ISSN 0118-9034

Philippine Heart Center Journal

Vol. 24 No. 2 July - December 2021

Official Publication of the Philippine Heart Center

EDITORS AND CONSULTANTS

The Philippine Heart Center Journal is published by the Philippine Heart Center.

PHILIPPINE HEART CENTER JOURNAL TABLE OF CONTENTS

Volume 24 # 2 July - December 2021

Editorial

Original Articles:

Case Report:

Cardiovascular Imaging Reviews --- *Irene S. Bandong, MD*

Editorial

Improving treatment outcomes do not come out of nowhere like rain on a summer day. It comes from a careful study of individual components or reflecting on the full extent of their sum to predict better or worse treatment outcomes. Determination of negative parameters initially that foretell on the basis of observation, evidence, or scientific reason is as important as introducing any disease intervention or any preventative interference to disease progression. Intervention is like an arrow, after it is launched, it would be technically almost impossible to arrest its trajectory.

The works of E. Yap, A. Salcedo, B. Causapin, C. Gayeta, P. Lopez, and E. Udaundo are excellent examples of the point of our discussion: studying and planning ahead before initiating any treatment is not only ethical but moral. Lives are at stake, let our science help. Wisdom comes from reflecting on our past experiences, meaning reviewing our charts. Their works attest to the fact that reflecting on our past will improve our future.

E. Domingo and D. Marmeto went full speed further and presented scoring systems to guide all practitioners about predicting positive treatment outcomes for TOF surgical corrections and cardiac rehabilitation. While A. Longos, N. Alegado, and J. Fongayao shared with us important case vignettes to be our intelligent guides to such rare cases.

We have started to include cardiovascular imaging reviews in this issue. We have a collection of images that will poke the interest of our readers.

Great works of art stimulate the emotions. These outstanding research outputs inside the pages of this edition tags not only emotions but entire lives and futures.

I hope you all enjoy reading through .

.

Gilbert Custodio Vilela, MD,
Editor-in-Chief

Effect of In-Patient Phase I Cardiac Rehabilitation on the Hospital Anxiety and Depression Scale Score (HADS) Among Cardiac Surgery Patients

Maria Donabel A. Marmeto, MD; Lucky R. Cuenza, MD; Edgardo E. Ebba, MD; Leandro C. Bongosa, MD; Marcelito L. Durante, MD; Minda Siasoco, MD; Mea Lovella B. Clara, MD; Benjamin Jose C. Quito, MD

Background **---** Depression and anxiety are prevalent co-morbidities in patients who are hospitalized due to heart disease and who have undergone cardiac surgery. These conditions can have significant impact on the patient's recovery, quality of life, treatment and prognosis. We aimed to determine the effect of an in-patient Phase I cardiac rehabilitation (CR) on the Hospital and Anxiety Depression Scores (HADS) of patients who underwent cardiac surgery.

Methods **---** A prospective cohort study of 100 patients who underwent cardiac surgery in our institution. Pre and post HADS score were taken from patients who were referred and not referred to Phase I Cardiac Rehabilitation. The two groups were compared for any significant changes of HADS score prior to discharge.

Results **---** Comparing the two groups, the decrease of post HADS scores was significantly greater in patients who were referred to Phase I Cardiac Rehabilitation (7.70 ± SD 3.0 vs 2.53 ± SD 1.4). The mean difference was 5.17 points with p = <0.001.Sub analysis of anxiety subscale was done. There was a significant decrease of post-HADS scores on patients who were referred to Phase I Cardiac Rehabilitation as compared with the other group (7.30 ± SD 3.2 vs 2.0 ± SD 1.2). The mean difference 5.17 points with p= <0.001.

Conclusion **---** Participation in an inpatient Phase I cardiac rehabilitation program prior to discharge may help in decreasing anxiety and depression levels in patients post cardiac surgery. ***Phil Heart Center J 2021;24 (2):1-8.***

Key Words: ■ Phase I Cardiac Rehabilitation ■ Post Cardiovascular surgery ■ HADS Score ■ Depression ■ Anxiety

Depression and anxiety are among the most common mental disorders specially for medically ill patients with a reported of prevalence of 10% - 50 %. These disorders result from a multitude of biological, psychological and social interactions. Prompt recognition should be sought because these can significantly hinder the course of management of patients.[1] Because of the stigma of medical illness as well as unwillingness of patients and healthcare provider to engage conversation regarding depression and anxiety, the existence of these conditions are often overlooked in many cardiac patients thus leading to sub-optimal outcomes in diagnosis and treatment. This has been showed significantly influence the course of medical illness, lengthen hospital stay duration, and lead to the patients'poor compliance to medication and treatment follow-ups.[1]

Cardiac rehabilitation (CR) is a medically supervised evidence-based intervention wherein a patient is restored to an optimal physical, psychological, social, emotional, and economic status. Cardiac rehabilitation programs consist of risk factor modifications, dietary interventions, psychological supports, exercise training, and education. It has already proven its benefits and effectiveness in terms of quality of life, reduction of mortality and its class I indication

1st place, Oral Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Maria Donabel A. Marmeto.*** Section of Cardiac Rehabilitation. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

from the American Heart Association/American College of Cardiology.[2] The Hospital Anxiety and Depression Scale (HADS) is a scoring system designed to recognize probable anxiety and depression among the in-hospital patients. It is a 14-item, self-assessment questionnaire composed of anxiety and depression subscales with 7 questions for each. For the interpretation, a score of 0-7 is normal, mild 8-10, moderate 11-14 and severe 15-21 as total HADS or for each subscale.[3] It has been validated as a measure of probable anxiety and depression in patients who had myocardial infarction and even in medically-ill patients. Correlational studies done in several aspects of medical illness and quality of life and it gave clinically meaningful results as a psychological screening tool. It showed high test-retest reliability make it appropriate for screening, monitoring and noted to be sensitive to changes during the course of the illness and in response to psychological management.[4]

More than 200 published studies worldwide used HADS score as tool, accepted in all facets of medical settings and translated in more than 50 different languages including Filipino language. It has been validated in the Philippines with a noted sensitivity of 75%, specificity of 70% and PPV of 75%.[5]

The typical cardiac rehabilitation program consists of 2 phases, where Phase 1 involves an in-patient phase emphasizing early recovery and ambulation in preparation for discharge, consisting strengthening exercises and basic instructions while Phase II is an outpatient comprehensive program consisting of exercise training, education and counselling.[6] While most of the studies focused on the effects of Phase II CR on outcomes, no published study to the best of our knowledge assessed the effects of Phase I Cardiac Rehabilitation (CR) in anxiety and depression results after cardiac surgery. The study may provide insight to use the HADS for in patients examining the postulated benefit of Phase I Cardiac Rehabilitation.

The objectives of the study are: (1) **t**o determine the effect of Phase I Cardiac Rehabilitation in HADS score of the post cardiovascular surgery patients. While the specific objectives are: (1) to determine the pre and post Hospital Anxiety and Depression Scale Scoring System (HADS Score) of post cardiac surgery patients who referred and not referred to Phase I Cardiac Rehabilitation; (2) to compare the mean difference of the pre and post Hospital Anxiety and Depression Scale Score (HADS Score) of post cardiac surgery patients who referred and not referred to Phase I Cardiac Rehabilitation.

METHODS

This was a prospective cohort study. The study protocol was approved by the Institutional Review Board and Institutional Ethics Review Board in our institution. The study was done in our institution from November 2017 to February 2018. Informed consent was obtained from the patients prior to the participation.

The respondents were chosen based on the following criteria: adult male or female patients with age of 19 to 70 years old, post cardiovascular (CABG, valve, vascular, trauma and congenital) surgical patients from private and service wards and on its third post-operative day where patients' clinical status was already stable.

We excluded patients who cannot read and write in English or Filipino, elderly patients (>70 years old), existing psychiatric disorders based on their medical histories, ongoing treatment of anti-anxiety and anti-depressant medications and prolonged hospitalization of >15 days due to complications. Each patient who agreed were given informed consent form. The attending physicians of each patient were also informed regarding the study.

The Hospital Anxiety and Depression (HADS) score scale, a 14-item, self-assessment questionnaire composed of 7-items for both the anxiety subscale and depression subscale. Pre and post HADS were taken for both groups. The total HADS score and its subscale were interpreted based on these ranges: normal (0-7), mild (8-10), moderate (11-14) and severe (15-21) and measured the changes from the baseline HADS score for both groups. (*Figure 1*).

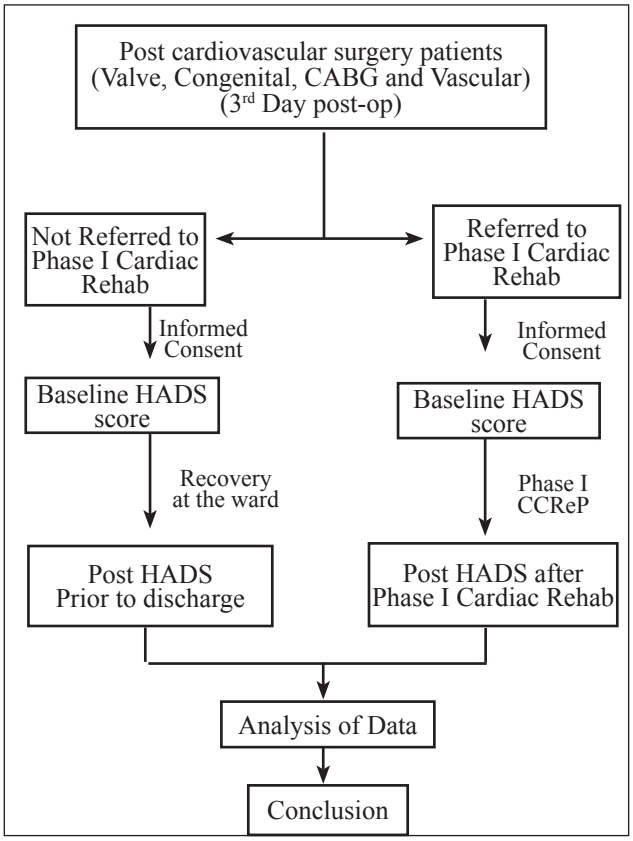

Figure 1. Study Maneuver

A. Phase I of Cardiac Rehabilitation - This is a hospital in-patient program which is initated after cardiac rehabilitation specialist assessed and diagnosed that patient is on stable medical condition after the cardiac event. The objectives of the program are to speed -up recovery and prevent complications like deconditioning due to prolonged bed rest, etc. Rehabilitation program includes health education, range of motion activities, intermittent sitting or standing and walking according to the level set by cardiac rehabilitation specialist.

B. Hospital Anxiety and Depression Scale Scoring System - The HADS score was designed to determine the presence of depression and anxiety disorders among the medically-ill patients which includes depression and anxiety symptoms, while the somatic items which could be attributed to the physical illness have been omitted. A 14-item self-assessment questionnaire. It is composed of 7-items for both the anxiety subscale and depression subscale. Scores on each scale can be interpreted in ranges: normal (0-7), mild (8-10), moderate (11-14) and severe (15,21).[3]

C. Age - refers to the chronological age of the patient. In the study of Stordal et al, suggested that age has relationship with persons' vulnerability/susceptibility to depression and anxiety.

D. Sex - refers to biological characteristics that differentiate man and woman. Studies suggest that there are differences in rate of depression between males and females through the ages.

E. Marital Status – refers to the relationship status of married couple as some studies suggest that interplay exists between marital status and depression.

F. Educational Attainment – refers to the level of schooling that an individual achieved and is observed as part of the risk factor for having depression as observed in some studies. The socio-economic status as a result of educational attainment could be the reason.

G. Occupation – refers to work that generates income. The highest rates of depressed workers were observed in sectors where the workers have low income and low morale.

H. Socio-economic Status–According to 2012 Family Income and Expenditure Survey (FIES), Philippine Statistics Authority, the following are the different socio-economic status class base on monthly income:

a. Poor – the income per capita was less than official poverty threshold amounting less than PHP 7,890 per month.

b. Low income (but not poor) – the income per capita was twice higher than the poverty line ranging from PHP 7,890 to PHP 15,780 per month.

c. Lower middle income - the income per capita was twice to four times higher than the poverty line ranging from PHP 15,780 to PHP 31,560 per month.

d. Middle class - the income per capita was four times to ten times higher than the poverty line amounting PHP 31, 560 to PHP 78,900 per month.

e. Upper income (but not rich) - the income per capita was fifteen times to twenty times higher than the poverty line ranging from

PHP 118,350 to PHP 157,800 per month.
f. Rich - the income per capita was equal or more than twenty times higher than the poverty line amounting at least PHP 157,800 per month.

