provides details to determine feasibility of surgical separation and assess shared brain tissues, vascular supply and venous drainage. Despite disastrous outcomes and perplexity of surgical separation of craniopagus, there have been reports of successful procedures due to recent advances in neuroimaging modalities and neurosurgical and endovascular techniques.[3]

The case presented is a pair of craniopagus twins for cerebral angiography. The authors aim to contribute in the advancement of knowledge in the evaluation and separation of the complex cases of craniopagus.

CASE

This is a case of conjoined twins who were born to a 27 year old via Caesarian delivery at 37 4/7 weeks age of gestation with a total birth weight of 4.2 kilograms. Prenatal screening revealed monozygotic twins with conjoined vertices. At birth, heads were conjoined, with separate thoraces and pelvises, complete separate pairs of upper and lower limbs.

The twins underwent radiography, computed tomography and magnetic resonance imaging in the referring institution. They were referred to the Philippine Heart Center for cerebral 4-vessel angiography to accurately map the shared intracranial vessels.

Babygram revealed fused calvaria at the occiput of Twin A and right parietal area of Twin B, separate thoraces, pelvises and extremities. Cranial CT done at 12 weeks and plain cranial axial MRI done at 16 weeks of age reveal separate brain parenchyma with intervening dura, each twin having her own pair

Winner, Oral Presentation - Case Report. 28th PHC Annual Research Paper Competition and Poster Presentation held on February, 2020 at Philippine Heart Center. Correspondence *to* ***Dr. Lyzyl Anne S Quinio.*** Department of Radiological Sciences. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

of cerebral hemispheres and the Twin B's right parietal structures partly housed by Twin A's calvarium with note of compression of the brain parenchyma of each twin.

Cerebral digital subtraction angiography

Under general anesthesia, cerebral angiograms of Twin A and Twin B were done via Seldinger technique through right transfemoral approach using French 4 Berenstein angled tip catheters. Selective and individual injections into the bilateral internal carotid and bilateral vertebral arteries were done in succession. In addition, the left external carotid artery angiogram was also performed. Contrast used was Iodixanol (Visipaque) 320 mg/mL non-ionic low osmolar contrast media with a total dose of approximately 12.5 mL for each twin.

Findings are as follows:

TWIN A: The vascular structures of Twin A are confined within her cranial vault, the visualized segments of the bilateral internal carotid arteries, bilateral middle cerebral arteries, bilateral anterior cerebral arteries and their branches of Twin A are unremarkable. Multiple branches of both external carotid arteries of Twin A were noted crossing into the scalp region of Twin B. No communication was noted between the intracranial arterial systems of Twin A and Twin B.

TWIN B: The parietal vascular structures of the right cerebral hemisphere of Twin B were seen protruding into the posterior cranial vault of Twin A. The bilateral internal carotid arteries, bilateral middle cerebral arteries, bilateral anterior cerebral arteries and their branches of Twin B are unremarkable.

There is shared superior sagittal sinus of Twin A and Twin B, located within the cranium of Twin A. There were no complications (i.e. contrast hypersensitivity reactions or bleeding) experienced during and after the procedure. The twins were discharged in stable conditions and transferred back to the referring institution.

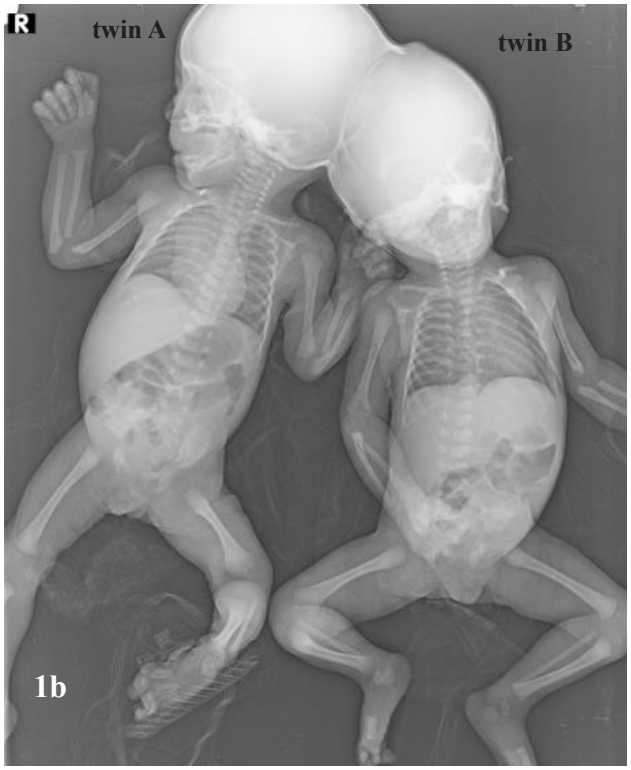


Figure 1. ***a.*** Photo of the 9 month old craniopagus twins ***b.*** Babygram of the twins at 12 weeks of age revealing shared calvaria between the occipital region of Twin A and the rightparietal area of Twin B, separate thoraces, pelvises and extremities.

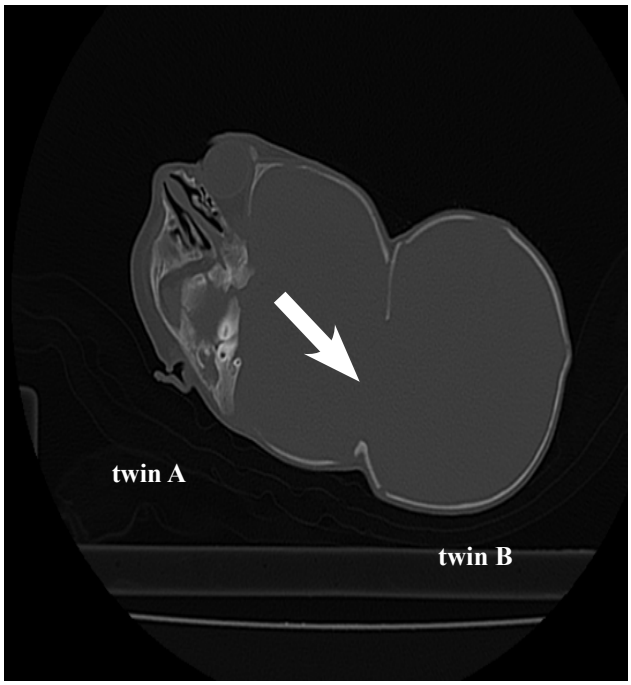


Figure 2. Cranial CT - Axial view of the twins at 12 weeks confirming the bony defect (arrow) between cranial vaults of the twins and fairly delineated shared brain parenchyma of the twins.

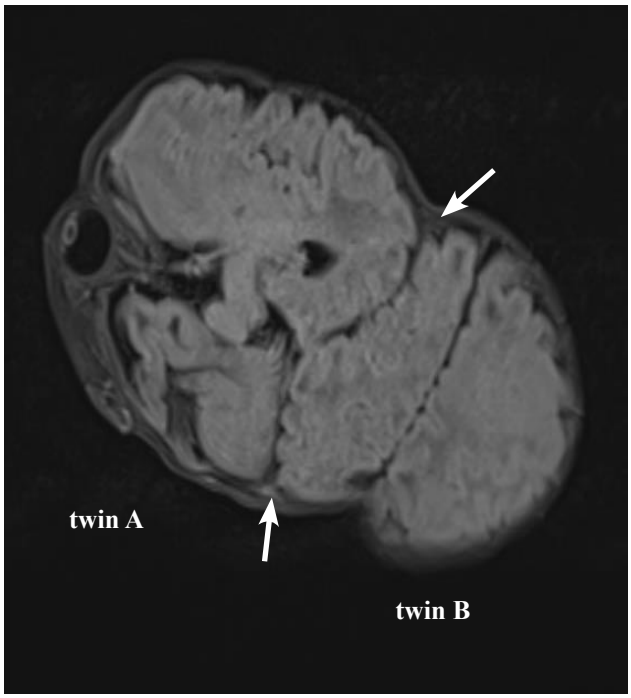
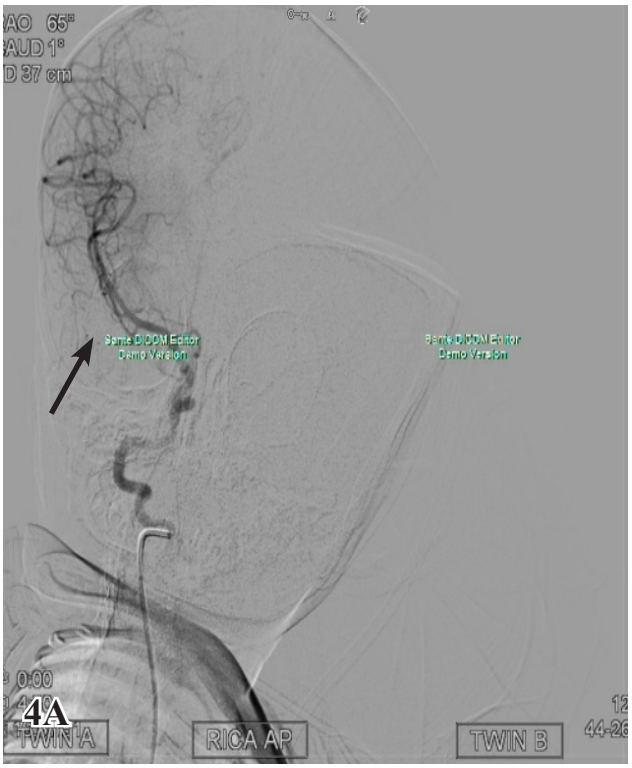
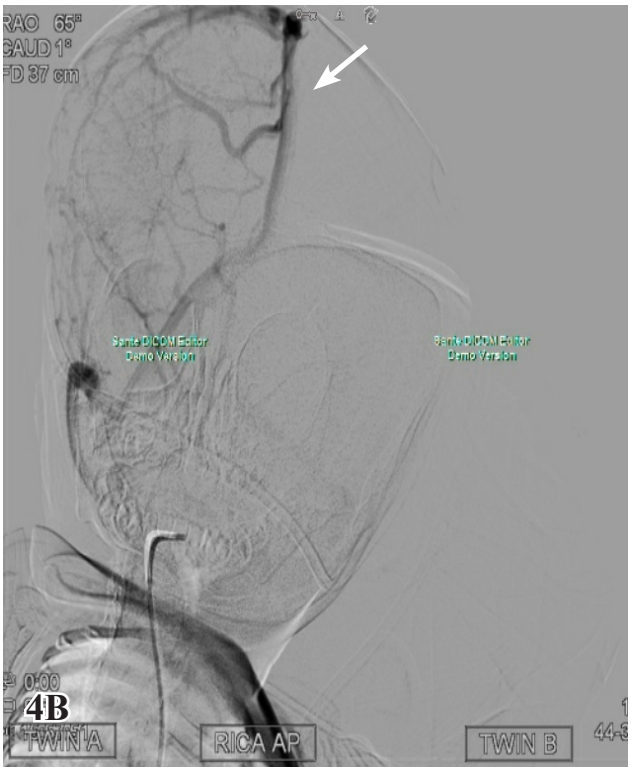
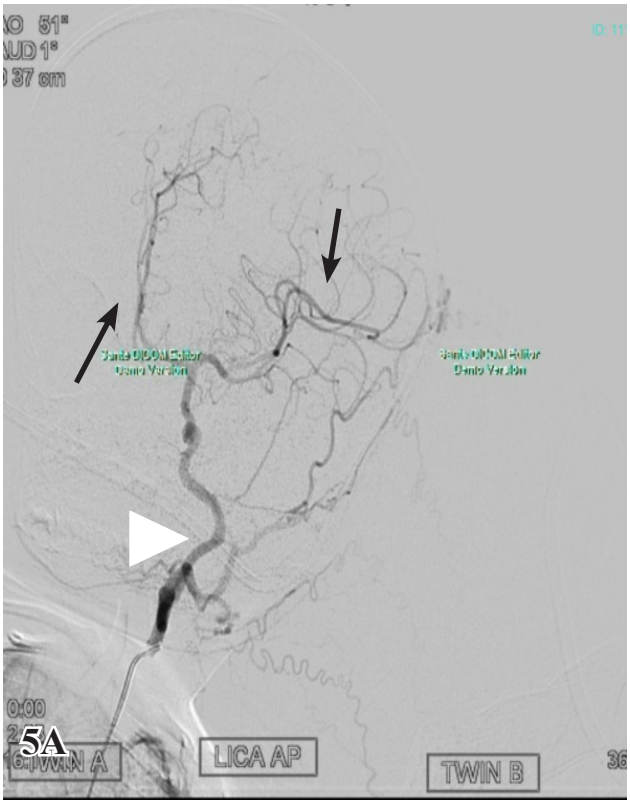


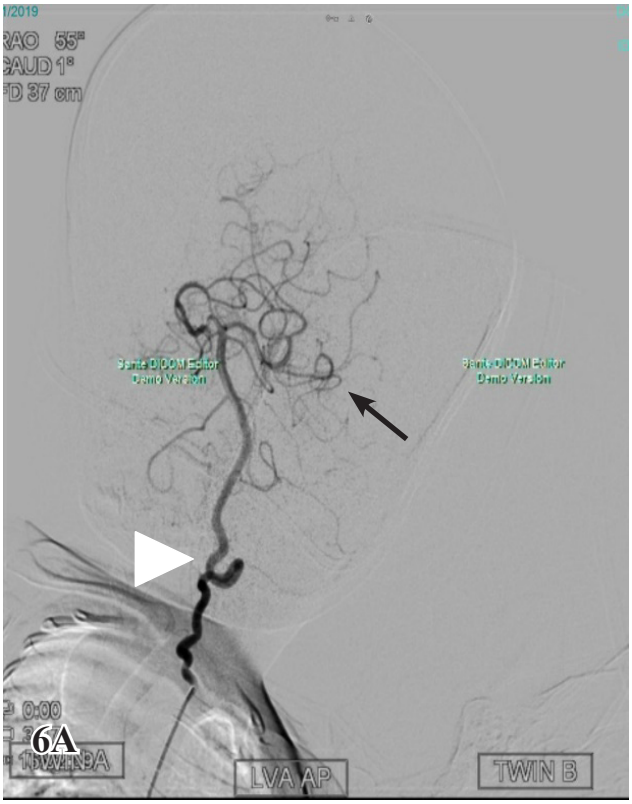
Figure 3. Plain Cranial Axial MRI T1-weighted image at 16 weeks of age revealing separate brain parenchyma with intervening dura, each twin having her own pair of cerebral hemispheres and the Twin B's right parietal structures partly housed by Twin A's calvarium with note of compression (arrows) of the brain parenchyma of each twin.

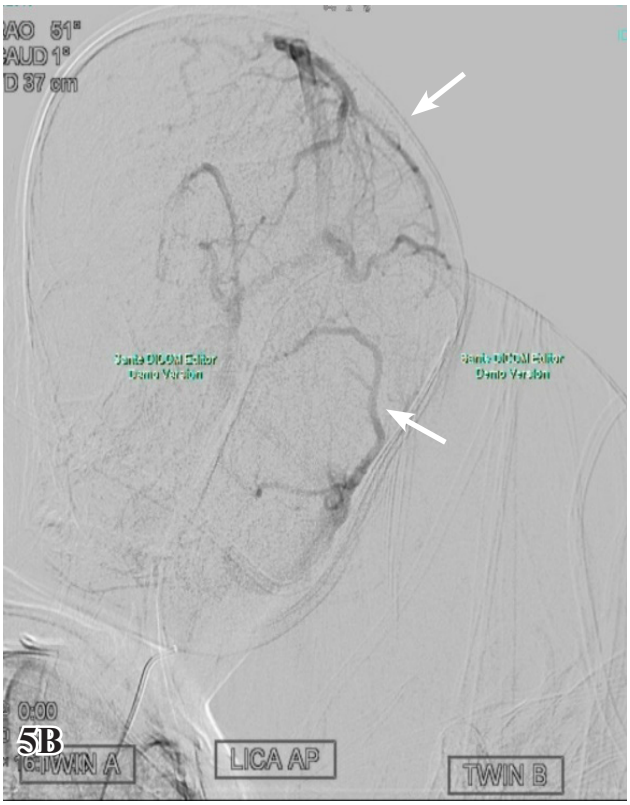


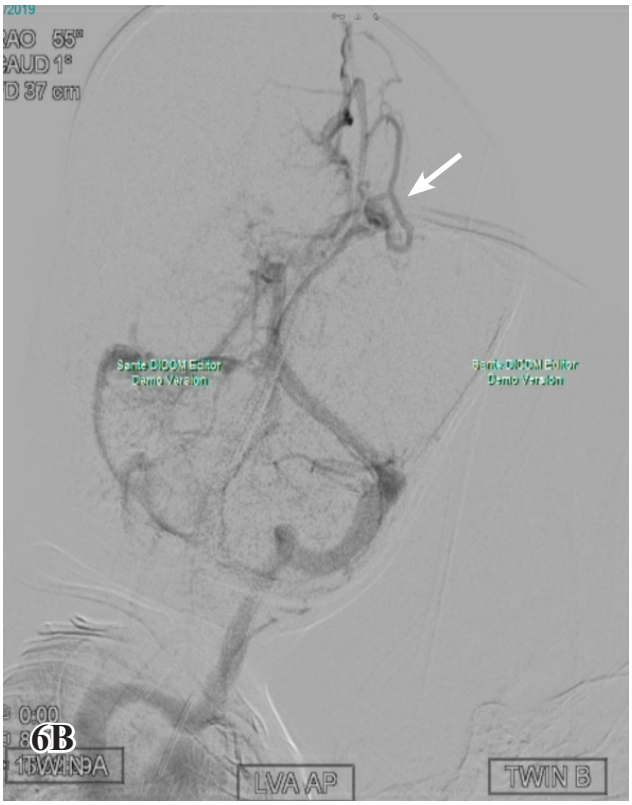


Figures 4A and 4B. Digital subtraction angiography-AP views show contrast injection into Twin A's right internal carotid artery (arrowhead) showing normal arterial supply (black arrow) and venous drainage (white arrow), respectively.



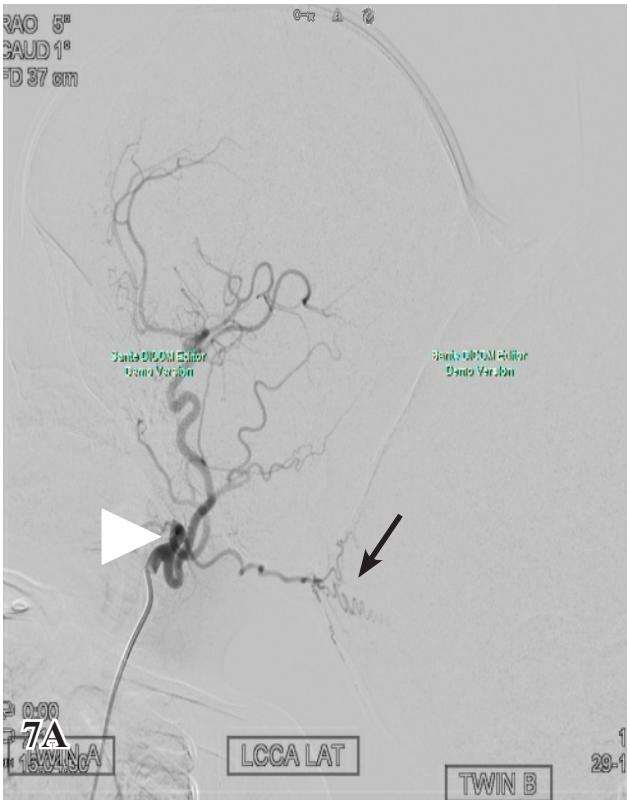


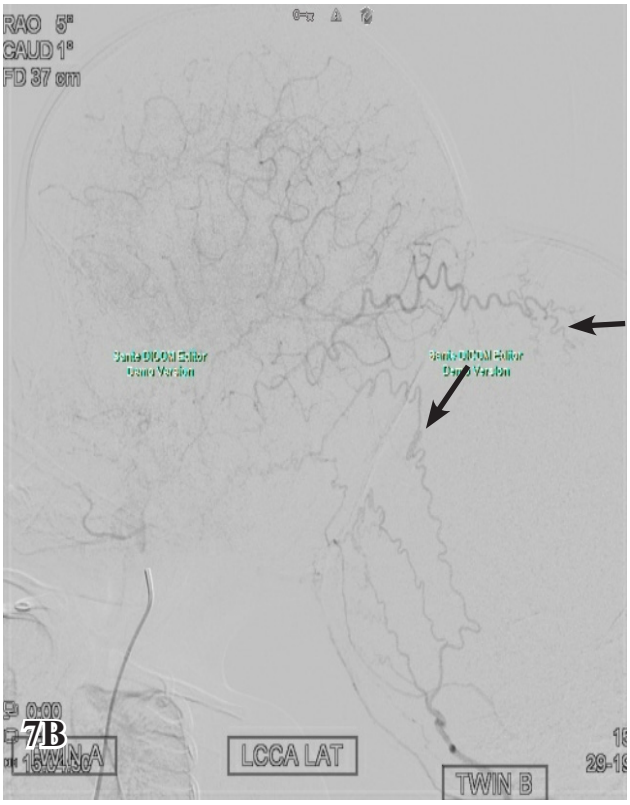




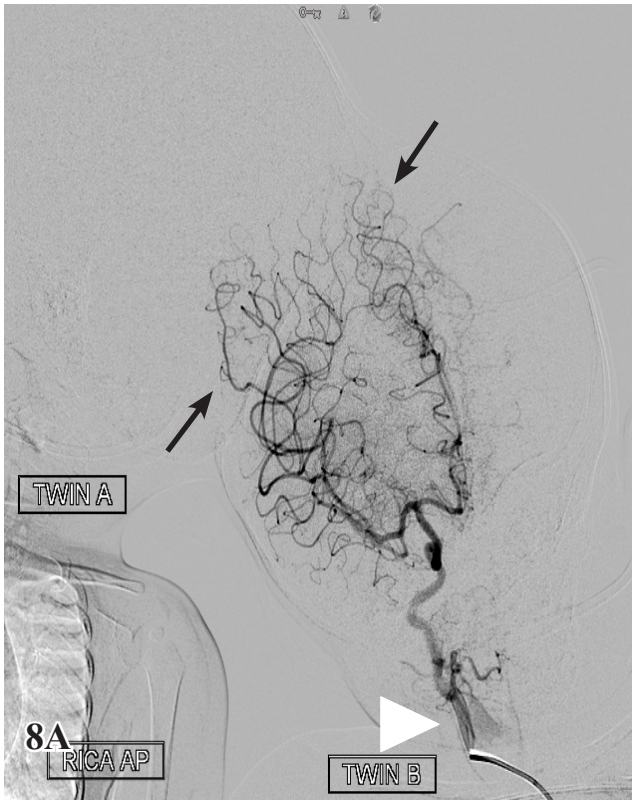
Figures 5A and 5B. Digital subtraction angiography- AP views show contrast injection into Twin A's left internal carotid artery (arrowhead) showing normal arterial supply (black arrows) and venous drainage (white arrows), respectively.

Figures 6A and 6B. Digital subtraction angiography- AP views show contrast injection into Twin A's left vertebral artery showing normal arterial supply (black arrow) and venous drainage (white arrow), respectively.





Figures 7A and 7B. Digital subtraction angiography- Lateral views show contrast injection into the left common carotid artery of Twin A (arrowhead) with multiple branches of external carotid arteries (black arrows) crossing into the scalp region of Twin B.