I. Physical Activity – refers to activities like exercise that helps to reduces stress, ward-off anxiety and feeling of depression, boost self-esteem and improves sleep. In this study the patients will be asked if they are actively doing exercise or not prior to their operation.

J. Cardiovascular surgery – composed of coronary artery bypass graft surgery, valve surgery, congenital heart disease surgery and vascular surgery.

K. Co-morbidities – presence of co-morbidities like hypertension, diabetes, cerebrovascular and previous psychological disorder can be a triggering factor for anxiety and depression.

L. Risk factors – smoking, alcoholic beverage drinking, and illegal drug abuse will be noted in study in which can have possible association with anxiety and depression.

M. Medications used – medications can be associated with depression and anxiety.
Use of Beta-blockers - refers to intake of drugs classified as beta-blocker, which is used in managing cardiac arrhythmias. Intake of this drug has been associated with increased risk of depression.
Use of anti-depressant drugs - this is part of treatment of depression. This includes Selective Serotonin Re-uptake Inhibitor (SSRI) such as Sertraline and Citalopram which are safe for patients with coronary heart disease (CHD) and effective for moderate, severe, or recurrent depression.

A minimum of 94 patients were required for the study, this was based on effect size of 0.49, alpha level of 0.05, power of 80%, pooled standard deviation of 3.4, and an assumed 0.875 correlation coefficient of pre and post cardiovascular rehabilitation program in terms of Anxiety on Psychosocial Score by Stauber.[9]

Descriptive statistics were used to summarize the clinical characteristics of the patients. Frequency and proportion were used or nominal variables, mean and SD for continuous varables. To show relationship/association, Independent and Paired Sample *T*-tests were used for continuous varables, and Fisher's Exact/Chi-square test were used to for categorical variables. Missing variables were neither be replaced nor estimated. Null hypothesis was rejected at 0.05 α-level of significance. STATA 13.1 was used for data analysis.

RESULTS

A total of 100 post-cardiovascular patients participated in the study, 85% of which referred for Phase I Cardiac Rehabilitation.

The total pre-HADS score of the two groups showed a mean of 11.86 ± 2.0 SD for those patients who were not referred and 10.45 ± 2.0 SD for those who referred to Phase I Cardiac Rehabilitation respectively. After the course of treatment and sessions, the mean HADS score for both groups significantly decreased, 9.33 ± 1.3 for patients who were not referred and 2.75 ± 2.5 points for patients who were referred to Phase I Cardiac Rehabilitation respectively. Comparing the two groups, the overall mean difference was significantly greater in patients who were referred to Phase I cardiac rehabilitation with mean difference of 5.17 points, p= <0.001. (*Table 2*) The mean changes in scores were graphically represented in Figure 2.

Sub-analysis of anxiety subscale was done. The mean pre-HADS score of the two groups were 10.87 ± SD 1.3 for those who were not referred vs 9.96 ± SD 1.3 for those who were referred. There was noted a significant decrease between the mean post-HADS anxiety subscale of the two groups, with the Phase 1 referred group having a greater decrease in the anxiety score (8.87 ± SD 1.2 vs 2.65 ± SD 2.5). The change in the anxiety subscale scores was significantly greater in the Phase 1 group with a mean change of 5.17 points (p=<0.001). The changes are graphically summarized in Figure 3.

Table 1. Profile of Post Cardiovascular Patients Who Underwent Cardiovascular Surgery.

	Without Phase I Cardiac Rehab (n=15) Frequency (%)	With Phase I Cardiac Rehab (n=85) Mean ± SD	P Value
Age in years	44 .3 ± 16	53. 5 ± 14	**0.025**
Sex			1.000
Male	5 (33.3)	26 (30.6)	
Female	10 (66.7)	59 (69.4)	
Marital Status			0.220
Single	5 (33.3)	12 14.2)	
Married	9 (60.0)	69 (81.18)	
Widowed	1 (6.6)	3 (81.8)	
Separated	0	1 (1.18)	
Occupation			0.381
with occupation	8 (53.3)	57 (67.1)	
without occupation	7 (46.7)	28 (32.9)	
Previous physical activity			0.222
with exercise	13 (86.7)	59 (69.4)	
without exercise	2 (13.3)	26 (30.6)	
Socioeconomic status			0.723
Poor	6 (40.0)	23 (27.1)	
Low income	6 (40.0)	28 (32.9)	
Lower middle income	1 (6.7)	7 (8.2)	
Middle class	2 (13.3)	20 (23.5)	
Upper income	0	7 (8.2)	
Rich	0	0	
Co-morbidities			
Hypertension	7 (46.8)	61 (71.7)	0.073
Diabetes	3 (20.0)	48 (56.5)	**0.012**
Asthma	0	2 (2.35)	1.000
COPD	0	0	-
Psychiatric disorder	0	0	-
Others	1 (6.67)	6 (7.06)	1.000
Medications			
Beta blockers	13 (86.7)	66 (77.6)	0.731
Anti-depressants	0	0	-
Type of cardiac surgery			0.052
CABG	4 (26.6)	46 (9.41)	
Valve surgery	4 (26.7)	8 (9.4)	
Vascular surgery	4 (26.7)	11 (12.9)	
Congenital surgery	3 (20.0)	9 (10.59)	
Combined surgery	0	10 (11.8)	
Trauma	0	1 (1.2)	

Table 1. Showed the baseline characteristics of the two groups. Patients who referred to Phase I Cardiac Rehabilitation (CR) were older (53.5 vs 44.3) and were more likely to be diabetic. The rest of the findings were all similar between the two groups.

Table 2. Total HADS of the Two Groups (With and Without Phase I Cardiac Rehabilitation)

	PRE HADS Mean ± SD	POST HADS Mean ± SD	Mean Difference	P-Value
WITHOUT Phase I Cardiac Rehabilitation	11.86 ± 2.0	9.33 ± 1.3	2.5	**<0.001**
WITH Phase I Cardiac Rehabilitation	10.45 ± 2.0	2.75 ± 2.5	7.7	**<0.001**
Mean Difference	1.41	6.58	5.17	**<0.001**

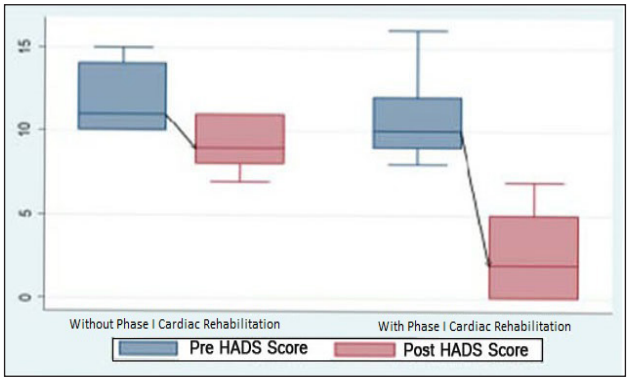

Figure 2. Box plot showing changes in pre and post total HADS score among patients without Phase I Cardiac Rehabilitation and with Phase I Cardiac Rehabilitation.

Table 3. HADS Score, Anxiety Subscale of the two groups

	PRE HADS Mean ± SD	POST HADS Mean ± SD	Mean Difference	P-Value
WITHOUT Phase I Cardiac Rehabilitation	10.87 ± 1.3	8.87 ± 1.2	2.0	**<0.001**
WITH Phase I Cardiac Rehabilitation	9.96 ± 1.3	2.65 ± 2.5	7.3	**<0.001**
Mean Difference	0.91	6.22	5.17	**<0.001**

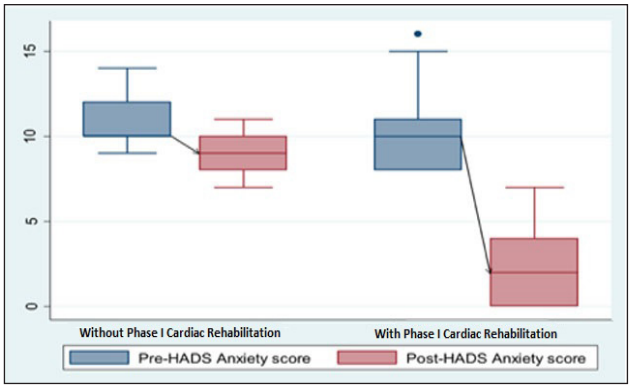

Figure 3. Box plot showing changes in pre and post anxiety sub-scale HADS score among patients without Phase I Cardiac Rehabilitation and with Phase I Cardiac Rehabilitation.

DISCUSSION

The Hospital Anxiety and Depression Scale Score (HADS) has been used in many settings: in the general population/community, in primary care settings, and in hospitalized patients particularly among those with cancer and cardiac problems.[7]

Patients who had post cardiac surgery are prone to develop anxiety and depression. Probable pathophysiology can be secondary to significant increase of inflammatory response during perioperative period. Both anxiety and depression were significantly associated with physical inactivity leading to increase of re-hospitalization as well as increase in morbidity and mortality. With this, recognition of this psychological condition should be recognize and addressed during early phase.[8]

In our study, the total post HADS of the two groups decreased compared from the baseline. Those patients referred to Phase I cardiac rehabilitation had a significantly higher mean difference of post HADS scores. Sub-analysis of anxiety subscale also showed significant higher mean change of post HADS scores in those patients who were referred to Phase I cardiac rehabilitation compared from the baseline. These results suggest possible improvement of anxiety of post cardiac patients even during at the early phase of cardiac rehabilitation. There was no depression sub-analysis done since all of the patients for both groups did not reach the level of probable depression during pre-HADS assessment and may not show any significant changes.

A study assessing psychosocial outcome in complete cardiac rehabilitation showed in 520 patients with Coronary Artery Disease (CAD) who were recruited for 12 week cardiac rehabilitation program and noted significant improvement with *p*-values of < 0.001. [9]

Another study using Spielberger State - Trait Anxiety Inventory Questionnaire (STAI), 51 patients with Acute Myocardial Infarction (AMI) were assessed after 2-3 weeks cardiac rehabilitation program. It resulted improvement in the 2-week rehabilitation group compared

with the control group (repeated ANOVA, $p = 0.0095$).[10]

Lastly, in a study conducted showing impact of cardiac rehabilitation on depression and anxiety and its underlying morbidity and mortality, around 3,975 patients were enrolled during Phases I and II of cardiac rehabilitation program. Only 379 (<10) participated in Phase II. However, after 6 years, median follow-up showed 20 risk reduction of mortality and morbidity for patients enrolled in Phase I and a 40 risk reduction for Phase II participants. [11]

The benifit s of exercise program on health are indisputable in the field of modern medicine and it said to be the first step in life-style modifications for the prevention and management of chronic diseases as well as psychological conditions like anxiety and depression. Understanding of the effects of exercise and physical activity on the mechanisms of anxiety disorders is important because it has effects not just psychological but also physiological changes in the body. Studies have shown that regular physical activity can lower sympathetic nervous system and hypothalamic -pituitary-adrenal (HPA) axis reactivity in which will further enhance gas exchange, endothelial and muscle function. Thus, this physiologic enhancements will increase patients' self-esteem and well-being in which an important factor to patients at their early phase of post cardiovascular recovery.[12]

Our results of possible evidence of some psychosocial benefit of an early Phase I program can serve as an adjunct to complete the cardiac rehabilitation program well into Phase II as these patients are expected to achieve a more complete physical and mental cardiovascular recovery.

Thus, this study showed that cardiac rehabilitation after cardiac surgery may be beneficial in reducing anxiety and depression levels, which in turn may help reduce morbidity and length of hospital stay and improve over all well being and quality of life.

Our study has certain limitations. This study is prospective cohort by its nature, it is just observational in design and only intended for hypothesis generating. The sample size is small, and the generalizability of the results may be limited.

Our results need to be further validated by a large randomized controlled trial to show definite causality of the effect of Phase I cardiac rehabilitation in the HADS score.

To the best of our knowledge there have been no published studies in our setting that determined the effects of a Phase I in-patient cardiac rehabilitation program in the HADS scores of cardiovascular surgery patients. However, studies consistently show that established the beneficial effect of both Phase I and Phase II cardiac rehabilitation in improving anxiety and depression.[14] Our results add knowledge to expanding the reach of an early in-patient referral for cardiac rehabilitation, so patients may optimize its benefits.

CONCLUSION

Participation in an in-patient Phase I Cardiac Rehabilitation program can help in decreasing hospital anxiety scale score levels in post cardiac surgery patients. Early referral to this program may benefit to aid not only in their cardiovascular, physical recovery but also in their mental and psychological recovery as well.