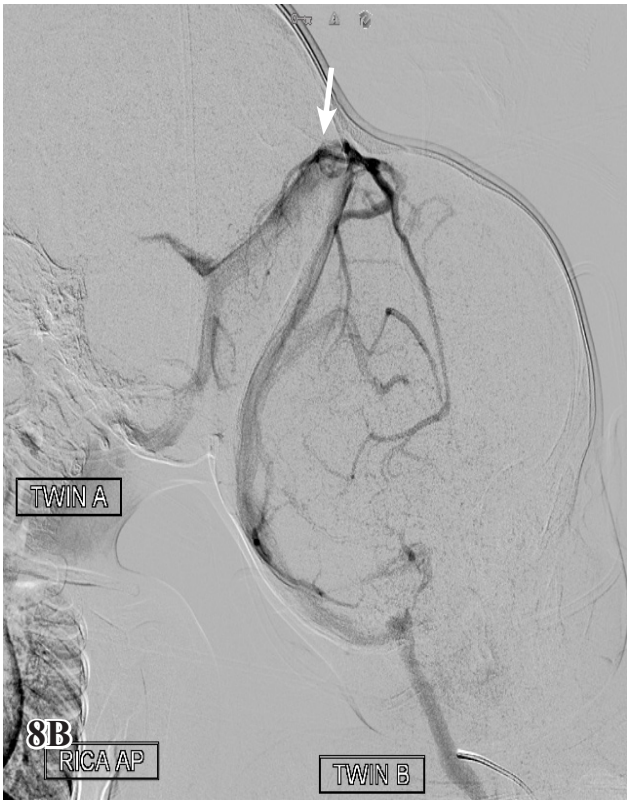
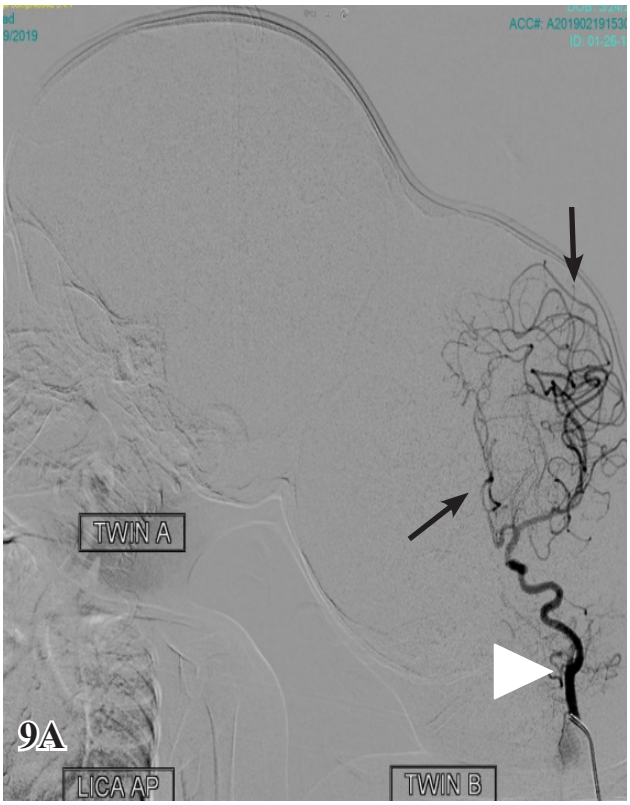
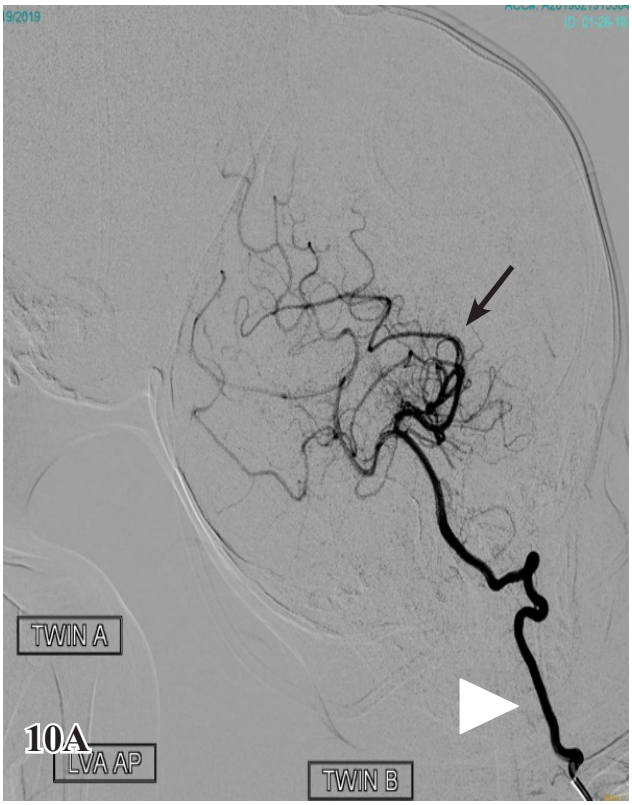
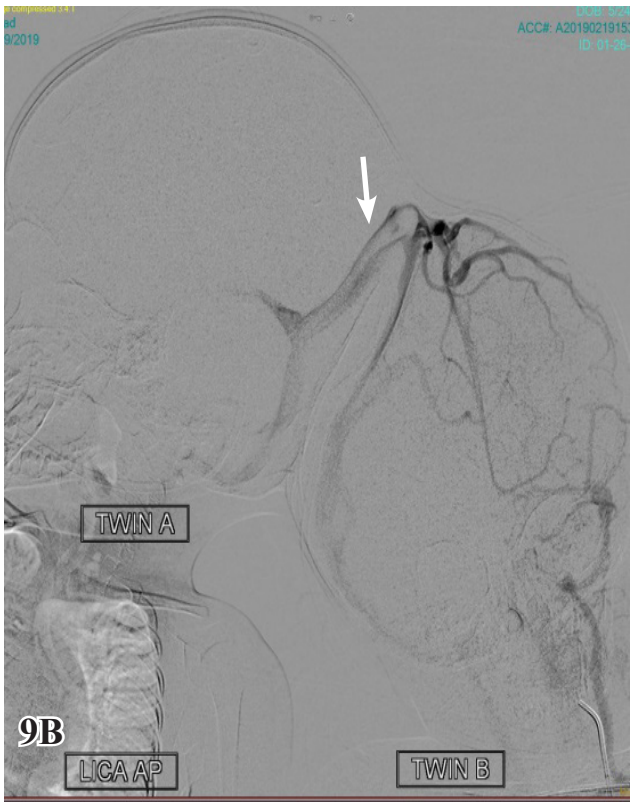


Figure 8A and 8B. Digital subtraction angiography- AP views: Contrast injection into Twin B's right internal carotid artery (arrowhead) showing parietal vascular structures of Twin B (black arrows) protruding into the posterior cranial vault of Twin A and venous drainage into the superior sagittal sinus (white arrow) within Twin A's cranial vault.







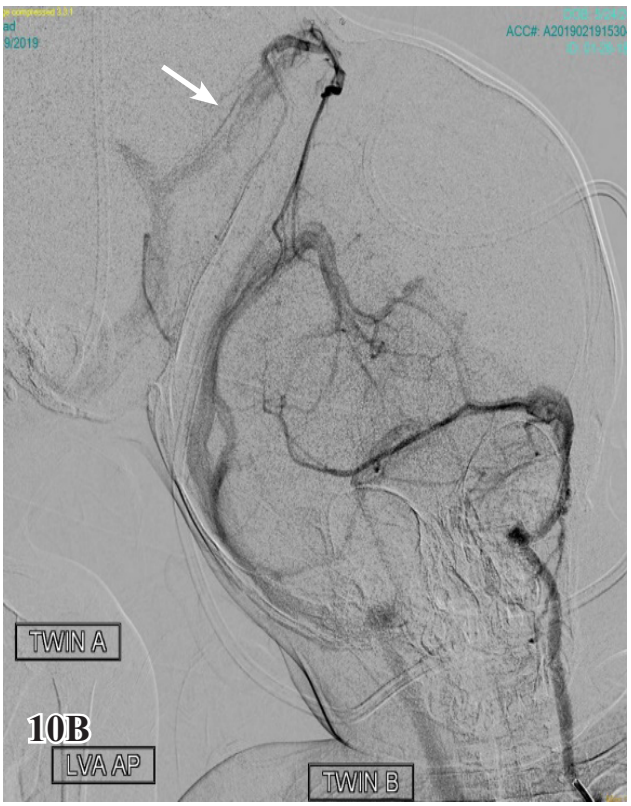


Figure 9. Digital subtraction angiography- AP views show contrast injection into the left internal carotid artery of Twin B (arrowhead) showing normal arterial supply (black arrows) with venous drainage into the superior sagittal sinus (white arrow) within Twin A's cranial vault.

Figure 10. Digital subtraction angiography- AP views show contrast injection into the left vertebral artery of Twin B (arrowhead) showing normal arterial supply (black arrow) with venous drainage into the superior sagittal sinus (white arrowhead) within Twin A's cranial vault.

DISCUSSION

Craniopagus is a type of conjoined twins who are fused at the skull, not including the face or foramen magnum. Although the exact mechanism of conjoined twinning remains unclear, the current accepted theory is the failure in the development of primitive structures during the later embryonic stage. Further, there are two proposals to explain the events of conjoined twinning. The fission theory explains that there is incomplete splitting of the embryo whereas the fusion theory proposes that there is merging of separate embryo.[1,2]

For an accurate assessment of cerebral vasculature of craniopagus prior to surgical separation, a three-dimensional digital subtraction angiography is a mainstay.[3] Our patient underwent cerebral angiography at 9 months of age.

To classify the twins in this case, the O'Connell's system was used, which is the most common classification based on the size of the union and extracranial or intracranial involvement. Partial craniopagus refers to a pair of twin with a smaller extracranial union limited to the dura or leptomeninges and total craniopagus refer to a pair of twin with a shared cranial vault housing two brains Total craniopagus type I: if the orientation of the faces are of the same direction; type II if orientation of the faces are opposite directions and type III if faces are intermediately oriented.[3,4] Our patient shared a cranial vault and superior sagittal sinus, hence the twins can be classified as total craniopagus.

Another classification is by Stone and Goodrich, based on the degree of shared dural venous and intertwin longitudinal axis; a) total –if with significant shared dural venous sinus and b) partial if with less significant shared dural venous sinuses. Vertical classification is based on O'Connell's subtypes. Angular type denotes intertwin longitudinal axis <140 degrees. In the present case, the intertwin longitudinal axis is less than 140 degrees, making them an angular type of total craniopagus.[4]

O'Connell suggested that venous drainage is one of the most problematic issues encountered during surgical separation.[1] In a study of surgical outcomes in total angular craniopagus, out of 14 pairs, mortality rate was 57% (68% who underwent single staged procedure versus 17% with multiple staged procedure). Among those who survived, 21 % had mild to moderate or normal outcome and 14% had severe disability.[5] Often, mortality from craniopagus separation is associated with venous dural sinus hemorrhage or thrombosis.[6] In a systemic review of cases from 1995-2015, they concluded that vertical type of craniopagus has the highest chance of successful separation. In addition, staged operation and early surgery (before 1 year of age) potentially increase the chance of successful separation.[4] The total angular craniopagus twins in our present case may be feasible to surgical separation, preferably in a multistage procedure and before 1st year of life, however, there is a high risk for poor prognosis.

In the advent of neuroendovascular procedures utilizing temporary and permanent balloon occlusion, stenting, liquid agent embolization and use of coils, there are reported cases of successful separation of total craniopagus. One successful surgery involves 5 month old female craniopagus twins O' Connell type I vertical craniopagus. Cerebral angiography shows cross filling of arterial channels and each twin has anterior superior sagittal sinus with anterior venous confluence. They underwent multiple staged procedures, utilizing temporary vascular clips for occlusion of venous channels aiming to promote deep venous drainage of Twin B (left with no venous inflow to the common sagittal sinus).[1] Another successful case involves O' Connell Type II vertical craniopagus twins who had separate cerebral hemispheres on one side and interdigitated brain on the contralateral side and they shared marginal dural sinuses on both sides with linked superior sagittal sinuses. They underwent 4 staged surgical procedures at 20, 21 , 26 and 30 months (first two stages included insertion of sheaths between two brain as well as arterial and venous ligation; third stage involved insertion of tissue expanders; last stage was the final separation) and two staged neurointerventional procedures at age 25 and 30 months (first stage was embolization of superior sagittal sinus of twin B using coils

and dominant venous lake of twin B using Onyx-18; second stage was the complete occlusion using the detachable coils and Onyx-18).[7] These neurovascular techniques can be applied to the twins in the case.

In addition to innovations in neurovascular procedures, new forms of technology such as computer-aided design, modeling and three-dimensional printing have been introduced in the recent years and were used as part of a successful multidisciplinary approach of separation of total angular craniopagus twins at 10 months of age.[8]

The primary physicians advised the twins to undergo surgical separation before age 1, parents' requested to delay the surgery and allow them to grow for a few more months. It may be less advantageous to delay the contemplated procedure because studies have shown that earlier separation lead to more successful outcomes.[1,4]

CONCLUSION

For cases of craniopagus, detailed and accurate mapping of shared and unshared anatomy, particularly the complex vascularity is of utmost importance. Comprehensive study of the case, planning and preparation are likewise necessary when contemplating separation of craniopagus to minimize the risk of vascular complications. Recent reports of surgical separation of craniopagus show a favorable outcome of the incorporating neuroendovascular techniques in the occlusion of shared venous connections in the craniopagus twins in multistaged operations. Modern neuroendovascular techniques and technologies as well as proceeding with a multistaged procedure and multidisciplinary team should be highly considered to achieve a successful separation.

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A Case of Partial Anomalous Pulmonary Venous Return (Scimitar Syndrome) In a Adult Female: A Case Report

Paul Martin M. Garcia, MD; Chris Albert N. Dy,MD; Ana Katarina C. Longos MD

Scimitar syndrome is a rare congenital anomaly that is a type of partial anomalous pulmonary venous return (PAPVR). Its presentation in adult patients usually includes symptoms of pulmonary hypertension and recurrent pulmonary infections.[1] Our case involves a 31-year old female presenting with symptoms of palpitations, dyspnea on exertion, recurrent pulmonary infection and syncopal attacks. Workup done for our patient included chest x-ray, 2D echocardiography, and cardiac MRI and all of which confirmed the diagnosis of Scimitar syndrome. She was subjected to surgery where on pump repair of Scimitar syndrome was done. Repair was done by creating a baffle using a portion of the pericardium and creating a tunnel from the opening of the anomalous vein in the inferior vena cava to the surgically created atrial septal defect. Postoperative course of the patient was unremarkable and patient was sent home improved. Patient followed up after three months with a postoperative cardiac MRI showing the patency of the repair.***Phil Heart Center J 2022;25(1):81-85.***

Key Words: ■ Scimitar syndrome ■ partial anomalous pulmonary venous return

Partial anomalous pulmonary venous return is a congenital disease entity that encompasses different variations of pulmonary venous return to the heart. The basic pathophysiology in PAPVR is that blood from one or more pulmonary veins that should drain to the left atrium drain into the right side of the heart thus producing a left to right shunt. The estimated overall incidence is at 0.7 percent of the whole population.[2] PAPVR has numerous anatomic variations wherein the anomalous pulmonary veins can drain to the left innominate vein, directly to the superior vena cava, coronary sinus, azygous vein or the inferior vena cava. When part or the entirety of the right pulmonary vein drain into the IVC, it is called Scimitar syndrome.[2]

Scimitar syndrome is usually diagnosed thru an abnormal radiologic finding of a crescent shaped shadow in the right hemi thorax suggesting an anomalous pulmonary vein. It can also be diagnosed thru 2D echocardiography and confirmed thru cardiac MRI or chest CT scan.[3,4] Once confirmed thru diagnostic imaging in a symptomatic adult, surgery is performed to repair the defect and to bring back normal physiologic blood flow. In this report we discuss an adult female diagnosed as a case of Scimitar syndrome and the approach to diagnosis, surgical treatment and follow up.

CASE PRESENTATION

We have a 31-year-old female, physically fit, who initially came in for consult with complaints of palpitations. Her symptoms started 3 years prior when she experienced palpitations, which would resolve spontaneously. These symptoms slowly progressed into palpitations accompanied with episodes of dizziness and syncopal attacks. This prompted

Finalist, Oral Presentation - Case Report. 28th PHC Annual Research Paper Competition and Poster Presentation held on February 2020 at Philippine Heart Center. Correspondence *to* ***Dr. Paul Martin M. Garcia .*** Department of Adult Cardiology. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

consult at a local hospital but workup revealed inconclusive findings. One year prior to admission, patient experienced persistent non-productive cough. Consult was done at a hospital abroad where chest x-ray, CT scan and 2D echo was done which showed that she had PAPVR for which she was advised close follow-up. (Fig. 1, 2) Her symptoms further progressed, this time she noted decrease in functional capacity from being able to engage in daily exercise to having difficulty laying flat on bed. She sought consult where a trans esophageal echocardiogram was done which revealed PAPVR however was still advised observation. She again sought consult with another physician where cardiac MRI (Fig. 3) was done which confirmed the diagnosis of PAPVR and was advised surgery hence was admitted for the contemplated procedure.

Patient was then subjected to surgery upon admission and pre operative preparation. Operation done was on pump repair of Scimitar syndrome. Preoperative trans esophageal echocardiogram was done which showed a large draining vessel into the superior vena cava (SVC) with consideration of an anomalous pulmonary venous drainage. Intraoperative findings showed an anomalous vein draining into the inferior vena cava (IVC). The goal of the repair was to construct a bridge for the blood to drain from the right heart to the left heart. Hence, repair of the defect was done by creating a baffle to divert the blood coming from the anomalous vein to the left atrium thru surgically created atrial septal defect (ASD). We used the patient's own pericardium as a conduit for the baffle. (Fig. 4) The pericardium was approximated to the posterior wall of the IVC and the opening of the ASD. (Fig. 5) Postoperative echocardiogram was done which showed no abnormal mosaic color flow seen draining into the IVC. The procedure went on smoothly andpatient was transferred to the surgical intensive care unit (SICU) post operatively with no untoward events. After three days in the SICU where all contraptions were removed and all medical support was discontinued, patient transferred to private room where she recuperated until was cleared for discharge. The patient came back for follow up after three months with a cardiac MRI. Results showed decrease in size of the anomalous pulmonary vein and a patent baffle.

ILLUSTRATIONS

List Of Figures

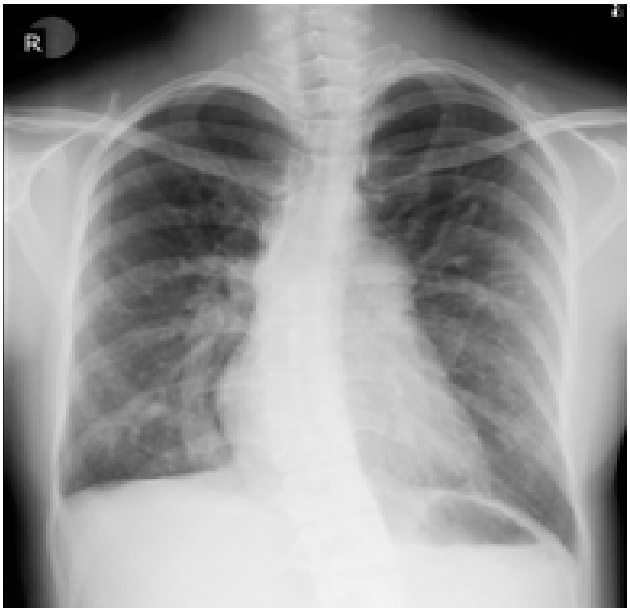

Figure 1. Chest X-ray (Posteroanterior View)

Pre operative chest radiograph in posteroanterior view showing a band like density in the right paracardiac area suggesting an anomalous pulmonary vessel.

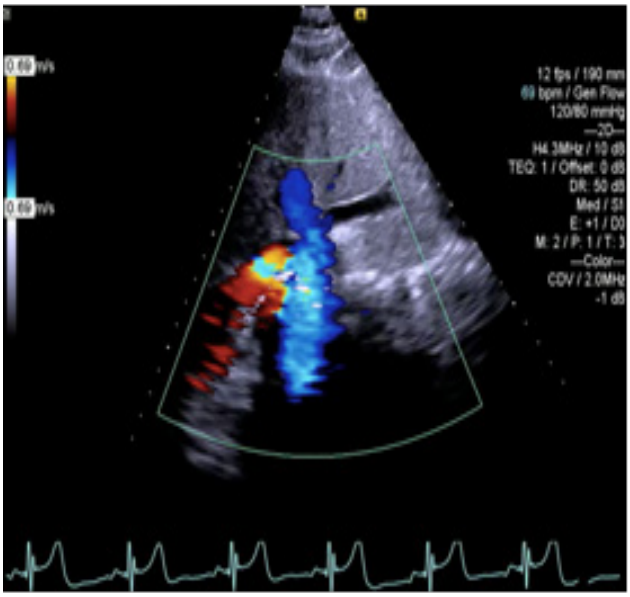

Figure 2. 2D-Echo

2D echo showing the anomalous vein draining into the IVC

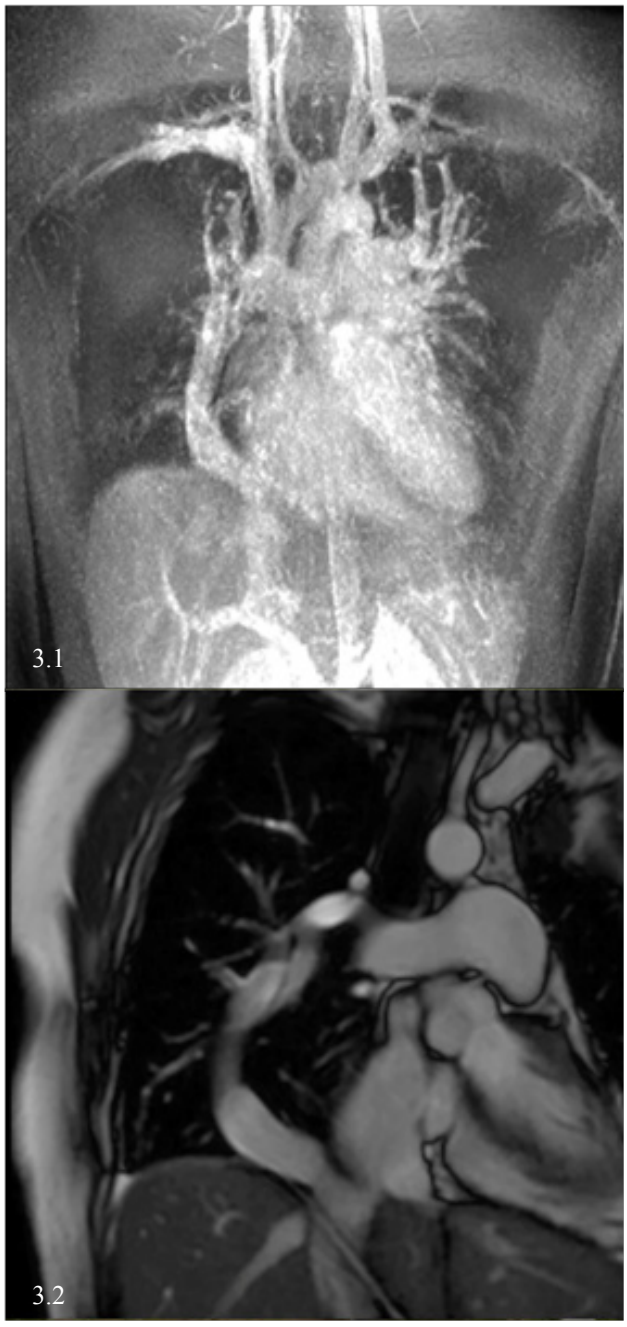

Figure 3. (3.1 and 3.2)Cardiac MRI

Cardiac MRI showing abnormal pulmonary venous connection in the right. Large anomalous pulmonary vein in the right spanning and with tributaries from the upper to lower lung measuring 20.6 mm in maximal diameter, which courses inferiorly to drain into the IVC at the diaphragmatic hiatus just above the level of the hepatic veins.