REFERENCES

1. Herrmann C, Buss U, Snaith RP. HADS-D. Hospital Anxiety and Depression Scale. Deutsche Version. Bern: Hans Huber. 1995.
2. Bahieh Moradi, MD. Physician-Related Factors Affect ing Cardiac Rehabilitation Referral. Echocardiography Research Center, Rajaie Cardiovascular, Medical and Research Center, Tehran University of Medical Sciences, Tehran, Iran. Iran Journal. 28 September 2011.
3. Roberts SB, Bonnici DM. Psychometric evaluation of the Hospital Anxiety and Depression Scale (HADS) among female cardiac patients. Br J Health Psychol. 2001 Nov;6(Part 4):373-383.
4. Johnston M, Pollard B, Hennessey P. Construct validation of the hospital anxiety and depression scale with clinical populations.J Psychosom Res. 2000 Jun;48 (6):579-84.
5. R. De Guzman. A validation of the Hospital Anxiety and Depression Scale (HADS) in the medically-ill. Acta Medica Philippina. 2013;47:3.
6. Taylor RS, Brown A, Ebrahim S. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. Am J Med 2004; 116: 682–692.

7. Snaith RP. The Hospital Anxiety and Depression Scale. Health Qual Life Outcomes. 2003 Aug 1;1:29.
8. O'Rourke A, Lewin B, Whitecross S, Pacey W. The effects of physical exercise training and cardiac education on levels of anxiety and depression in the rehabilitation of coronary artery bypass graft patients. Int Disabil Stud. Jul-Sep 1990;12(3):104-6.
9. Stauber S, Guéra V, Barth J, Schmid JP, Saner H, Znoj H, et al. Psychosocial outcome in cardiovascular rehabilitation of peripheral artery disease and coronary artery disease patients. Vasc Med. 2013 Oct; 18(5): 257-62.
10. Yoshida T, Yoshida K, Yamamoto C, Nagasaka M, Tadaura T, Meguro T, et al. Effects of a two-week, hospitalized phase II cardiac rehabilitation program on physical capacity, lipid profiles and psychological variables in patients with acute myocardial infarction. Jpn Circ J. 2001 Feb;65(2):87-93.
11. Millani RV, Lavie CJ. Impact of cardiac rehabilitation on depression and its associated mortality. Am J Med. 2007 Sep;120(9):799-806.
12. Astrand P. Physiological bases of exercise. In Textbook of work physiology. Champaign: Human Kinetics Publishers, 2003.
13. Turner A, Philips L, Hambridge JA, Baker AL, Bowman J, Colyvas K. Clinical outcomes associated with depression, anxiety and social support among cardiac rehabilitation attendees. Aust N Z J Psychiatry. 2010 Jul;44(7):658-66.
14. Harrison R. Psychological assessment during cardiac rehabilitation. Nurs Stand. 2005 Mar 16-22;19(27):33-6.
15. Ceccarini M, Manzoni GM, Castelnuovo G. Assessing depression in cardiac patients: what measures should be considered? Depress Res Treat. 2014;2014: 148256.
16. Pietrzyk E, Gorczyca-Michta I, Michta K, Nowakowska M, Wożakowska-Kapłon B. Depression in patients after coronary artery bypass grafting] [Article in Polish] Psychiatr Pol. Sep-Oct 2014;48(5):987-96.
17. Anderson E, Shivakumar G. Effects of exercise and physical activity on anxiety.Front Psychiatry. 2013 Apr 23;4:27.
18. Aquarius AE, Smolderen KG, Hamming JF, De Vries J, Vriens PW, Denollet J. Type D personality and mortality in peripheral arterial disease: a pilot study. Arch Surg. 2009 Aug;144(8):728-33.
19. Smolderen KG, Hoeks SE, Pedersen SS, van Domburg RT, de Liefde II, Poldermans D. Lower-leg symptoms in peripheral arterial disease are associated with anxiety, depression, and anhedonia. Vasc Med. 2009 Nov;14(4):297-304.
20. Bjellad I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002 Feb; 52(2):69-77.
21. Bullinger M, Alonso J, Apolone G, Leplège A, Sullivan M, Wood-Dauphinee S, et al. Translating health status questionnaires and evaluating their quality: the IQOLA Project approach. International Quality of Life Assessment. J Clin Epidemiol. 1998 Nov;51(11):913-23.
22. Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992 Jun;30(6):473-83.
23. Cohen J. Statistical power analysis for the Behavioral Sciences. Diagnostic and statistical manual of mental disorders. 5th ed. PA: American Psychiatric Association. 2003.
24. Brubaker PH, Miller Jr HS, Rehabilitation outcomes: post PCI patient. Coronary artery revascularization. Pollock's textbook of cardiovascular disease and rehabilitation. 1995; 291-292.
25. Stordal E, Mykletun A, Dahl AA. The association between age and depression in the general population: a multivariate examination. Acta Psychiatr Scand. 2003 Feb;107(2):132-41.
26. Carney RM, Rich MW, teVelde A, Saini J, Clark K, Freedland KE. Prevalence of major depressive disorder in patients receiving beta-blocker therapy versus other medications. Am J Med. 1987 Aug;83(2):223-6.
27. Peyrot WJ, Lee SH, Milaneschi Y, Abdellaoui A, Byrne EM, Esko T, et al. The association between lower educational attainment and depression owing to shared genetic effects? Results in ~25,000 subjects. Mol Psychiatry. 2015 Jun;20(6):735-43.
28. Esguerra MD. Phases of Cardiac Rehabilitation. Annual Comprehensive Workshop on Cardiac and Pulmonary Rehabilitation. Philippine Association of Cardiac and Pulmonary Rehabilitation (PACPR).
29. Piccinelli M, Wilkinson G. Gender differences in depression. Critical review. Br J Psychiatry. 2000 Dec; 177:486-92.
30. Bressert, S. Depression Symptoms (Major Depressive Disorder). Psych Central. [Internet]. Available at: https://psychcentral.com/depression/depression-symptoms-major-depressive-disorder#whats-next Retrieved on September 2017.
31. Bulloch AG, Williams JV, Lavorato DH, Patten SB. The relationship between major depression and marital disruption is bidirectional. Depress Anxiety. 2009; 26(12):1172-7.
32. Kessler RC, Berglund P, Demler O, Jin R, Merikangas R, Walters EE. DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005 Jun;62(6):593-602.

Clinical Outcomes and Predictors of In-Hospital Mortality Among Patients with Infective Endocarditis at a Tertiary Referral Center

Emily Mae L. Yap, MD; Ana Beatriz D. Medrano, MD; Raquel Victoria M. Ecarma, MD; Lucky R. Cuenza, MD

Background **---** Infective endocarditis (IE) continues to be a fatal disease if inappropriately diagnosed or managed. This study aims to determine the incidence, clinical features, outcomes and predictors of mortality among those with IE in our institution.

Method **---** This was a cross-sectional analytical study of 283 patients admitted and diagnosed with definite and possible IE based on the modified Duke's criteria from January 1, 2007 to December 31, 2016 at a tertiary referral center.

Results **---** The 10-year prevalence rate of IE was 0.21% with 21 cases for every 10,000 person days. The mean age was 40 ± 16.5 years old with a male predominance (59%). Fever (47%) and dyspnea (36%) were the most common clinical presentation. One half of the patients received empiric antibiotics prior to admission. Blood cultures were negative in 62% of cases. *Streptococcus spp*. was the most common isolated organism. Betalactams as monotherapy or in combination with aminoglycosides were the most common antibiotics given. Acute kidney injury (AKI) (18%), septic shock (15%), and acute heart failure (12%) were the most common major adverse events during hospitalization. The in-hospital mortality rate was 30%. On multivariate analysis, positive blood culture (OR 8.7, 95% CI 1.68-45.26, p=0.010), AKI (OR 5.0, 95% CI 1.04-24.15, p=0.045) and septic shock (OR 2.58, 95% CI 1.33-5.01, p=0.005) were predictors of mortality. Surgical management for an emergent or urgent indication (OR 0.22, 95% CI 0.05-0.90) was a predictor of survival.

Discussion **---** IE continues to be associated with significant morbidity and mortality. Early recognition, identification of patients at risk for complications, and aggressive medical or surgical management are needed to improve survival. ***Phil Heart Center J 2021;24(2):9-15.***

Key Words: ■ Infective endocarditis ■ native valve endocarditis ■ prosthetic valve endocarditis ■ outcome

Infective endocarditis (IE) is defined as a microbial infection of the endocardial surface of the heart which commonly involves one or more valves, mural endocardium damaged by aberrant jets of blood or foreign bodies, or intracardiac devices. Complications may occur at the involved valve or at extra-cardiac locations that can result in serious morbidity and mortality. IE continues to be fatal if left untreated or inappropriately treated. [1-3]

The annual incidence of Infective Endocarditis at the Philippine Heart Center was previously reported to be 10 cases per 10,000 person days, with an equal male to female distribution and a mean age of 30 years.[4] The more widespread availability of diagnostic tests for IE has facilitated earlier recognition of this condition, yet mortality remains high. [4-13]

Limited studies on Infective Endocardities in Southeast Asia, particularly in the Philippines, are largely outdated.[4] As the clinical and microbiologic spectra of IE have evolved, so have the epidemiological trends and mortality rates reported in other countries.[8-13] This study aims to

Finalist, Oral Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Emily Mae L.Yap.*** 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

provide the most comprehensive update on the clinical profile, microbiologic spectra, echocardiographic features, complications and factors associated with in-hospital outcomes and mortality among Filipinos with IE at our institution.

METHODS

A cross-sectional analysis was done at a tertiary referral center, Quezon City, Philippines, on adult patients ≥ 19 years old who were admitted with an adjudicated diagnosis of IE based on the Modified Duke's criteria, [14] either definite (i.e., fulfilling 2 major criteria, or 1 major criterion and 3 minor criteria, or 5 minor criteria) or possible (i.e., fulfilling 1 major criterion and 1 minor criterion), between January 1, 2007 to December 31, 2016. This study was conducted in compliance with the ethical principles set forth in the Declaration of Helsinki. Prior to study initiation, the study protocol was reviewed and approved by the Institutional Ethics Review Board of our institution.

Clinical, demographic, echocardiographic and microbiologic data were extracted from patient medical records. The primary outcome sought to identify the predictors of in-hospital mortality, while secondary outcomes sought to determine the incidence and prevalence rates, echocardiographic features, blood culture results, complications, and clinical outcomes.

Statistical Analysis: Data were encoded in Microsoft Excel 2015 and analyzed in IBM SPSS v13.1. Categorical variables such as demographics, predisposing factors, duration of hospitalization, outcome, management, etiologic agent, echocardiographic features and complications were described using frequency and percentages. Continuous variables were described using mean and standard deviation if normally distributed, or median and absolute range if non-normally distributed. Factors associated with the in-hospital outcome were determined using binary logistic regression analysis. The level of significance was set at 5%.

RESULTS

Table 1 highlights the baseline characteristics, clinical features, in-hospital course, and clinical outcomes of patients presenting with IE at our institution.

Incidence, Prevalence, and Baseline Characteristics of IE: A total of 283 adult patients were identified with a diagnosis of definite or possible IE from 2007-2016. The incidence of IE ranged from 0.14% to 0.29% (*Figure 1*), with a 10-year prevalence of 0.21% (283/137,574) or 21 cases of IE for every 10,000 person days.

The majority of patients with IE involved native heart valves: 168 patients with definite IE and 89 patients with possible IE had native valve endocarditis (NVE), while 20 patients with definite IE and 6 patients with possible IE had prosthetic valve endocarditis (PVE). Sixty percent (n=155) of the patients with NVE were male, with a mean age of 39.1 ± 16.4 years. By contrast, fifty-four percent (n=14) of the patients with PVE were female, with a mean age of 49.7 ± 14.6 years.