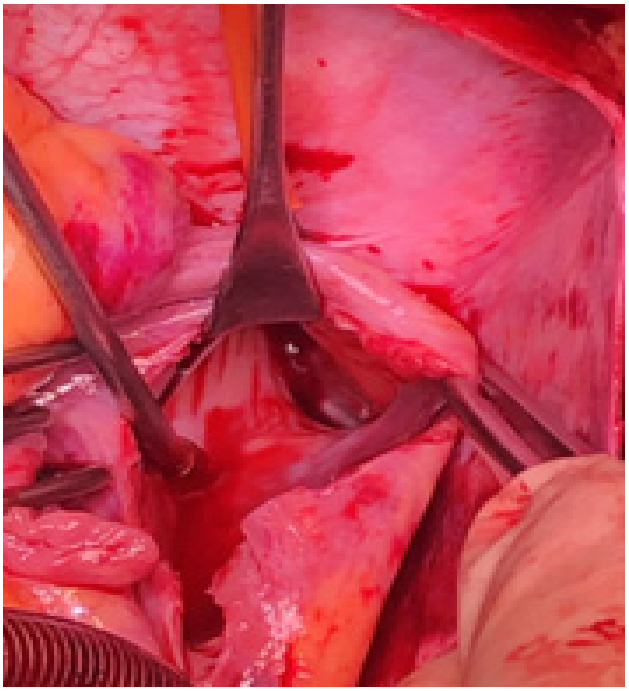

Figure 4. Intraoperative picture of the anomalous vein draining into the IVC

An intraoperative picture showing the defect in the posterior wall of the IVC

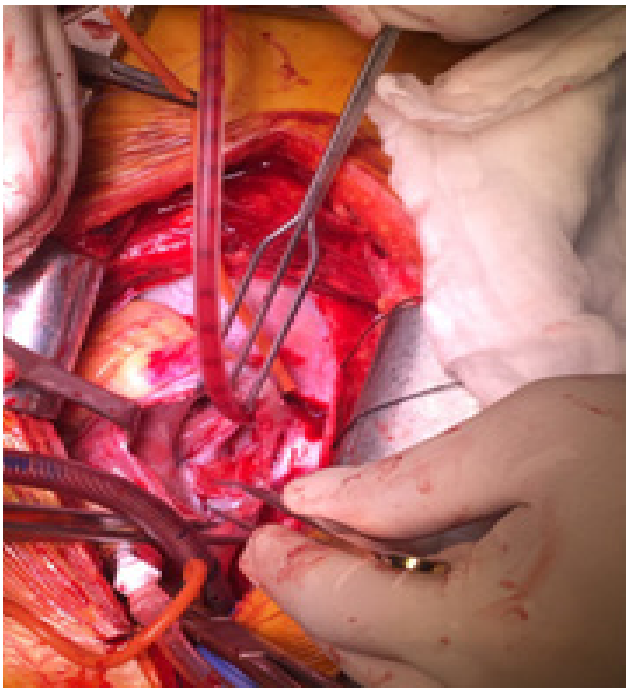

Figure 5. Intraoperative picture of baffle

Intraoperative photo of the baffle being sewn into place from the opening in the posterior wall of the IVC to the surgically created FO.

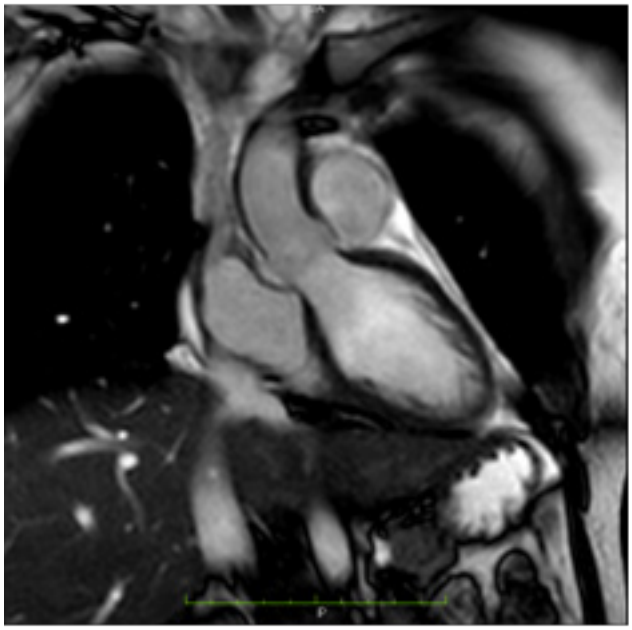

Figure 6. Postoperative cardiac MRI

DISCUSSION

Scimitar syndrome is a congenital disease, which is under the umbrella of partial anomalous pulmonary venous return. In this anomaly pulmonary veins abnormally connect to systemic veins or the right atrium instead of the normal variant which is the left atrium. Scimitar syndrome is a rare disease and is characterized as an anomalous connection of the right pulmonary vein to the inferior vena cava.[5,6,7] This abnormal connection causes left to right shunting and can cause right-sided volume overload, which in turn produces pulmonary hypertension and right-sided heart failure. Scimitar syndrome can be diagnosed early in infancy and can also manifest as symptomatic or asymptomatic adults. Literature has stated that early diagnosis usually in the infantile population has a worse prognosis than diagnosing it in the older or adult population.[5,7] In the adult population with scimitar syndrome, they are usually asymptomatic or have mild symtoms of excertional dyspnea and have good prognosis after surgical treatment.[5,7,8]

Diagnosis of scimitar syndrome can be done thru a wide array of diagnostic exams. The initial test where we usually have a suspicion for this condition is with a chest x-ray. In the chest x-ray of these patients, we get to appreciate a crescent shaped shadow in the right lower lung similar to a Scimitar or a saber like shape. In our patient this finding is very prominent. [Fig. 1] You can also appreciate the anomalous venous drainage with a 2D echocardiogram as was also seen in our patient. [Fig. 2] The use of 3D imaging is also of value for confirmation and for better defining the anatomy for proper surgical planning. The use of CT scan and cardiac MRI has been cited in literature and its use as a means for confirming the anomalous pulmonary venous drainage have been very helpful to the physician.[3,4] In our case, cardiac MRI was done and was very useful in terms of preoperative surgical planning.

With the confirmation of the diagnosis of scimitar syndrome, the main approach to treatment is surgical correction. The goal of surgical treatment is to bring back the normal physiologic drainage of the pulmonary veins to the left atrium thus removing the left to right shunting and the volume overload to the right side of the heart. With delayed surgery, prolonged right side volume overload can manifest as symptoms of right-sided heart failure and pulmonary hypertension hence the need for surgery once diagnosed.[9] Surgical technique for correction of anomalous pulmonary venous drainage has varied depending on the type of defect.[10] For scimitar syndrome, surgical correction mainly involves the creation of a tunnel connecting the opening of the anomalous pulmonary vein to the left atrium via a surgically created ASD. Doty described this technique and the important step in the repair is to keep in mind to make the pericardial patch wide enough to allow it to bulge in the atrium so as to provide unobstructed blood flow.[11] Several reports have also used this technique with good postoperative outcome.[12]

CONCLUSION

Scimitar syndrome is a rare congenital anomaly that can cause heart failure and pulmonary hypertension if not treated promptly upon

diagnosis. In the adult population, surgical treatment is the standard and prognosis based on literature is favorable. We presented a 31-year old female, adult, diagnosed as scimitar syndrome by chest x-ray, echocardiography and cardiac MRI who underwent surgical repair of scimitar syndrome by creating a baffle connecting the anomalous pulmonary vein to the left atrium thus obliterating the left to right shunt. With proper detection and surgical repair of this rare disease, patients can have better outcomes and have a longer life with a healthy heart.

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A Successful Three Dimensional Transesophageal Echocardiographic-guided Percutaneous Transmitral Commissurotomy in Rheumatic Mitral Stenosis with Coexistent Cor Triatriatum Sinister

Catherine P. Cataluña, MD; Shandi Mar L. Basiri, MD; Cherisse Ann P. Panlilio, MD; Aurora L. Lorenzana, MD; Abigail P. Bantoc-Cudel, MD; Vergel A. Quiogue, MD, Edwin S. Tucay, MD, Dodee Nino V. Rigor, MD, Rowena G. Cacas-Rebollido, MD

Introduction **---** Studies on combined or multiple valve diseases are limited precluding the availability of evidence-based guidelines. Accurate measurement of pressure gradients is pivotal in assessing the hemodynamic burden of these lesions. The Pulmonary Artery Pulsatility Index (PAPi) is calculated by dividing the difference of the pulmonary artery systolic and diastolic pressures with the right atrial pressure.

Case Report **---** We present a case of a 60-year old female diagnosed with rheumatic mitral stenosis and with incidental finding of non-obstructing cor triatriatum sinister who underwent a successful three dimensional transesophageal echocardiographic-guided percutaneous transmitral commissurotomy.

Conclusion **---** Cor triatriatum is uncommon congenital anomaly and its coexistence with rheumatic mitral stenosis makes it extremely rare. This anomaly is very challenging in doing PTMC, which needed well-trained invasive and non-invasive cardiologists. For nonobstructive or mild restrictive membrane, PTMC is possible. Transesophageal echocardiogram (TEE) is needed intraprocedural to best provide anatomic information.
Phil Heart Center J 2022;25(1):86-92.

Key Words: ■ Cor triatriatum ■ Rheumatic mitral stemosis ■ Percutaneous transmitral commissurotomy

Cor triatriatum is uncommon congenital heart disease rarely seen in adult patients comprising 0.1% of cases of congenital heart anomaly.[1] It was first described by Church in 1868 as a fibromuscular membrane dividing the left atrium into a posterosuperior chamber, which receives the return of all pulmonary veins, and an anteroinferior chamber, which is a true left atrium and communicates with the mitral valve.[2] It causes left ventricular oinflow obstruction and mimic mitral stenosis. Its coexistence with rheumatic heart disease, specifically mitral stenosis, is extremely rare. Such coexistence becomes a challenge to perform percutaneous transmitral commissurotomy (PTMC). PTMC for rheumatic MS with coexisting cor triatriatum has been reported in two cases by Devidutta et al.[3,4] Both cases presented with heart failure symptoms but were attributed to the rheumatic mitral stenosis. On transthoracic echocardiography showed an incidental finding of a transmembrane dividing the left atrium into a small proximal accessory membrane and a larger distal true left atrium. Transesophageal echocardiography (TEE) was done to evaluate the anatomy better. PTMC was done in both cases successfully guided with trans thoracic echocardiography. Here, We present a case of a 60-year old female, initially diagnosed with rheumatic heart disease, severe mitral stenosis, who had an incidental finding of a fenestrated cor triatriatum on three dimensional transesophageal echocardiography (3D TEE) and eventually underwent a successful 3D TEE guided PTMC to relieve the obstruction at the mitral valve level.

Finalist, Poster Presentation - Case Report. 28th PHC Annual Research Paper Competition and Poster Presentation held on February 2020 at Philippine Heart Center. Correspondence *to* ***Dr. Catherine P. Cataluña.*** Department of Adult Cardiology. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

CASE

A 60-year old female presented with a history of 11 years progressive easy fatigability and dyspnea. She was diagnosed with rheumatic mitral stenosis on two-dimension echocardiography with doppler studies. She is known hypertensive for 10 years and was maintained on an Angiotensin II receptor blocker. She is a 10 pack years smoker who stopped for almost 5 years and a non alcoholic beverage drinker. On clinical examination, the blood pressure is 120/70 millimeters of mercury (mmHg), heart rate of 69 beats per minute and respiratory rate of 20 breaths per minute. On auscultation noted irregulary irregular rhythm with grade 2/6 low pitched holodiastolic rumbling murmur best heard at the apex with loud S1 and short A2-OS. No loud P2 and no heaves nor thrills appreciated.

Electrocardiogram confirmed atrial fibirillation in controlled ventricular response (Figure 1), thus maintained on Vitamin K antagonist (VKA). Chest radiography showed cardiomegaly with left atrial prominence (Figure 2).

Two dimensional transthoracic echocardiography (Figure 3) revealed thickened mitral valve leaflets with diastolic doming motion of the anterior leaflet and restriction of the posterior leaflet. Calcifications scattered along the leaflet margins with mild subvalvar involvement. Both commissures are fused with mitral valve area of 1.0 cm^2 by planimetry and 0.79 cm^2 by pressure half time with mean valve gradient of 21.2 mmHg. The patient's Wilkin's score is 8. Patient then proceeded with TEE, which showed no thrombus neither more than mild mitral regurgitation. On 2D and 3D TEE, a thin, fenestrated, continuous membrane was noted bissecting the left atrium into a posterosuperior chamber and an anteroinferior chamber with no gradient across it upon application of colors (Figure 4,5). Pulmonary venous anatomy showed that the right upper and lower pulmonary veins drain into the posterosuperior chamber and the left upper and lower pulmonary veins drain into the anteroinferior chamber (Figure 6).

Patient was then referred to Invasive service for the plan of PTMC. A conventional coronary angiography and hemodynamics were done prior to PTMC and showed an angiographically normal coronary arteries and no significant step up in between chambers and great vessels respectively. Patient then underwent a successful 3D TEEguided PTMC via a transseptal approach below the membrane. A decrease in gradient to 5 mmHg from 21 mmHg and increase in mitral valve area to 2.0 cm^2 from 1.0 cm^2 was documented (Figure 7). Patient was then discharged with improved functional capacity. Figure 7A.

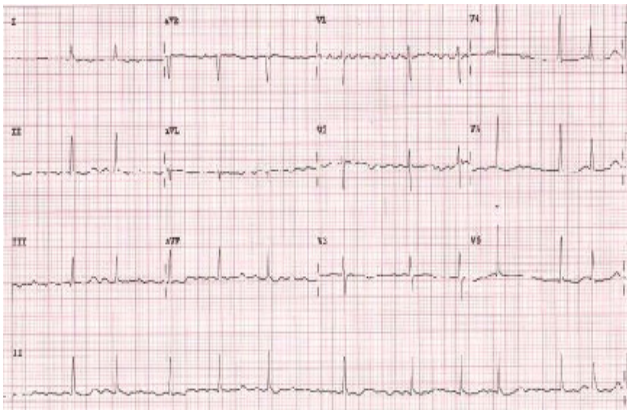

Figure 1. ECG-12 leads showed atrial fibrillation in controlled ventricular response.

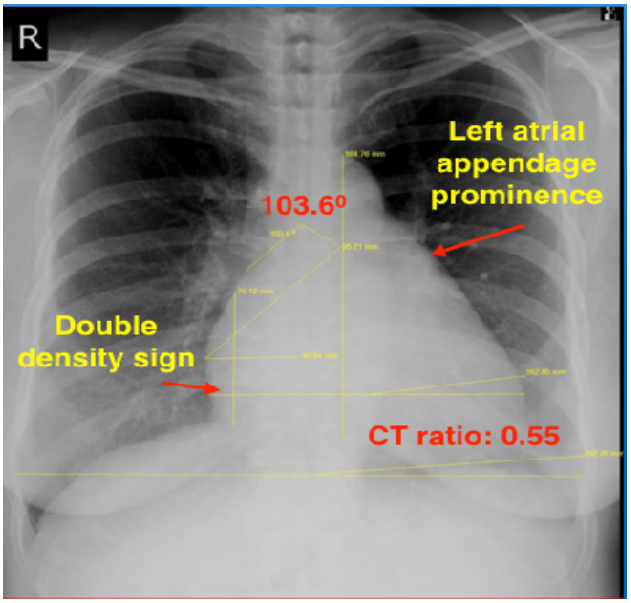

Figure 2. Chest radiography taken posteroanterior view showed cardiomegally with left atrial prominence as noted by straightening of the cardiac waistline with left atrial appendage prominence, widening of the carinal angle and double density sign.

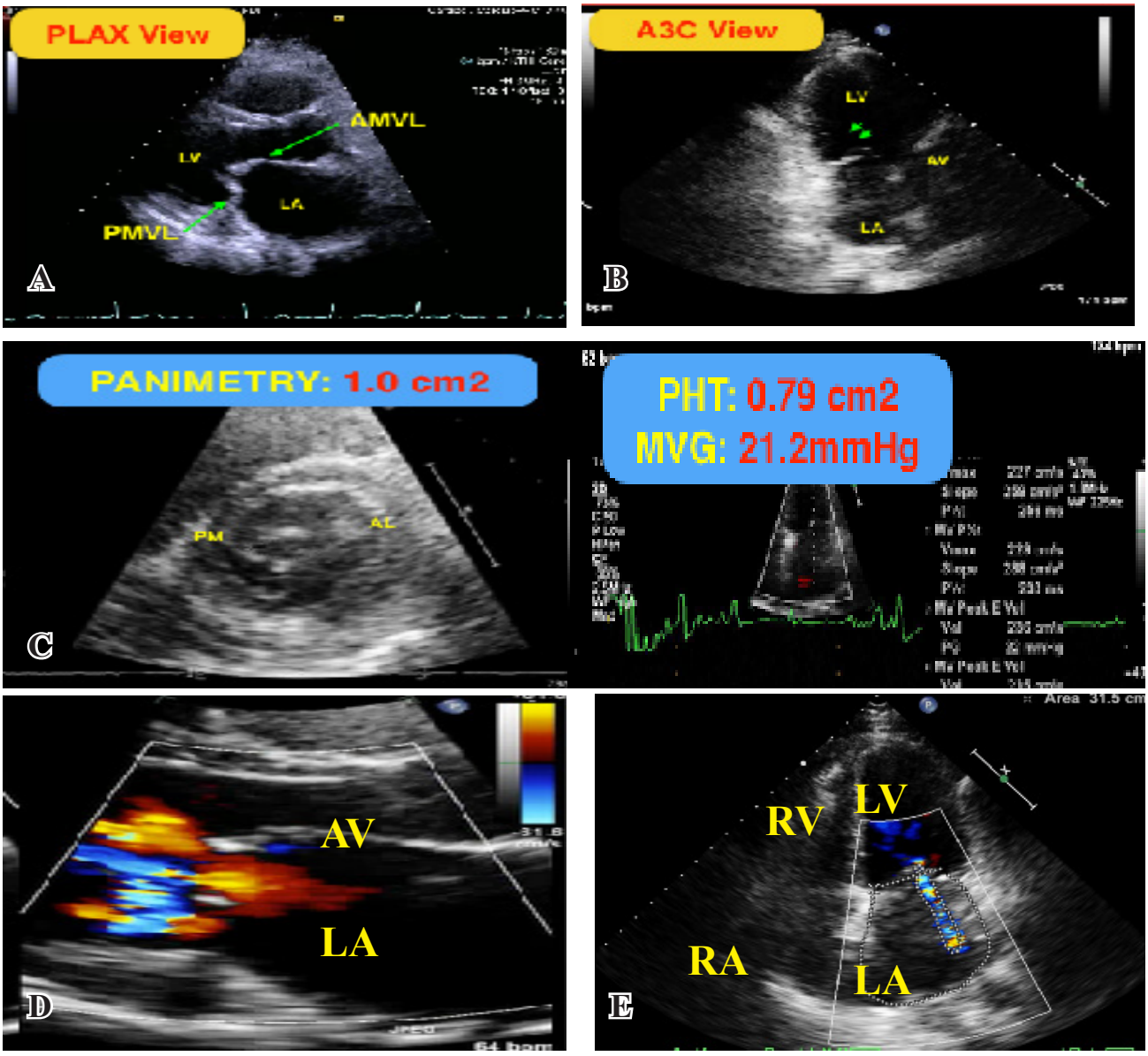

Figure 3. Two dimensional transthoracic echocardiography showed (**A**) thickened mitral valve leaflets with diastolic doming motion of the anterior leaflet and restricted posterior leaflet with calcifications scattered along leaflet margins and (**B**) mild subvalvar involvement; (**C**) both commissures are fused with mitral valve area of 1cm^2 by planimetry and 0.79cm^2 by pressure half time (PHT) with mean valve gradient (MVG) of 21.2 mmHg; (**D, E**) mosaic color flow display seen across the mitral valve during systoleand diastole

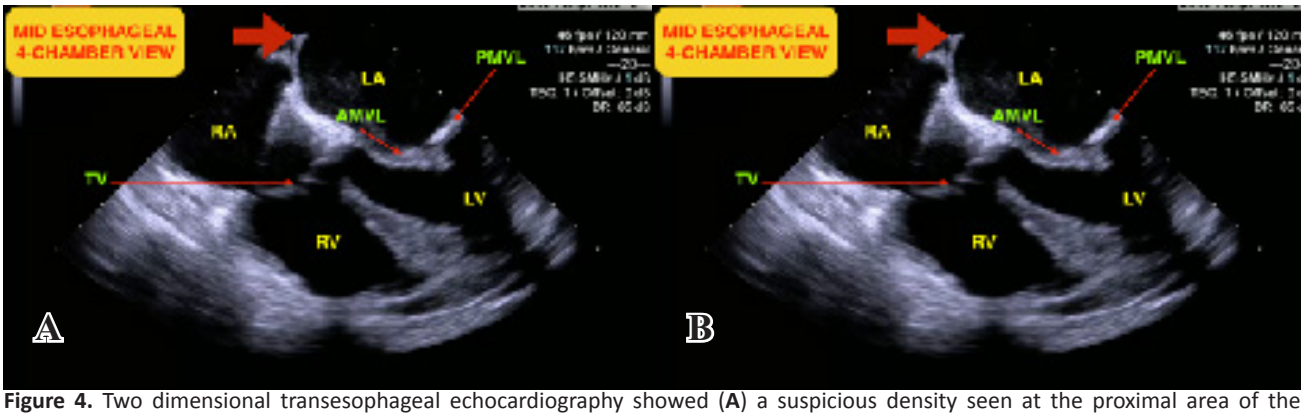

Figure 4. Two dimensional transesophageal echocardiography showed (**A**) a suspicious density seen at the proximal area of the left atrium; (**B**) at mid esophageal AV SAX view showed a thin membrane bissecting the left atrial cavity into an upper and lower chamber

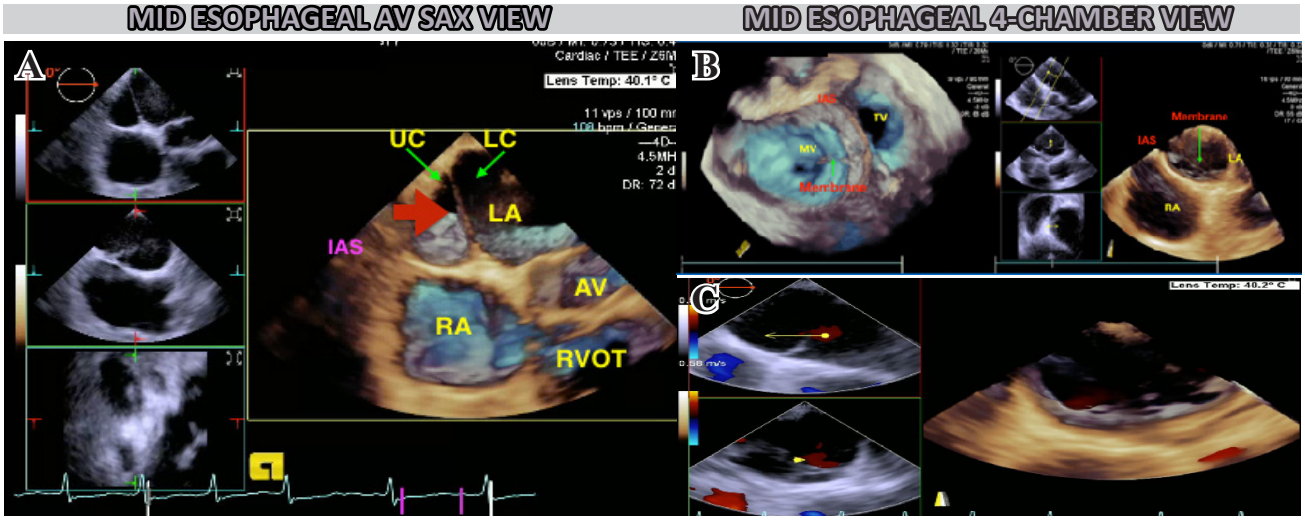

Figure 5. Three dimensional transesophageal echocardiography showed (**A**) the thinmembrane dissecting the left atrial cavity and upon interrogation (**B**) the membrane was noted as a continuous membrane with fenestration; (**C**) applying color, no gradient across it was noted