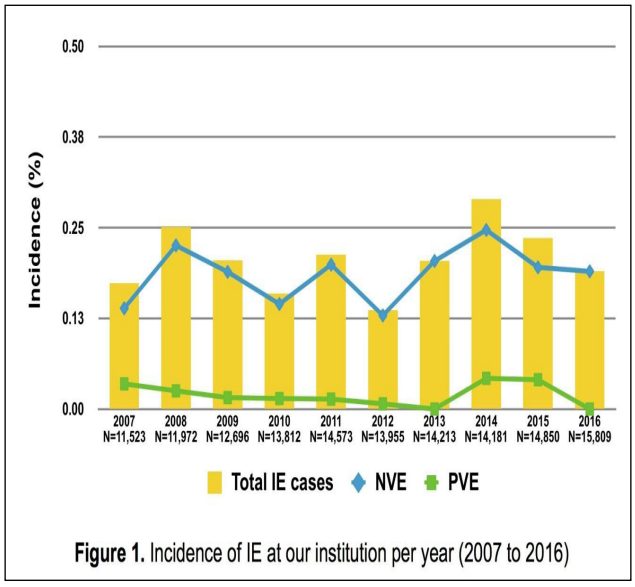

Figure 1. Incidence of IE at our institution per year (2007 to 2016)

Clinical Features and In-hospital Course of IE: Fever (T>38C) was the most common reason for admission (NVE- 44%, PVE- 77%), followed by dyspnea (NVE- 38%, PVE- 12%) and left or right-sided weakness as neurologic manifestations (NVE- 4%, PVE- 8%). The most common predisposing factors leading to NVE in order of prevalence included: 1. rheumatic heart disease (48%, n=124) with multi-valvular involvement (27%, n=70) being more common than single valve lesions (16%, n=42); 2. congenital heart disease (30%, n=78), with patent ductus arteriosus (8.9%, n=23), ventricular septal defect (7.8%, n=20) and bicuspid aortic valve (4.3%, n=11) as the three most common etiologies; and 3. non-rheumatic valvular heart disease (19%, n=50) with mitral valve prolapse notable in 47 cases (18%) and calcific aortic stenosis in 3 cases (1%). Conversely, non-rheumatic valvular heart disease was the most common predisposing condition (50%, n=13) leading to PVE, followed by rheumatic heart disease (31%, n=8).

Forty-nine percent (n=127) of the patients with NVE and 58% (n=15) of patients with PVE had received antibiotics prior to hospitalization. Blood cultures were positive in 36% (n=92) of NVE cases, and in 58% (n=15) of PVE cases. Streptococcus spp. (11%, n=28) were the most common organisms isolated among those with NVE, followed by Cogulase-negative Staphylococcus spp. (CONS) (7%, n=17), Methicillin-Sensitive *Staphylococcus Aureus* (MSSA) (4%, n=11) and gram negative bacilli (4%, n=10). By contrast, among those with PVE, gram negative bacilli were the most common microorganisms isolated (27%, n=7), followed by MSSA (12%, n=3), CONS (8%, n=2) and *Enterococcus spp* (8%, n=2). Betalactams, either as monotherapy (NVE:39%,n=100; PVE: 35%, n=9) or in combination with aminoglycosides (NVE: 38%, n=98; PVE: 35%, n=9), were most commonly used to treat both NVE and PVE.

Infection of a single valve predominated in both sub-groups of IE (NVE: 65%, n=167; PVE: 81%, n=21). In particular, the mitral valve was most frequently affected (NVE: 32%, n=82; PVE: 42%, n=11) followed by the aortic valve (NVE: 26%, n=68; PVE: 31%, n=8). In the majority of cases (NVE: 60%, n=155; PVE: 69%, n=18), the associated vegetations were small measuring <10mm. A small subset of patients with NVE (19%, n=50) or PVE (8%, n=2) had large vegetations >10mm. The mean size of the vegetations associated with NVE was 12.9 ± 8.6mm, whilst that with PVE was 6.0±1.7mm. Six cases (2%) of NVE and 1 case (4%) of PVE were associated with valvular abscesses.

Management and Clinical Outcomes of IE: The median duration of hospitalization was 14 days (range 0-92 days) for NVE, and 17 days (range 1-62 days) for PVE. Most of the patients survived to hospital discharge (NVE: 67%, n=173; PVE: 61%, n=16) while 29% (n=75)of NVE cases and 35% (n=9)of PVE cases died. Seven (3%) patients with NVE went home against medical advice, and 2 (1%) cases of NVE and 1 case (4%) of PVE were transferred to another hospital.

Predictors of Outcome: Table 2 summarizes the adverse events associated with IE at our institution, while Table 3 highlights the predictors of in-hospital mortality. The most common complications associated with both NVE and PVE included AKI (18%, n=51), septic shock (15%, 42), and acute decompensated heart failure (12%, n=33).

On univariate analysis, patients with positive blood culture (OR 1.694, 95% CI 1.005-2.856, p=0.047) and growth of Methicillin-Resistant *Staphylococcus Aureus* (OR 7.192, 95% CI 1.421-36.416, p=0.006) were directly associated with in-hospital mortality. Furthermore, development of acute kidney injury (OR 21.79, 95% CI 8.67-54.76, p <0.001) and acute decompensated heart failure (OR 11.22, 95% CI 2.37-53.15, p=0.002) were also directly associated with mortality during admission.

On multivariate analysis, growth on blood culture (OR 8.71, 95% CI 1.68-45.26, p=0.010), development of septic shock (OR 2.58, 95% CI 1.33-5.01, p=0.005) and acute kidney injury (OR 5.01, 95% CI 1.04-24.15, p=0.045) were significant predictors of mortality. Patients who underwent surgery with an emergent or urgent indication had significantly better survival (OR 0.22, p 0.035).

Table 1. General characteristics of patients with IE at our institution, 2007-2016.

Demographics	NVE f (%) n=257	PVE f (%) n=26	Total f (%) N=283
Total number of cases			
Definite IE	168 (65)	20 (77)	188 (66)
Possible IE	89 (35)	6 (23)	95 (34)
Gender			
Female	102 (40)	14 (54)	116 (41)
Male	155 (60)	12 (46)	167 (59)
Age, years			
Mean ± SD	39.1 ± 16.4	49.7 ± 14.6	40 ± 16.5
Clinical presentation			
Fever	113 (44)	20 (77)	131 (47)
Dyspnea	98 (38)	3 (12)	101 (36)
Neurologic manifestations	11 (4)	2 (8)	13 (5)
Edema	7 (3)	0 (0)	7 (2)
Generalized body weakness	7 (2)	1 (4)	8 (3)
Chest pain	6 (2)	0 (0)	6 (2)
Arthralgia	2 (1)	0 (0)	2 (1)
Duration of hospitalization, days			
Median	14	17	14
Absolute range	0-92	1-62	0-92
Antibiotics given before admission	127 (49)	15 (58)	142 (50)
Blood culture results			
Positive	92 (36)	15 (58)	107 (38)
Negative	165 (64)	11 (42)	176 (62)
Management			
Medical	183 (71)	22 (85)	205 (72)
Emergent or urgent surgery	17 (7)	1 (4)	18 (6)
Elective surgery	48 (19)	3 (11)	51 (18)
Refused surgery	9 (3)	0 (0)	9 (3)
Outcome			
Improved	173 (67)	16 (61)	189 (67)
Died	75 (29)	9 (35)	84 (30)
Home against medical advice	7 (3)	0 (0)	7 (2)
Transferred	2 (1)	1 (4)	3 (1)

Table 2. Major adverse in-hospital events of patients with IE, 2007-2016.

Complications	NVE f (%) n=257	PVE f (%) n=26	Total f (%) N=283
Acute kidney injury	42 (16)	9 (35)	51 (18)
Septic shock	36 (14)	6 (23)	42 (15)
Acute decompensated heart failure	30 (12)	3 (12)	33 (12)
Stroke	25 (10)	3 (12)	28 (10)
Arrhythmias	20 (8)	2 (8)	22 (8)
Seizures	12 (5)	2 (8)	14 (5)
Acute limb ischemia	3 (1)	0 (0)	3 (1)
Cardiac abscess	6 (2)	1 (4)	7 (2)
Cardiac tamponade	1 (0)	0 (0)	1 (0)
Pulmonary thromboembolism	1 (0)	0 (0)	1 (0)
Brain abscess	1 (0)	0 (0)	1 (0)

Table 3. Univariate and multivariate analysis.

Predictor	Crude OR (95% CI)	p-value
Positive blood culture (>2)	1.694 (1.005-2.856)	0.047
Methicillin-Resistant Staphylococcus aureus	7.192 (1.421-36.416)	0.006
Stroke	3.41 (1.32-8.82)	0.011
Acute kidney injury	21.79 (8.67-54.76)	<0.001
Acute decompensated heart failure	11.22 (2.37-53.15)	0.002
Surgical management	0.151 (0.053-0.435)	<0.001
Predictor	**Adjusted OR (95% CI)**	**p-value**
Positive blood culture (>2)	8.71 (1.68-45.26)	0.010
Septic shock	2.58 (1.33-5.01)	0.005
Septic shock	5.01 (1.04-24.15)	0.045
Surgical management	0.22 (0.05-0.90)	0.035

DISCUSSION

Our study provides a comprehensive and contemporary description of the clinical profile of Filipinos diagnosed with IE, in addition to identifying the key predictors of in-hospital mortality among those who were admitted with IE. The incidence of IE in our institution has doubled in the past decade from 10 to 21 cases per 10,000 person days.[4] The authors ascribe this to early recognition of the disease and the more widely available diagnostic tests. Ninety-one percent of our patients had NVE. As expected, there were lesser cases of PVE (9%, n=26), similar to the rates shown in the study by Krecki et al.[5] Significantly higher rates of PVE ranging from 16% to 44% were reported in other studies. [6-11] The lower incidence of NVE in these latter studies could be attributed to better outcomes in their patients with NVE, resulting in a relative increase in PVE.[6-11]

The mean age of patients in our study was 40 ± 16.5 years, which is comparable to that in the study by Ibrahim et al.[12] Younger mean ages, ranging from 27.5 to 34.6 years, were reported by other studies.[8-9,13] Studies done in Asia[9,12,13] reported rheumatic heart disease as the most common predisposing factor, explaining the younger age of the patients with IE. On the other hand, studies from Europe and South America reported more cases of degenerative valvular disease and prosthetic valve involvement, which could explain the disparity in the age at the time of IE in these latter instances.[5,7]

Fever was the most common presentation (47%, n=131) associated with IE.[7-12] This was followed by dyspnea (36%, n=101),[8] often accompanying patients who presented with acute decompensated heart failure on admission. Other studies reported constitutional symptoms such as anorexia and weight loss to be more common.[7, 10]

Our results showed more culture-negative IE cases (62%) similar to studies in India[8] and Pakistan.[13] The practice of administration of empiric antibiotics prior to obtaining blood cultures could be a plausible explanation in our setting. Conversely, studies in Western countries have higher blood culture positive rates reflective of their good clinical practices and compliance to the guidelines.[6-7] The presence of positive blood cultures on ≥ 2 samples (OR 1.69, p 0.047) and growth of community-acquired or hospital-acquired Methicillin-Resistant *Staphylococcus Aureus* (MRSA) (OR 7.19, p 0.006) sensitive to Vancomycin, were significant univariate predictors of mortality. In addition, the former was also a multivariate predictor of mortality (OR 8.71, p 0.010). Positive blood cultures despite antibiotics was reflective of inadequate antibiotic coverage given prior to admission in our cohort. While previous studies suggested that positive blood cultures may be a harbinger of virulence, sepsis and adverse outcomes,[15] some studies have implied that culture negative IE cases have similar and equivalent prevalence and outcomes to culture positive IE.[16] Given the availability of antimicrobial susceptibility testing, culture guided antibiotics given at the soonest possible time should be part of general practice.[17]

Studies done in different countries reported similar complications, but with varying frequency.[9-13,18-19] The most commonly reported major in-hospital adverse event in our study was acute kidney injury (AKI) (18%, n=51) similar to the complications reported by Tariq et al [13] and Sherpa et al[19] AKI was a significant univariate (OR 21.79, p <0.001) and multivariate (OR 5.01, p 0.045) predictor of mortality in our study. While etiologies of AKI were not reported in most studies, we surmise that in our study, this was possibly due to the development of other complications such as prolonged hypotension among those who developed septic shock (15%, n=42), acute decompensated heart failure (12%, n=33) with cardiorenal implications, and the use of nephrotoxic agents such as the glycopeptide Vancomycin and aminoglycoside Gentamicin. A sizeable number of our patients developed stroke (10%, n=28), which was due to peripheral embolization, and arrhythmias (8%, 22) in the form of varying degrees of atrioventricular block and atrial fibrillation. These extracardiac complications were reported in other studies as well.[8, 10, 12]

Septic shock, a common complication of IE, developed in 15% of our patients (n=42). This was a significant multivariate predictor of mortality in our study (OR 2.58, p 0.005). This underscores the need for more aggressive measures among patients presenting with sepsis to avert the development of septic shock. In addition to obtaining blood cultures prior to administration of empiric antibiotics appropriate for IE, the use of the latest Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock could improve survival.[20]

The in-hospital mortality of IE remains high despite advancements made in the diagnostic and therapeutic approach to IE. We reported a rate of 30% similar to studies done in India[8] Brazil[10] Turkey[11] and Malaysia[12] ranging from 29 to 35%. Acute decompensated heart failure developed in 33 patients (12%); this was a significant univariate predictor of mortality (OR 11.22, p 0.002) herein. Most of these patients required emergency and urgent valvular surgery. Surgical management of IE was a significant predictor of survival in both univariate and multivariate analysis in our study. Therefore, it is important to emphasize adherence to class I indications for surgery among those with heart failure, uncontrolled infection and large vegetations as published in the guidelines.[17]

Our study was conducted in only one center, which may limit generalizability. The retrospective nature is an inherent limitation since completeness of data cannot be ascertained. A multicenter prospective study with long term follow-up is suggested by the authors to describe the course of the disease as well as to determine short and long-term outcomes. Local guidelines can then be formulated to further improve mortality outcomes of this devastating disease.