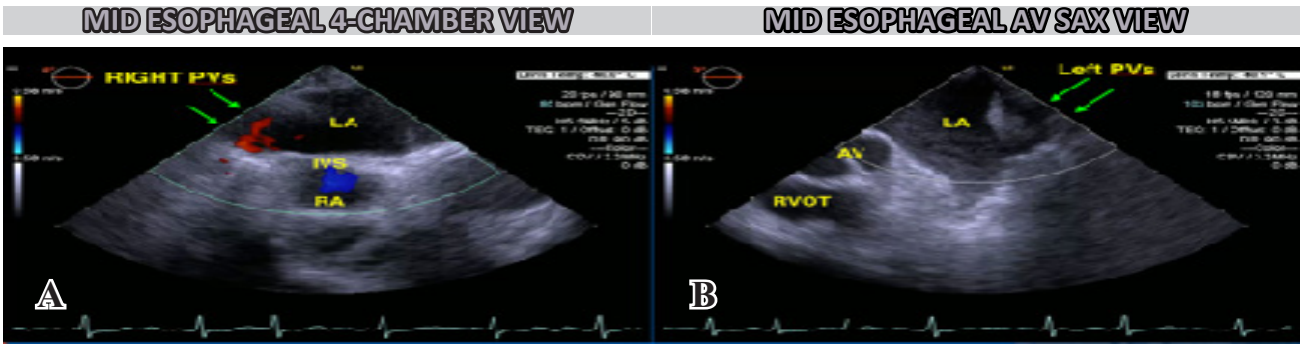

Figure 6. Pulmonary venous anatomy showed that (**A**) the right upper and lower pulmonary veins drain into the posterosuperior chamber and (**B**) the upper and lower leftpulmonary veins drain into the anteroinferior chamber

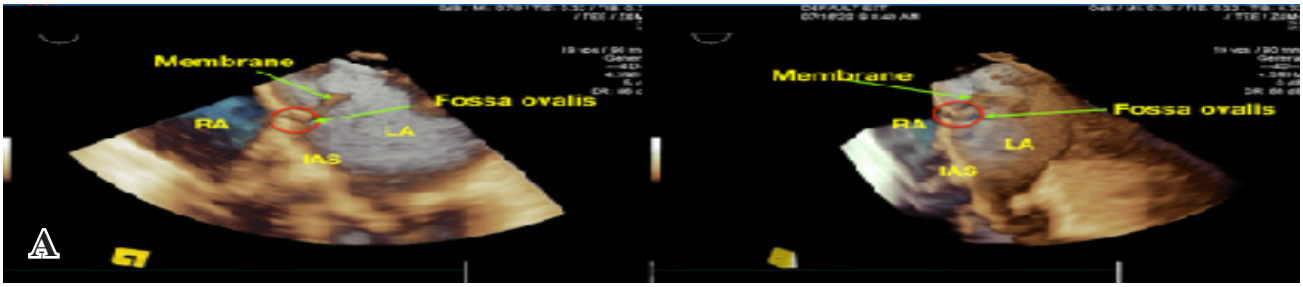

Figure 7A. Transseptal puncture site in the fossa ovalis was selected under online TEE guidance

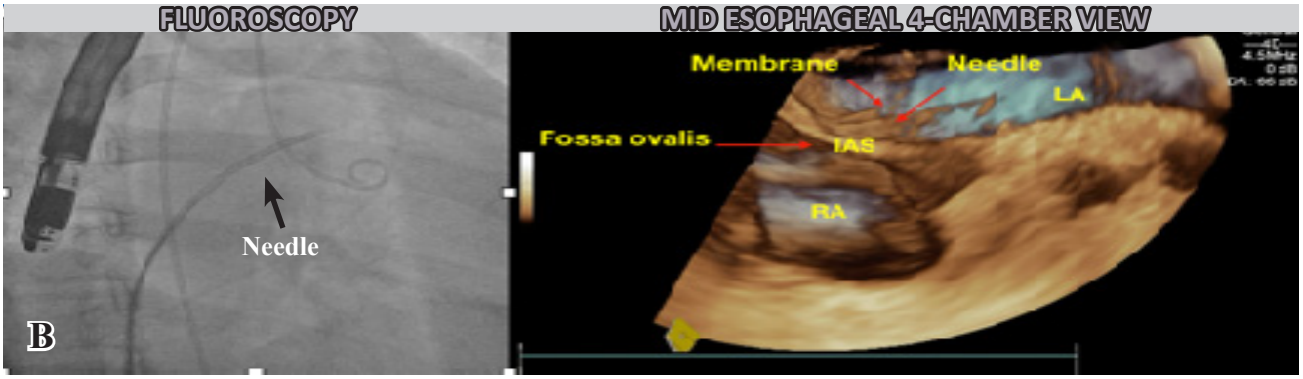

Figure 7B. The puncture needle was carefully advanced and was noted its placement just above the dosa ovalis but below the membrane

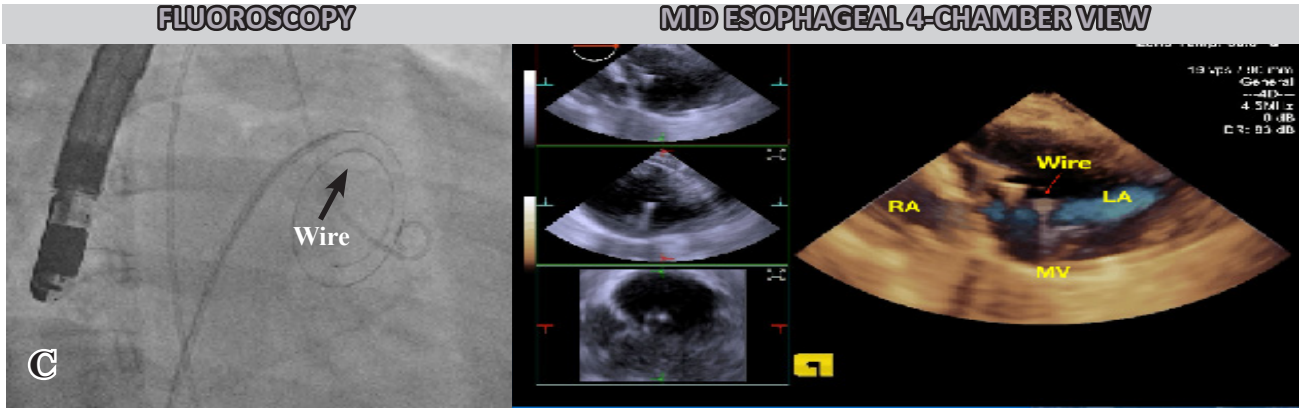

Figure 7C. A spring-tip guide wire was coiled into the left atrium

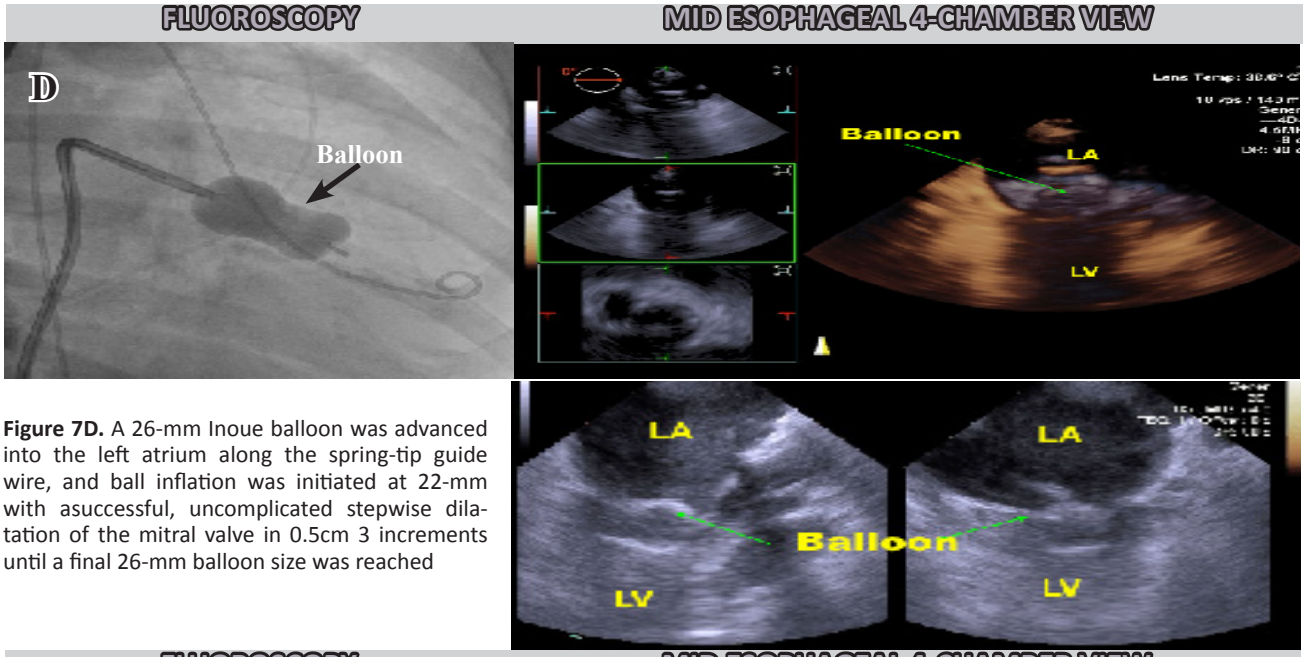

Figure 7D. A 26-mm Inoue balloon was advanced into the left atrium along the spring-tip guide wire, and ball inflation was initiated at 22-mm with asuccessful, uncomplicated stepwise dilatation of the mitral valve in 0.5cm 3 increments until a final 26-mm balloon size was reached