The strength of our study lies in its sample size collected over a period of 10 years, which to the best of our knowledge, is the largest reported single center study on IE in the Southeast Asia. It adds to our knowledge regarding the clinical characteristics, microbiologic spectra, echocardiographic features and factors that affect in-hospital outcomes; these accrued data can guide clinicians in management and prognosis.

CONCLUSION

IE continues to be associated with significant morbidity and mortality. The results of this study underscore the need for early recognition, to identify patients who are at high risk of complications, as well as for more aggressive medical and surgical management to improve outcomes.

DISCLOSURE

The authors have no conflict of interest in conducting this study.

REFERENCES

1. Brusch J. Infective Endocarditis: Practice Essentials, Background, Pathophysiology [Internet]. Emedicine. medscape.com. 2016 [cited 2 July 2016]. Available from: http://emedicine.medscape.com/article/216650-overview.
2. Karchmer AW. Infective endocarditis. Harrison's principles of internal medicine. 19th ed. McGraw-Hill; 2015:816-827.
3. Baddour L, Freeman W, Suri R and Wilson W. Infective endocarditis. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 10th ed. WB Saunders Co; 2015:1524-1543.
4. Pasaporte BB. and Pena AC. Association of Infective Endocarditis with age: a 21 years experience. Phil J Microbial Infect Dis 2002; 31(1):17-26.
5. Krecki R, Drozdz J, Ibata G, Lipiec P, Ostrowski S, Kasprzak J, et al. Clinical profile, prognosis and treatment of patients with infective endocarditis--a 14-year follow-up study. Pol Arch Med Wewn. 2007 Nov-Dec;117(11-12):512-20.
6. Hoen B, Alla F, Selton-Suty C, Béguinot I, Bouvet A, Briançon S et al. Changing profile of infective endocarditis: results of a 1-year survey in France. JAMA. 2002;288(1):75-81.
7. Ferreiros E, Nacinovich F, Casabé JH, Modenesi JC, Swieszkowski S, Cortes C, et al. Epidemiologic, clinical, and microbiologic profile of infective endocarditis in Argentina: a national survey. The Endocarditis Infecciosa en la República Argentina-2 (EIRA-2) Study. Am Heart J. 2006 Feb;151(2):545-52.
8. Jain SR, Prajapati JS, Phasalkar MA, Roy BH, Jayram AA, Shah SR, et al. Clinical spectrum of infective

endocarditis in a tertiary care centre in western India: a prospective study. Int J Clin Med. 2014;05(05):177-187.
9. Assiri AS. Clinical and microbiological profiles of infective endocarditis in a tertiary hospital in Aseer region, Saudi Arabia. J Saudi Heart Assoc. 2011 Oct;23(4):207-11.
10. Nunes MCP, Gelape CL, Ferrari TCA. Profile of infective endocarditis at a tertiary care center in Brazil during a seven-year period: prognostic factors and in-hospital outcome. Int J Infect Dis. 2010 May;14(5):e394-8.
11. Erbay AR, Erbay A, Canga A, Keshin G, Sen N, Atak R, Demir AD, et al. Risk factors for in-hospital mortality in infective endocarditis: five years' experience at a tertiary care hospital in Turkey. J Heart Valve Dis. 2010 Mar;19(2):216-24.
12. Ibrahim KS, Ismail JR, Yusol Y, Yuhana Y, Saman MAS, Khir NR, et al. Pattern and predictors of outcomes for infective endocarditis in North Kuala Lumpur. Heart India. 2017;5(1):12-16.
13. Tariq M, Siddiqui BK, Jadoon A, Alam M, Khan SA, Atiq M, et al. Clinical profile and outcome of Infective Endocarditis at the Aga Khan University Hospital. Int J Collaborative Research on Int Med Public Health. 2009;1(3):84-99.
14. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis. 2000 Apr;30(4):633-8.
15. Phua J, Ngerng W, See K, Tay C, Kiong T, Lim H, et al. Characteristics and outcomes of culture-negative versus culture-positive severe sepsis. Crit Care. 2013 Sep 12;17(5):R202.
16. Ferrera C, Villacosta I, Fernández C, López J, Olmos C, Sarriá C, et al. Reassessment of blood culture-negative endocarditis: its profile is similar to that of blood culture-positive endocarditis. Rev Esp Cardiol (Engl Ed). 2012 Oct;65(10):891-900. [Article in English, Spanish]
17. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015 Nov 21; 36 (44): 3075-3128.
18. Iqbal MA, Fahim M, Ikramullah, Khan N, Hafizullah M. In-hospital outcome of patients with Infective Endocarditis: a retrospective analysis. Khyber Med Univ J. 2015; 7(3):120-123.
19. Sherpa K, Shah P, Khati Y, Jha SK, Sharma SK, Karki P. Clinical Profile and Outcome of Infective Endocarditis Patients Admitted in a Tertiary Care Center in Eastern Part of Nepal. J Inst Med. 2016 Aug-Dec; 38:2-3.
20. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving sepsis campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017 Mar;43(3):304-377.

Subjective Global Assessment as a Tool in Predicting Outcomes of Valve Surgeries in Tertiary Cardiovascular Center

Alma Cristina A. Andin-Salcedo, MD; Chito Permejo, MD; Samuel Andin, MD; James Ho, MD

Background --- Preoperative nutrition status remains to be a less identified risk factor for postoperative adverse outcomes in cardiac valve surgeries. SGA represents an overall concept of nutritional status. This study aims to determine the association of SGA scores and outcome of valve surgery patients.

Methods --- This is a prospective cohort study done in 112 patients with valvular heart disease admitted for valve repair or replacement. Evaluation of nutritional status was done using the 'Modified Subjective Global Assessment Form' tool. Charts were reviewed for postoperative complications (i.e. infection, re-intubation, and organ failure), and length of hospital stay. The 30-day vital status were determined via phone call.

Results --- Most valve patients were middle-aged males (48.3 ± 14.92 years old), with normal BMI (22.88 ± 3.72 kg/m^2). Etiology wise there was more non-rheumatic than rheumatic (52% vs 48%) subjected for valve surgery. There was significant difference in the BMI (p 0.007) and albumin levels (p <0.001) of patients from the malnourished (MN) than in the nourished (N) group. Most patients in the N group underwent single valve repair/replacement compared with the MN group (47.46% vs 16.98%). Post-operative complications (OR 8.27, p <0.001), length of ICU stay (OR 2.05, p <0.001), length of hospital stay (OR 1.14, p 0.001), and the 30-day all-cause mortality (OR 6.63, p <0.018) were higher in the MN group. The rheumatic etiology had longer ICU stay compared with the non-rheumatic etiology (OR 1.21, p 0.032).

Conclusion --- The SGA scoring is a simple and effective tool in assessing the nutritional status of patients who will undergo valve surgery. This tool can predict adverse post-operative outcomes, longer ICU and hospital stay, and 30-day mortality in malnourished patients. ***Phil Heart Center J 2021;24(2):16-22.***

Key Words: ■valve surgery ■SGA ■post-operative outcome ■nutrition

Cardiac valve surgery accounts for 30 to 40% of thoracic cardiovascular surgery procedures in Philippine Heart Center annually. In the age of public awareness, well-allocated and capable diagnostic clinics at district level, and financial access to health care through goverment assistance, there has been a steady increase in surgery referrals for both rheumatic and non-rheumatic etiologies. Inspite of guideline directed approach in identifying indications for valve procedures, we have observed a higher in-hospital complications and/or mortality compared to other cardiac surgeries.

There have been identified preoperative clinical characteristics that independently increased the risk of morbidity and mortality in patients receiving valve surgery such as age, renal failure, multi-valve procedure, previous cardiac operation(s), pulmonary hypertension, salvage status and peripheral vascular disease.[1] Preoperative nutrition status on the other hand remains to be a less identified risk factor for postoperative adverse outcomes in cardiac valve surgeries. The body mass index (BMI) as a parameter for malnutrition had been used in studies and showed that lower body mass index was a significant independent predictor for both in-hospital and long-term mortality in after valve surgery.[2-3] Hence, patients with malnutrition must be considered a high-risk population that warrants careful risk stratification to opt for preoperative build-up strategies, or even consider less invasive valve therapies.

Winner, Poster Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Alma Cristina A. Andin-Salcedo.*** 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

Subjective Global Assessment, or SGA, represents an overall concept of nutritional status and is the only screening tool that recommended by the American Society for Parenteral and Enteral Nutrition (ASPEN) and Philippine Society for Parenteral and Enteral Nutrition (PhilSPEN).[4,15] It is simple, economical, internet-available and well-validated. It only needs bedside history and physical examination assessment, and yet has been found to be highly predictive of nutrition-associated complications.[5,15] SGA in literatures has shown to be substantially predictive of outcomes in association with mechanical ventilation, cancer, cancer surgery and palliation in advanced cancer, chronic kidney disease and dialysis, liver transplantation, geriatric care, radiotherapy, and stroke.[6-14] There are no reports on the use of SGA for malnutrition screening and evaluated its usefulness in predicting post operative outcomes following cardiac valve surgery.

METHODS

The study was conducted in compliance with the ethical principles set forth in the Declaration of Helsinki, and was reviewed and approved by the Philippine Heart Center Institutional Ethics Review Board (PHC-IERB). A written informed consent was obtained after adequate explanation of the aims, methods and anticipated benefits of the study.

The study was done from May 2017 to January 2018. The population included all adult cardiology patients >19 years old, with diagnosis of valvular heart disease admitted for valve repair or replacement. Inclusion criteria were patients with rheumatic or non-rheumatic heart disease, undergoing any valve (mitral, aortic, tricuspid, pulmonic) replacement using mechanical or bioprosthetic valve, or repair, alone, multiple or in combination with CABG. Exclusion criteria were patients who need to undergo emergency/salvage procedures, who had active infective endocarditis, or other debilitating co-morbidities such as chronic lung disease, liver failure and chronic renal failure. Sample size calculation was done using Stata SE version 13, the minimum sample size requirement is at least 112, based on the percentage of complication in the well-nourished and malnourished groups: 23% and 48% respectively[17] with alpha level 5% and power 80%.

All adult valve patients for surgery were screened for eligibility. Patient interview and chart review were facilitated to acquire important demographic and clinical information. Evaluation of nutritional status were done using the 'Modified Subjective Global Assessment Form' tool. The patients were classified initially as SGA A (weight gain, no change or mild weight loss); SGA B (moderate weight loss); and SGA C (severe weight loss). These classifications were then divided into 2 groups as 'nourished' (SGA A), or 'malnourished' (SGA B or C). The patients' charts were reviewed after valve surgery to follow-up their outcomes in terms of post-operative complications (i.e. infection, reintubation, and organ failure), and length of hospital stay. The 30-day vital status were determined via phone call. The study maneuver as written above was done solely by the primary investigator.

The dependent or outcome variables are divided as to the (1) postoperative complications [18] (i.e. infection, re-intubation or prolonged extubation (>42 hours), and organ failure), (2) length of hospital stay, and (3) post-operative mortality. Infection was defined as respiratory tract infection, urinary tract infection, mediastin'tis, surgical site infection. Organ failure is defined as acute kidney injury, neurologic failure, hepatic failure, hematopoietic failure or bleeding. Length of hospital stay was the duration in days from the date of the index surgery to the date of discharge. The post-operative mortality (30days) was death due to any cause within 30 days of index surgery.

Statistical data analysis was performed in Stata SE version 13. Quantitative variables were summarized as mean and standard deviation, while qualitative variables as frequency and percentage. Comparison of characteristics between well-nourished (SGA A) and malnourished (SGA B and C) were done using the independent exact test for qualitative variables. Association between SGA and outcomes was done using logistic regression analysis. Associations between post-operative outcomes and rheumatic and non-rheumatic etiologies was analyzed using logistic regression

analysis. The level of significance was set at 5%.

RESULTS

During the 9 months period between May 2017 to January 2018, 123 patients indicated for valve surgery were screened for eligibility. Nine patients were excluded due to active infective endocarditis, emergency procedure, COPD in exacerbation, renal failure, and STEMI. The data of 114 patients were collected, however 2 patients were lost to follow-up 30 days after surgery. The data of remainder 112 patients were analyzed. (*Figure 1*)

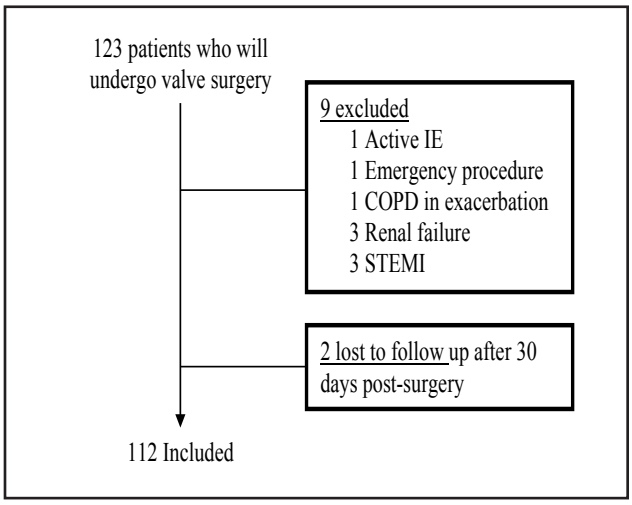

Figure 1: Flow of data collection

The baseline characteristics summarized in Table 1 show that most valve patients were middle-aged (48.30 ± 14.92), where 53.57% were males and 46.43% were females. Majority had normal BMI (60.71%) while the rest constituted the overweight (23.21%) and severely malnourished (16.07%). There was slightly more non-rheumatic (58%) than rheumatic (54%) in etiology. Among the valve patients, atrial fibrillation (40.18%), hypertension (33. 04%), and coronary artery disease (24.11%) were the most frequent comorbidities. The pre-operative laboratory and ancillaries revealed that all had normal TLC, and majority still had adequate eGFR, normal albumin and pre-served ejection fraction. Multiple valve repair/ replacement (47.32%) was the most indicated operative procedure, followed by single valve repair/ replacement (33.04%), and least was

Table 1. Baseline characteristics (n=112)

Characteristics	Frequency (%); Mean + SD
Age	48.30 + 14.92
Sex	
Male	60 (53.57)
Female	52 (46.43)
Medical history	
BMI	22.88 + 3.72
Normal	68 (60.71)
Overweight	26 (23.21)
Severely malnourished	18 (16.07)
Comorbidity	
Hypertension	37 (33.04)
Diabetes mellitus	15 (13.39)
Atrial fibrillation	45 (40.18)
Coronary artery disease	27 (24.11)
Chronic infective endocarditis	1 (0.89)
Congenital heart disease	14 (12.50)
Atrial septal defect	6 (42.86)
Bicuspid aortic valve	7 (50)
Pulmonary stenosis	1 (7.14)
Etiology	
Rheumatic heart disease	54 (48.21)
Other non-Rheumatic heart disease	58 (51.79)
Laboratory and ancillaries	
Total leukocyte count	8,074.82 + 2,688.65
Serum albumin	35.43 + 6.50
eGFR (CKD-EPI)	85.16 + 26.28
EF Simpsons (2DE)	57.59 + 12.49
Operative procedure	
Single-valve repair/ replacement	37 (33.04)
Multiple valve repair/ replacement	53 (47.32)
Combination valve + CABG	22 (19.64)

Notes: BMI- Body Mass Index; eGFR- estimated Glomerular Filtration Rate; Normal BMI 18.5-25 kg/m^2; overweight BMI 25.1-30 kg/m^2; severely malnourished BMI <18.5 or>30 kg/m^2

the combination of valve surgery with CABG (19.64%).

The comparison on clinical characteristics based of modified SGA score is summarized in Table 2. Among the study samples, 53% comprised the nourished (N) group with SGA A, while 47% comprised the malnourished (MN) group with SGA B&C.

Most in the MN group were older male patients although not statistically significant. There was significant difference in the BMI of patients from the MN group classified as "severely malnourished" compared with those from the N group where BMI was classified as "normal and overweight" (p 0.007). The serum albumin in the N group was also significantly higher compared with the MN group (p <0.001). Also, most patients in the N group significantly underwent only single valve repair/replacement compared with the MN group (p 0.001).

Conversely, no differences between the N and MN groups were observed in terms of comorbidities, etiology, laboratory tests such as total leukocyte count, eGFR and ejection fraction, and indication for multiple valve and combination of valve + CABG procedures.

The association between SGA score and post-operative outcomes showed positive correlation as shown in Table 3. There were 8.27 times more complications in the MN group than in the N group in terms of occurrence of infection, prolonged extubation or re-intubation, bleeding, organ failure and mortality immediately post-surgery (p<0.001).

The most common cause of infection was pneumonia. There

Table 2. Comparison of Clinical Characteristics Based on Nutritional Status by Modified SGA Score (n=112)

Variables	Nourished (n=59)	Malnourished (n=53)	P-value
	Frequency (%); Mean + SD		
Age	46.19 ± 14.37	50.66 ± 15.31	0.114
Sex			0.322
Male	29 (49.15)	31 (58.49)	
Female	30 (50.85)	22 (41.51)	
Medical history			
BMI	23.77 ± 3.21	21.88 ± 4.01	**0.007**
Normal	41 (69.49)	27 (50.94)	**0.016**
Overweight	14 (23.73)	12 (22.64)	
Severely malnourished	4 (6.78)	14 (26.42)	
Comorbidity			
Hypertension	18 (30.51)	19 (35.85)	0.549
Diabetes mellitus	6 (10.17)	9 (16.98)	0.291
Atrial fibrillation	23 (38.98)	22 (41.51)	0.785
Coronary artery disease	10 (16.95)	17 (32.08)	0.062
Chronic infective endocarditis	0	1 (1.87)	-
Congenital heart disease	6 (10.17)	8 (15.09)	0.431
Atrial septal defect	2 (33.33)	4 (50)	0.767
Bicuspid aortic valve	3 (50)	4 (50)	
Pulmonary stenosis	1 (16.67)	0	
Etiology			
Rheumatic heart disease	26 (44.07)	28 (52.83)	0.354
Other non-Rheumatic heart disease	33 (55.93)	25 (47.17)	
Laboratory and ancillaries			
Total leukocyte count	8,185.59 ± 2,341.05	7,951.51 ± 3,0347	0.648
Serum albumin	38.43 ± 4.61	32.08 ± 6.69	**<0.001**
eGFR (CKD-EPI)	89.71 ± 22.79	80.10 ± 29.07	0.053
EF Simpsons (2DE)	59.75 ± 11.41	55.19 ± 13.30	0.054
Operative procedure			
Single-valve repair/ replacement	28 (47.46)	9 (16.98)	**0.001**
Multiple valve repair/ replacement	23 (38.98)	30 (56.60)	0.062
Combination valve + CABG	8 (13.56)	14 (26.42)	0.087

was 3.88 times more risk for organ failure (p 0.016) in the MN group, with acute kidney injury being the most common cause. There was 8.83 times risk of mortality immediately post-surgery (p 0.045), with cardiac dysrhythmia related to right or left ventricular failure as the most common cause. The length of ICU stay (OR 2.05, p <0.001), length of hospital stay (OR 1.14, p 0.001), as well as the 30-day all-cause mortality (OR 6.63, p 0.018), were also significantly higher in the MN group.

Table 4 summarizes the association between the valve etiology and post-operative outcomes. The rheumatic etiology significantly had 1.21 times risk of longer ICU stay compared with the non-rheumatic etiology (p 0.032). However rheumatic and non-rheumatic etiologies were not discriminated in terms of post-operative complications, length of hospital stay and 30-day all-cause mortality.

Table 3. Association between SGA scores and post-operative outcomes

Variables	Malnourished (n=53)	Nourished (n=59)	Crude Odds ratio	95% CI	P-value
	Frequency (%); Median (IQR)				
Post-operative complications	40 (75.47)	16 (27.12)	8.27	3.54 to 19.33	<0.001
Infection	36 (67.92)	14 (23.73)	6.81	2.96 to 15.64	<0.001
Re-/prolonged intubation	15 (28.30)	0	-	-	-
Bleeding	6 (11.32)	0	-	-	-
Organ Failure	14 (26.42)	5 (8.47)	3.88	1.29 to 11.66	0.016
Post-operative mortality	7 (13.21)	1 (1.69)	8.83	1.05 to 74.32	0.045
Length of ICU stay	4 (2 to 6)	2 (2 to 3)	2.05	1.37 to 3.06	<0.001
Length of hospital stay	12 (9 to 21)	7 (6 to 10)	1.14	1.06 to 1.23	0.001
30-day mortality	10 (18.87)	2 (3.39)	6.63	1.38 to 1.12	0.018

Table 4. Association post-operative outcomes of and rheumatic and non-rheumatic etiologies

Variables	Rheumatic (n=54)	Non-Rheumatic (n=58)	Crude Odds ratio	95% CI	P-value
	Frequency (%); Median (IQR)				
Post-operative complications	26 (48.15)	30 (51.72)	0.87	0.41 to 1.82	0.705
Infection	24 (44.44)	26 (44.83)	0.98	0.47 to 2.08	0.967
Re-/prolonged intubation	9 (16.67)	6 (10.34)	1.73	0.57 to 5.25	0.330
Bleeding	4 (7.41)	2 (3.45)	2.24	0.39 to 12.76	0.364
Organ Failure	7 (12.96)	12 (20.69)	0.57	0.21 to 1.53	0.280
Post-operative mortality	4 (7.41)	4 (6.90)	1.08	0.26 to 4.55	0.916
Length of ICU stay	3 (2 to 4)	2 (2 to 3)	1.21	1.02 to 1.45	0.032
Length of hospital stay	10 (7 to 14)	9 (6 to 12)	1.03	0.98 to 1.07	0.275
30-day mortality	5 (9.26)	7 (12.07)	0.74	0.22 to 2.50	0.632

DISCUSSION

In our study, there were more patients with SGA score of A (nourished) than those with SGA score of B and C (malnourished). The lesser proportion of malnourished valve patients who underwent surgery was not reflective of the overall malnourished population who have valvular heart disease. The clinician's decision to optimize the nutritional status and delay elective surgery in severely malnourished patient may had been a factor, hence lesser malnourished patients were included in this study.

Those in the malnourished group had severely abnormal BMI <18.5 kg/m^2. This chronic and progressive weight loss or wasting syndrome termed as cardiac cachexia has affected valve patients leading to neuroendocrine, inflammatory and metabolic disturbances.[19] The BMI as a parameter for malnutrition in our study was consistent with other studies reflecting that lower body mass index was a significant independent predictor for both in-hospital and long-term mortality in after valve surgery.[2-3]

The SGA scores which were simplified as the nourished (SGA A) and malnourished (SGA B and C) were significantly associated with post-operative complications, length of ICU and hospital stay, immediate post-operative mortality and mortality after 30 days. This result is consistent with other studies which were substantially predictive of outcomes in association with other procedures and diseases such as in mechanical ventilation, cancer, cancer surgery and palliation in advanced cancer, chronic kidney disease and dialysis, liver transplantation, geriatric care, radiotherapy, and stroke.[6-14]

The limitation of the study however are the interrelated factors that may affect surgical outcomes such as the total bypass time and aortic cross-clamp time which was associated with post-operative complications and mortality.[20]

In all, this study implicates that valve patients with malnutrition must be considered to be a high-risk population that warrants careful risk stratification to opt for preoperative build-up strategies, or even consider less-invasive valve therapies.

CONCLUSION

The SGA scoring is a simple and effective tool in assessing the nutritional status of patients who will undergo valve surgery. This tool can predict adverse post-operative outcomes, longer ICU and hospital stay, and 30-day mortality in malnourished patients.