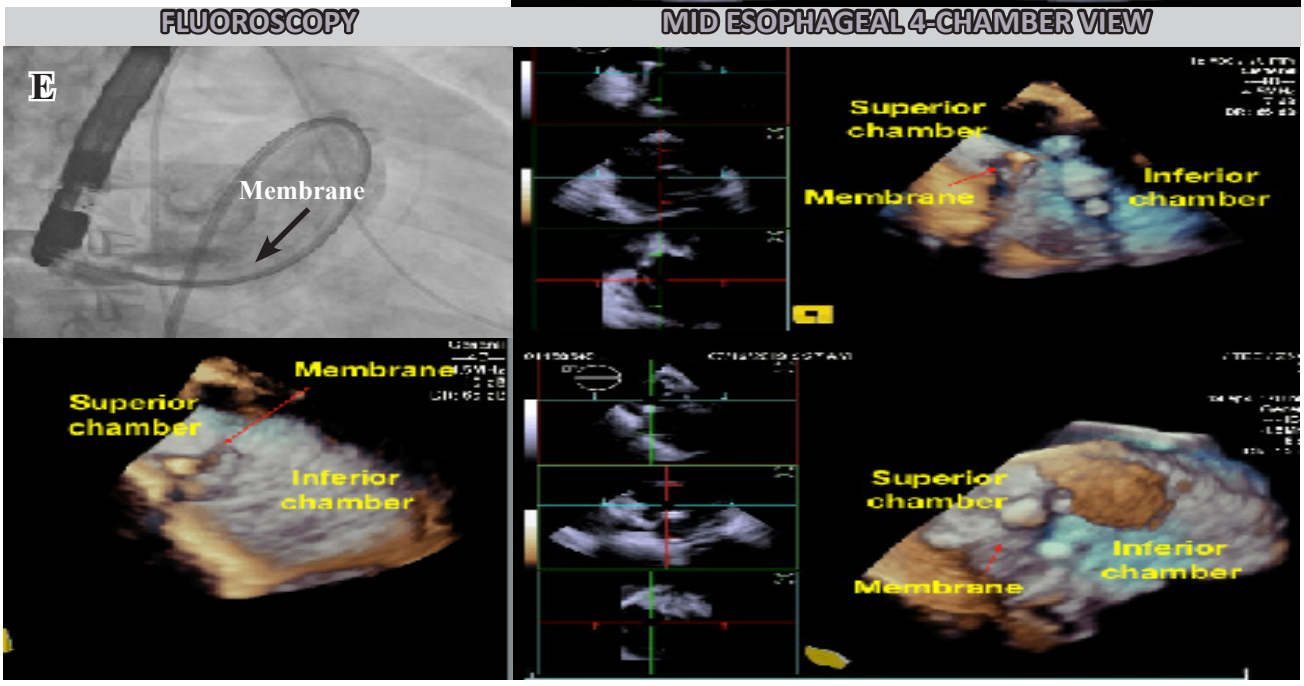

Figure 7E. Membrane was patent after introducing a contrast dye

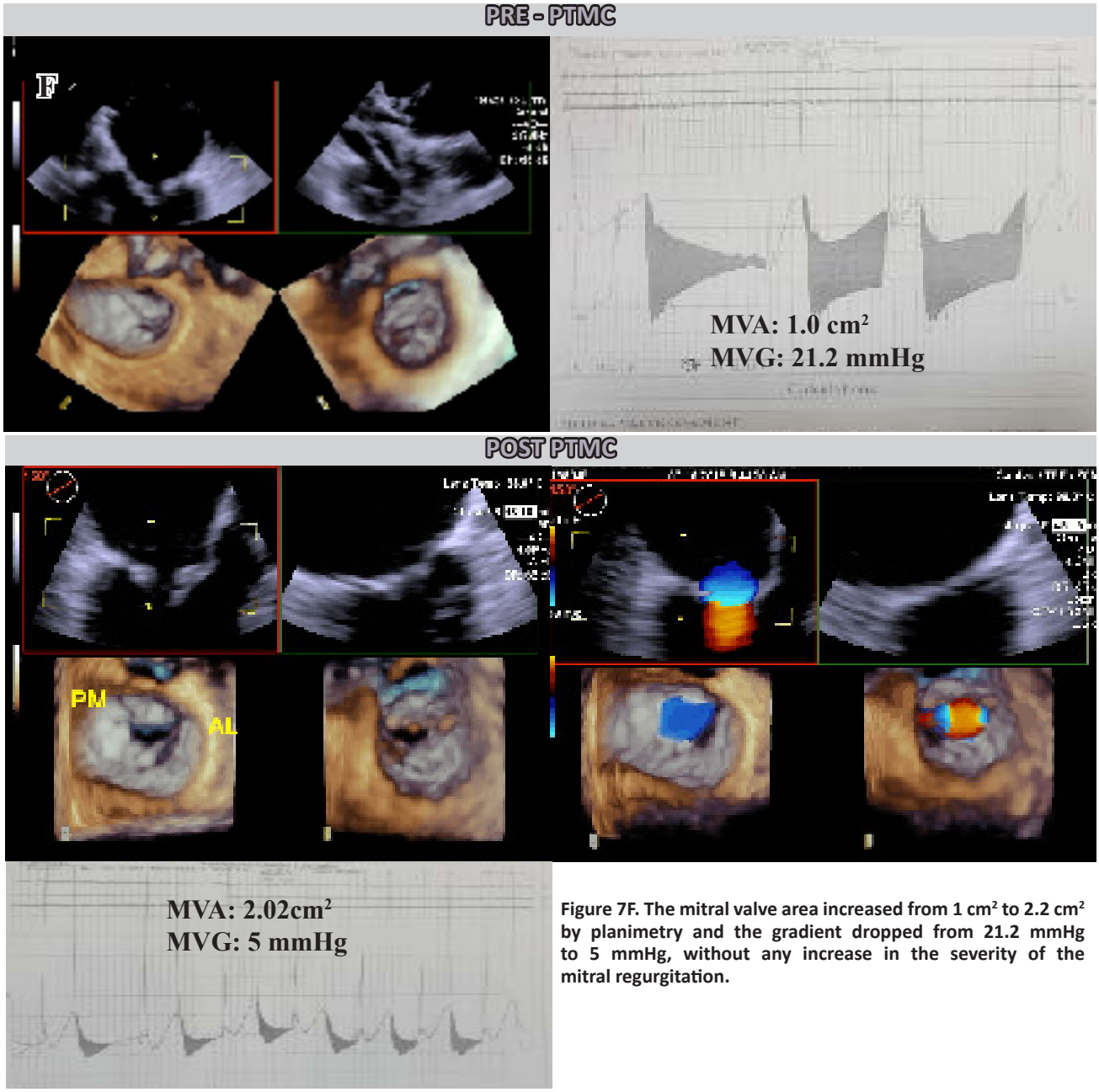

Figure 7F. The mitral valve area increased from 1 cm² to 2.2 cm² by planimetry and the gradient dropped from 21.2 mmHg to 5 mmHg, without any increase in the severity of the mitral regurgitation.

DISCUSSION

Cor triatriatum sinister is a rare congenital heart disease comprising only 0.1% of cases of congenital heart disease.[1] It is first described by Church in 18682. It is a fibromuscular membrane dividing the left atrium into a posterosuperior chamber, which receives the return of all pulmonary veins, and an anteroinferior chamber, which is a true left atrium and communicates with the mitral valve.[2]

Based on the embryology, cor triatriatum is due to the failure of the common pulmonary veins to regress and become incorporated into the posterior left atrial wall, giving rise to the accessory atrium.[2,6,7] It is usually present in infancy and early childhood and few case remain asymptomatic and are diagnosed in adulthood. Approximately 75% of infants with classic cor triatriatum, which is severely restricted and mimics mitral stenosis, without surgical intervention die.[1,2]

A pressure gradient is created across the membrane due to its obstructive nature leading to an increase in pulmonary venous and arterial pressures, thus mimicking mitral stenosis.[4] Presentation age and severity of symptoms depends on the membrane fenestrations.[5] Usually those with larger membrane fenestrations presented with lesser transmembrane flow obstruction and became symptomatic at later life.

Cor triatriatum in coexistence with rheumatic mitral stenosis is uncommon. Devidutta et al presented two case reports of rheumatic mitral stenosis associated with cor triatriatum who underwent successful PTMC. The anomaly showed an incomplete non-obstructive membrane. They did a transthoracic echocardiogram guided PTMC, wherein they puncture the upper part of the interatrial septum and balloon was negotiated across themembrane and into the left ventricle. As in our case, another report of rheumatic mitral stenosis associated with cor triatriatum was presented by Alfonso et al where they did a lower atrial septal puncture to avoid entry into the proximal accessory chamber. The same technique was done in our patient through TEE guided. A brokenbrough needlewas introduced above the fossa ovalis but below the membrane. The inoue balloon was then inserted through the inoue wire then serially inflated until significant reduction of gradient across the mitral valve was achieved. In the Invasive point of view, it is difficult to entry into the left ventricle when the point of entry is into the proximal chamber. This is because of two reasons: First, it is difficult to cross the membrane most especially if the membrane is restrictive.[3,4] Second, if the membrane orifice and the mitral valve are not aligned coaxially it is difficult to negotiate the balloon across the mitral valve. [3,4] Thus, to avoid entry into the proximal atrial chamber, an intraprocedural TEE may best provide a key anatomic information.

CONCLUSION

Cor triatriatum is an uncommon congenital anomaly and its coexistence with rheumatic mitral stenosis makes it extremely rare. Echocardiography is still the mainstay of diagnosis with transthoracic echocardiography as the first line of choice. Transesophageal echocardiography is a valuable diagnostic tool to further assess the classification and severity of the condition as well as guide an appropriate management strategy. Doing PTMC is very challenging in this kind of anomaly. But still it is possible as long as the membrane is non-obstructive or with mild restriction . A well trained invasive and non-invasive cardiologists are needed to perform such delicate procedure. Routine follow-up with echocardiography is warranted given that, in less than 20%, patients who underwent PTMC may have restenosis after 10 years.

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Information for Authors

EDITORIAL POLICY

Scope of the Journal

The Philippine Heart Center Journal is devoted to the publication of original articles related to cardiovascular diseases and allied fields. The scope of articles includes original publications, editorials, current reviews, meta-analysis, critically appraisal (CATs) and case reports.

General Policies

Contributions are reviewed by a group of cardiologists, cardiovascular surgeons and physicians of allied specialties with recognized academic and clinical expertise. Each manuscript is evaluated by at least two reviewers and may be edited for scientific accuracy and clarity. Statements and opinions expressed in articles and communications are those of the author(s) and do not necessarily reflect those of the editor or publisher. Neither the publisher nor the editor guarantee any product or service advertised in the publication. No part of the articles and communications published in the journal may be reproduced without the written permission of the publisher.

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MANUSCRIPT PREPARATION AND SUBMISSION

Manuscripts and all communications to the Editor should be addressed to:

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Editor-in-Chief
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9th Floor, Medical Arts Building
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East Avenue, Quezon City, Philippines

Submitting the manuscript in the correct format will expedite the reviewing process and obviate undue delay in publication. Please adhere to the following requirements:

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One original and two duplicate manuscripts and three full sets of tables and labelled illustrations should be submitted to the above address. The Editorial Office will be responsible for the proper handling of manuscripts so that confidentiality is preserved. Manuscripts and figures will be returned only upon the written request of the authors. Please provide a self-addressed stamped envelope for this purpose. Manuscripts should be typed double-spaced throughout (including title page, abstract, text, references, tables and legends) one side only on 22 x 28 cm (8 1/2 x 11 inches) opaque bond paper with 3 cm (1 1/4 inch) margins all around. The manuscript should be arranged as follows:

1. Title page
2. Abstract page
3. Text
4. Acknowledgement (if any)
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6. Figures and legends
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Number the pages consecutively on the upper right corner beginning with the title page.

Title Page

The title page must contain:
1. Title of the article
2. Names of authors plus highest academic degree of each
3. Each author's official academic and/or clinical title and institutional affiliation
4. Name and address of the institution/s where the research work was conducted
5. Name, address and telephone/fax number of the author to whom correspondence should be sent

Abstract

All original articles must contain an abstract of not more than 250 words. The abstract should include statements on the background, objectives, method of study, results and conclusion. Abstracts for case reports should be shorter (75-80 words). Include several (3-7) keywords to assist in cross-indexing the article.

Text

Generally, the text should be organized as follows:
a. Introduction
b. Materials and Methods
c. Results
d. Discussion or comments
e. Conclusion

The ***Introduction*** should describe the purpose of the study and its relation to previous work in the field. It should not include an extensive literature review. The description of the ***Methods*** should be concise, but sufficiently detailed to permit repetition by other investigators. ***Results*** should present positive and relevant negative findings of the study, supported when necessary by reference to tables and figures. The ***Discussion*** should interpret the results of the study, with emphasis on their relation to the original hypothesis and to previous studies.

Abbreviations or acronyms such as CAD, AMI, LVH may be used after the terms are spelled out once each in the abstract and text followed by the abbreviation or acronym in parentheses. All measurements should use the International System (SI) of units. Alternative units may be indicated in parentheses if necessary.

Manuscripts that describe studies on humans must indicate that the study was approved by an institutional review committee and that subjects gave their written, informed consent. Studies on both humans and animals must indicate that the procedures followed were in accordance with the institutional guidelines.

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a. For Journal References: Surname and initial of author(s), title of article, name of journal, volume number, first page or inclusive pages. If there are more than three authors, list the first three authors and add et al.

Braunwald E and Rutherford JD. Reversible ischemic left ventricular dysfunction: evidence for the "hibernating myocardium." J Am Coll Cardiol 1986;8:1467-1470.

Dilsizian V, Rocco TP, Freedman NM et al. Enchanted detection of ischemic but viable myocardium by the reinjection of thallium after stress -redistribution imaging. N Engl J Med 1990;323:141-146.

b. For Books: Surname and initial of author(s), title and subtitle, editor, city, publishing house page, year as specific reference.

Dillman WH. The Cardiovascular System in Thyrotoxicosis. In Braverman LE and Utiger RD, eds. The Thyroid - A fundamental and Clinical Text. 6th ed. Philadelphia: JB Lippincott Co; 1991,759-770.

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Illustrations should complement the text. The illustrations should be sharp and professionally rendered. Letters, numbers and symbols must be clear and of sufficient size to retain legibility after reduction. Glossy photographs of the original artwork, between 3-1/2 x 5 in. and 8 x 10 in. in size, should be submitted. Each illustration should be numbered and cited consecutively using Arabic numerals. Colored photographs will be considered for publication.

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Tables

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