REFERENCES

1. Edwards FH, Peterson ED, Coombs LP, DeLong ER, Jamieson WR, Shroyer ALW, Grover FL. Prediction of operative mortality after valve replacement surgery. J Am Coll Cardiol. 2001 Mar 1;37(3):885-92.
2. Vaduganathan M, Beckham AJ, Andrei AC, Lapin B, Stone NJ, McGee EC, et al. Relation of body mass index to late survival after valvular heart surgery. Am J Cardiol . 2012 Dec 1;110(11):1667-78.
3. Thourani VH, Keeling WB, Kilgo PD, Puskas JD, Lattouf OM, Chen EP, et al. The impact of body mass in dex on morbidity and short- and long-term mortality in cardiac valvular surgery. J Thorac Cardiovasc Surg. 2011 Nov;142(5):1052-61.
4. ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN J Parenter Enteral Nutr. Jan-Feb 2002;26(1 Suppl):1SA-138SA.
5. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA, et al. What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr. Jan-Feb 1987;11(1):8-13.
6. Sheean PM, Peterson SJ, Gurka DP, Braunschweig CA. Nutrition assessment: the reproducibility of subjective global assessment in patients requiring mechanical ventilation. Eur J Clin Nutr. 2010 Nov;64(11):1358-64.
7. de Mutser R, Grootendorst DC, Boeschoten EW, Brandts H, van Manen JG, Netherlands Cooperative Study on the Adequacy of Dialysis-2 Study Group. Subjective global assessment of nutritional status is strongly associated with mortality in chronic dialysis patients. Am J Clin Nutr . 2009 Mar;89(3):787-93.
8. Shirodkar M, Mohandas KM. Subjective global assessment: a simple and reliable screening tool for malnutrition among Indians. Indian J Gastroenterol. Nov-Dec 2005;24(6):246-50.
9. Persson C, Sjödén PO, Glimelius B. The Swedish version of the patient-generated subjective global assessment of nutritional status: gastrointestinal vs urological cancers. Clin Nutr. 1999 Apr;18(2):71-7.
10. Thoresen L, Fjeldstad I, Krogstad K, Kaasa S, Falkmer UG Nutritional status of patients with advanced cancer: the value of using the subjective global assessment of nutritional status as a screening tool. Palliat Med. 2002 Jan;16(1):33-42.

11. Stephenson GR, Moretti EW, El-Moalem H, Clavien PA, Tuttle-Newhall JE. Malnutrition in liver transplant patients: preoperative subjective global assessment is predictive of outcome after liver transplantation. Transplantation. 2001 Aug 27;72(4):666-70.
12. Sacks GS, Dearman K, Replogle WH, Cora VL, Meeks M, Canada T. Use of subjective global assessment to identify nutrition-associated complications and death in geriatric long-term care facility residents. J Am Coll Nutr. 2000 Oct;19(5):570-7.
13. Isenring E, Bauer J, Capra S. The scored Patient-generated Subjective Global Assessment (PG-SGA) and its association with quality of life in ambulatory patients receiving radiotherapy. Eur J Clin Nutr. 2003 Feb;57(2):305-9.
14. Davis JP, Wong AA, Schulter PJ, Henderson RD, O'Sullivan JD, Read SJ. Impact of premorbid undernutrition on outcome in stroke patients. Stroke 2004;35:1930-5.
15. Navarette DR. The results of the validation process of a Modified SGA (Subjective Global Assessment) Nutrition Assessment and Risk Level Tool designed by the Clinical Nutrition Service of St. Luke's Medical Center, a tertiary care hospital in the Philippines.
16. Beghetto MG, Luft VC, Mello ED, Polanczyk CA. Accuracy of nutritional assessment tools for predicting adverse hospital outcomes. Nutr Hosp. 2009 Jan 1;24(1):56-62.
17. Warnold I, Lundholm K. Clinical significance of preoperative nutritional status in 215 noncancer patients. Annals of surgery. 1984 Mar;199(3):299-305.
18. van Venrooij LM, de Vos R, Borgmeijer-Hoelen MM, Haaring C, de Mol BA. Preoperative unintended weight loss and low body mass index in relation to complications and length of stay after cardiac surgery. Am J Clin Nutr. 2008 Jun;87(6):1656-61
18. von Haehling S, Doehner W, Anker SD. Nutrition, metabolism, and the complex pathophysiology of cachexia in chronic heart failure. Cardiovasc Res. 2007 Jan 15;73(2):298-309.
20. Salsano A, Giacobbe DR, Sportelli E, Olivieri GM, Natali R, Prevosto M, Del Bono V, Viscoli C, Santini F. Aortic cross-clamp time and cardiopulmonary bypass time: prognostic implications in patients operated on for infective endocarditis. Interact Cardiovasc Thorac Surg. 2018 Sep 1;27(3):328-335.

Correlation of Chest Radiograph Tracheal Index with Severity of Chronic Obstructive Pulmonary Disease

Ernesto C. Udaundo, Jr., MD; Omohaire T. Dilangalen, MD; Sarah Victoria L. Zampaga, MD

Background **---** Chest radiographs, spirometry and computed tomography scan are mainstay in the evaluation of patients with pulmonary disease. Patients with chronic obstructive pulmonary disease develops saber sheath trachea due to repetitive cartilaginous injury from excessive coughing and elevated intrathoracic pressure causing degeneration and ossification of the tracheal cartilage.[6] This study is done to determine the correlation of chest radiograph tracheal index (coronal tracheal diameter/sagittal tracheal diameter) with COPD severity using the GOLD staging system.

Method **---** One hundred and two patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD) wherein spirometry and, posteroanterior and lateral chest radiograph were done within six months of each other were included in the study. GOLD staging system using spirometry and tracheal index using chest radiographs were determined.

Results **---** There is low correlation between chest radiograph tracheal index and COPD severity (r=-0.1074).

Conclusion **---** Among patients with COPD, there is very low correlation of chest radiograph tracheal index and severity of COPD, hence, this index obtained by chest radiograph may not be useful in assessing for severity of COPD. ***Phil Heart Center J 2021;24(2):23-28.***

Key Words: ■ Tracheal index ■ GOLD staging system ■ Saber-sheath trachea ■ Chronic Obstructive Pulmonary Disease) ■ PA (posteroanterior) and Lat (Lateral) chest radiograph ■ Spirometry

Chronic obstructive pulmonary disease ranks 7th among the top 10 leading cause of death in the Philippines,[1] and projected to climb to be the third leading cause of death by the year 2030.[2] According to the data gathered by the Global Adult Tobacco Survey (GATS), the prevalence of cigarette smoking in the Philippines was estimated at 28% or around 17.3 million Filipino adults.[1] Only 2% of COPD cases in the Philippines are diagnosed by physicians,[3-4] and thus, the available data on the true prevalence of COPD in the country remain sunderdiagnosed/underestimated. COPD has been defined as a "persistent, largely irreversible airway obstruction in which the underlying pathophysiology is not precisely well known" or "a chronic, slowly progressive airway obstructive disorder resulting from some combination of pulmonary emphysema and irreversible reduction in the caliber of small airways in the lungs".[5]

Besides the clinical findings in COPD, several diagnostic modalities are available to the clinicians to aid in the diagnosis of COPD, this includes spirometry, plain upright chest radiograph and computed tomography. Spirometry remains the gold standard for diagnosing and functional classification of COPD. Tracheal index is the coronal to sagittal ratio of the segment of trachea 1 cm above the aortic arch (normal value of >2/3). Saber-sheath trachea (tracheal index or coronal to sagittal ratio < 2/3) has long been associated with COPD and is postulated to be due to repetitive cartilaginous injury from excessive coughing and elevated intrathoracic pressure causing degeneration and ossification of the tracheal cartilage.[6] Chronic remodeling of the trachea in COPD leads to alteration of the tracheal morphology. Saber-

Finalist, Poster Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Ernesto C. Udaundo, Jr.*** Division of Cardiovascular Radiological Sciences. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

sheath trachea was observed to be a specific diagnostic parameter for the diagnosis of COPD (specificity, 92.9%), although sensitivity (39.1%) was low.[7] Tracheal index has also been correlated with functional residual capacity and was concluded to be a sign of hyperinflation in COPD. [8]

The current statistical data on prevalence of COPD remains underdiagnosed and underestimated, hence the need for a quick and confident assessment via chest radiograph is an asset not only in determining severity of COPD but to rule out alternative diagnosis. This study aims to provide clinicians of alternative index to gauge the severity of COPD at its presentation and identifying those who are at risk of having future exacerbations.

The general objective of this study is to determine the correlation of chest radiograph tracheal index with COPD severity using the GOLD staging system. While its specific objectives was to determine tracheal index among COPD patients; determine the severity of COPD among the patients in the study using the GOLD staging system and to correlate tracheal index with COPD severity using the GOLD staging system.

METHODS

This is a cross-sectional study conducted at the Philippine Heart Center during the period of January 2014 to March 2018. Included in the study were adult Filipinos diagnosed with age 40 years old and above, either inpatient or outpatient, who were classified according to GOLD staging for COPD severity and has undergone a satisfactory digital chest x-ray in PA and lateral view done in our institution taken within the six months as the pulmonary function test were included in the study.

Excluded in the study were patients with distorted tracheal morphology secondary to causes besides COPD (i.e intrathoracic superior mediastinal mass or neoplasm, thoracic aortic aneurysm, congenital tracheobronchial anomalies, connective tissue diseases etc), on mechanical ventilation, unable to tolerate upright chest x-ray, with inherent contraindications to radiation exposure (i.e pregnant) and with moderate to severe thoracic cage deformities (e.g. scoliosis, gibbus deformity, pectus excavatum, straight back syndrome)

Sample Size Calculation: Using EPI Info version 7, the minimum sample size requirement is determined to be at least 92 based on prevalence of saber-sheath trachea among COPD patients = 40% (Gupta et al)[9] with confidence level of 95% and margin of error of 10%.

Description of Data Collection: The chest radiographs and pulmonary function test results of patients 40 years old and above, diagnosed with COPD January 2014 to September 2017 will be utilized.

Inter-Observer Variability: Intra/interobserver variability for the radiographic measurements of the tracheal index will be calculated using kappa test.

Chest Radiograph: Shimadzu sonial vision will be used this study. Images will be done with potential difference of 84 kV, current of 4 mAs, exposure time of 6.3 msec at 72 inches SID (source to image distance). Patients will be placed in the postero-anterior and left lateral view, and instructed to hold their breath after maximal inspiration.

Pulmonary Function Test: Pulmonary function test results will be gathered at the pulmonary laboratory. The FEV1/FVC ratio will be used to determine the presence of irreversible airway obstruction in patients with COPD and FEV1 will be used to determine COPD severity based on GOLD staging system.

Descriptive Outcome: The results of this study will determine the prevalence of saber-sheath trachea in COPD patients and among different stages by GOLD criteria.

Data Handling: The collected data will be encoded using Microsoft Excel 2016. All data will be entered as values suitable for statistical analysis. The generated excel file will be checked for completeness, consistency and accuracy. Results obtained from the processed data will be presented appropriately as tables, graphs and figures.

Identification of Study Variables:

i. Independent/Exposure

Tracheal index obtained from digital chest radiograph (tracheal coronal and sagittal diameters measured approximately 1 cm above the aortic arch).

ii. Dependent/Outcome

GOLD staging system for COPD severity

iii. Probable Confounders

Demographics (i.e. age, sex, asthma, smoking and PTB history)

Statistical Analysis: Data analysis was performed in STATA SE version 13. Quantitative variables were summarized as mean and standard deviation, while qualitative variables were tabulated as frequency and percentage. Intra/interobserver variability for the radiographic measurements of the tracheal index were analyzed using dependent t-test. Spearman correlation between saber-sheath trachea and COPD severity were determined using Spearman rank correlation. A p-value ≤ 0.05 was considered statistically significant.

Ethical Considerations: The study was conducted in compliance with the ethical principles set forth in the Declaration of Helsinki. Prior to the study invitation, the protocol shall be reviewed and approved by the Philippine Heart Center Institutional Ethics Review Board (PHC'IERB). The investigator requested for the waiver of informed consent for the following reasons: difficulty of obtaining individual authorization since the last contact with research subjects.

The risk to the subject's privacy was minimal and no sensitive information were obtained. The investigator ensured that the subjects' anonymity is maintained. Data was obtained from by review of the PFT record from the Department of Pulmonary Medicine and Critical Care and chest radiographs was reviewed from the Cardiovascular Radiological Sciences Division. Patient's data were dealt with utmost confidentiality.

RESULTS

A total of 102 patients were included in this study. Table 1 shows the demographic characteristics of the patient's included in this study. Measurement of tracheal indices were done by 2 radiologists with no significant inter-observer variability (*Table 2 and 3*). There is good agreement between measurements of the coronal and sagittal tracheal diameters by both radiologists using the dependent *t*-test.

Table 1. Demographic Characteristics of Patients in the Study

	Frequency (%); Mean ± SD
Age	66.31 + 10.49
Sex	
Male	94 (92.16)
Female	8 (7.84)
Co-morbidities	
Asthma	8 (7.84)
PTB	9 (8.82)
Hypertension	76 (74.51)
Diabetes Mellitus	33 (32.35)
Smoking	68 (66.67)
Severity of COPD	
Stage I (Mild)	17 (16.67)
Stage II (Moderate)	55 (53.92)
Stage III (Severe)	27 (26.47)
Stage IV (Very Severe)	3 (2.94)

Table 2. Correlation of Tracheal Index with COPD severity (n=102)

Correlation coefficient	Level of association	P-Value
-0.1074	Low correlation	0.2826

Table 3. Inter-Observer Variability Between Radiologist A and Radiologist B

Correlation coefficient	Mean difference	95% Confidence Interval	Range	P-value
Coronal Diameter	0.016	-0.001 to 0.032	-0.148 to 0.179	0.492
Sagittal Diameter	0.005	-0.009 to 0.019	-0.140 to 0.149	0.720
Tracheal Index	0.006	-0.003 to 0.014	-0.080 to 0.092	0.943

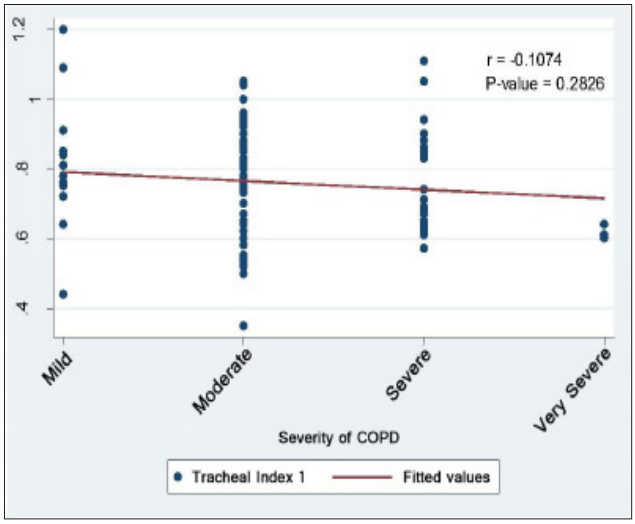

Figure 1. The study showed that there is low correlation of chest radiograph tracheal index and COPD severity (r = -0.1074).

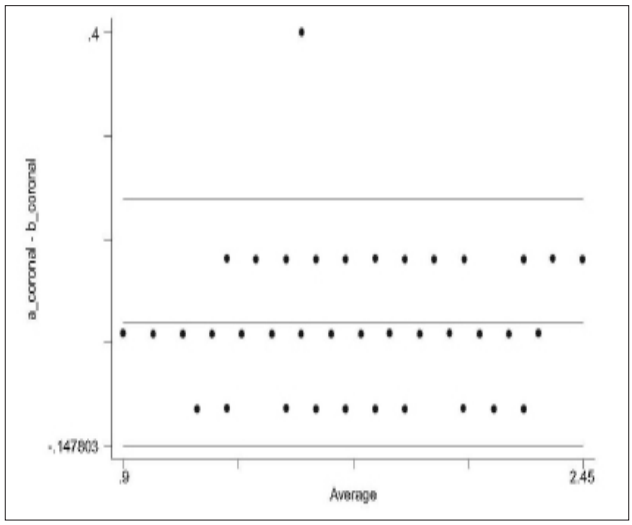

Figure 2. Coronal diameter agreement between 1st Radiologist and 2nd Radiologist

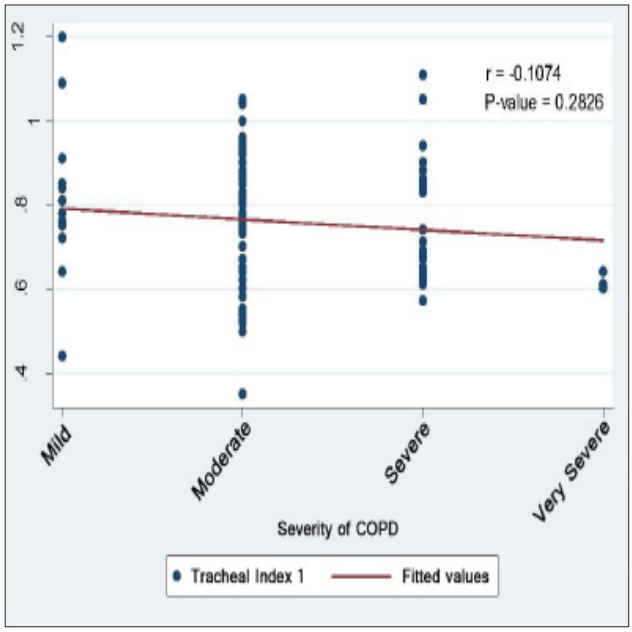

Figure 3. Sagittal Diameter Agreement between 1st Radiologist and 2nd Radiologist

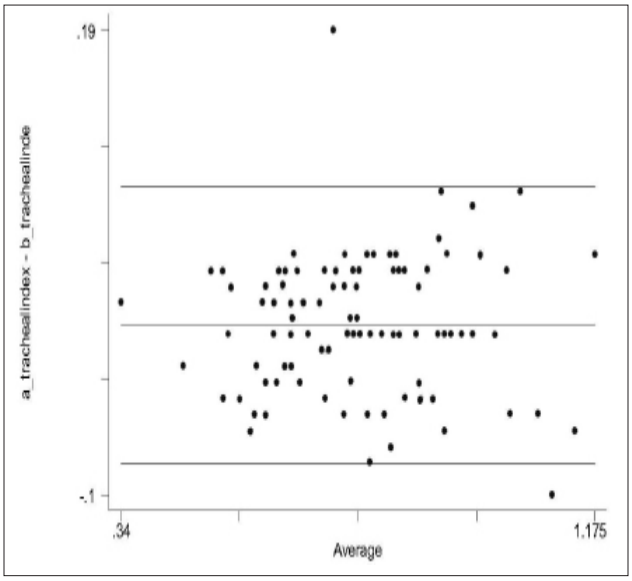

Figure 4. Tracheal Index Agreement between 1st Radiologist and 2nd Radiologist

DISCUSSION

Patients with chronic obstructive pulmonary disease overtime develops narrowing of the coronal tracheal diameter and widening of the sagittal tracheal diameter, the so called "saber-sheath trachea (Tracheal index = <2/3)". Chronic remodeling of the trachea in COPD leads to alteration of the tracheal morphology postulated to be due to repetitive cartilaginous injury from excessive coughing and elevated intrathoracic pressure causing degeneration and ossification of the tracheal cartilage.[6] The present study has shown a low correlation between chest radiograph tracheal index and COPD severity.

Although a previous study showed lower tracheal indices among COPD patients in comparison to a control group even in the early stages/lower severity of COPD.[10] The present study yielded different results. A possible explanation for this is that changes in the tracheal morphology are dependent on whether a particular chest radiograph was taken on maximal inspiration (which is the usual practice on our institution) or on maximal expiration. These differences in tracheal cross-sectional area was observed among healthy volunteers with no history of smoking exhibiting mean cross-sectional area decrease on expiration at the upper (54.34% ± 18.6) and lower trachea (56.14% ± 19.3).[11] Although it was thought that decrease in the tracheal indices can be seen even early stages of COPD, the extent to which it is decreased does not satisfy the criteria for saber-sheath trachea.

Saber-sheath trachea, despite its low correlation to COPD severity, remains as a specific diagnostic parameter for the diagnosis of COPD (specificity, 92.9%), although sensitivity (39.1%) was low.[7]

RECOMMENDATION

It is recommended that subsequent studies explore the possibility of conducting a prospective study by performing inspiratory and expiratory examinations on COPD patients utilizing the modalities available at our institution (Chest radiography and Computed Tomography). Baseline and follow-up chest radiograph on both anteroposterior and lateral views are suggested as a routine examination on COPD patients to monitor tracheal morphological changes.

CONCLUSION

Among patients with COPD, there is a low correlation (Spearman correlation coefficient = -0.1074) between chest radiograph tracheal index and COPD severity.

ACKNOWLEDGEMENT

The author would like to thank, first and foremost, Dr. Carolina Abesamis-Drilon and Dr. Sarah Victoria L. Zampaga for their guidance throughout the conduction of this research. Gratitude is also extended to Dr. Omohaire Dilangalen of the Pulmonary Medicine Division, Department of Education, Training and Research, Institutional Ethics Review Board of the Philippine Heart Center and the residents/consultants of the Cardiovascular Radiological Sciences Division for their tireless effort and contributions.

REFERENCES

1. Philippines GA. Philippines' Global Adult Tobacco Survey: Country Report. 2009.
2. Pauwels R. Global initiative for chronic obstructive lung diseases (GOLD): time to act. Eur Respir J. 2001 Dec;18(6):901-2.
3. Idolor LF, De Guia TS, Francisco NA, Roa CC, Ayuyao FG, Tady CZ, et al. Burden of obstructive lung disease in a rural setting in the Philippines. Respirology. 2011 Oct;16(7):1111-8.

4. Buist AS, McBurnie MA, Vollmer WM, Gillespie S, Burney P, Manninno DM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet. 2007 Sep 1;370(9589):741-50.
5. Muller N, Fraser R, Colman N, Pare PD Radiologic diagnosis of diseases of the chest. c2001.
6. Tunsupon P, Dhillon SS, Harris K, Alraiyes AH. Saber-sheath trachea in a patient with severe COPD. BMJ Case Rep. 2016 Feb 24;2016:bcr2016214648.
7. Tsao TC, Shieh WB. Intrathoracic tracheal dimensions and shape changes in chronic obstructive pulmonary disease. J Formos Med Assoc. 1994 Jan;93(1):30-4.
8. Trigaux JP, Hermes G, Dubois P, Van Beers B, Delaunios L, Jamart J. CT of saber-sheath trachea. Correlation with clinical, chest radiographic and functional findings. Acta Radiol. 1994 May;35(3):247-50.
9. Yadav R, Verma M, Agarwal D, Kumar M. Correlation between high-resolution computed tomography features and patients' characteristics in chronic obstructive pulmonary disease. Ann Thorac Med. 2008 Jul;3(3):87-93.
10. Eom JS, Lee G, Lee HY, Oh JY, Woo SY, Jeon KThe relationships between tracheal index and lung volume parameters in mild-to-moderate COPD. Eur J Radiol. 2013 Dec;82(12):e867-72.
11. O'Donnell CR, Bankier AA, Ernst A, Millet ME, Potemkin A, Loring SH. Tracheal collapsibility in healthy volunteers during forced expiration: assessment with multidetector CT Radiology. 2009 Jul;252(1):255-62.

Comparison of Clinical Outcome of Transcatheter Closure of Ventricular Septal Defect Using Antegrade and Retrograde Approaches

Babie Catherine R. Causapin, MD; Jean Antonio Villareal, MD; Juan Reganion, MD; Juliet J. Balderas, MD

Background --- Transcatheter device closure became a trending treatment for ventricular septal defect (VSD) for perimembranous and muscular type with satisfactory results and low morbidity rates. In most centers, the procedure is performed using antegrade method or transvenous approach. In adult patients, recent studies of transcatheter VSD closure via retrograde or transarterial approach had been successful; however in pediatric patients this kind of approach have insufficient data available. This study aims to compare the clinical outcome of transcatheter device closure of ventricular septal defect using antegrade and retrograde approaches among patients of our institution from January 2013 to July 2018.

Methods --- To compare the outcomes of two approaches, we retrospectively evaluated early and mid-term results of device closure for VSD in 72 patients divided into 2 groups (A and B) composed, respectively, of 37 patients (antegrade) and 35 patients (retrograde).

Results --- Procedure time between groups with group A 39.2 ± 13.8 min and with Group B 27.3 ± 10.8min ($p<0.0001$) were found to be significant. There is a significant difference in clinical outcome between the groups with number of complications in Group A is 10 (83.33%) and in Group B is 2 (16.6%). Antegrade patients were more likely to have complications compare to retrograde patients with a p-value of 0.027. Embolization of the device was the early adverse events observed on both groups. Data from mid-term follow-up showed that, in antegrade group, new-onset valvular insufficiency and residual shunts were more frequent.

Conclusion --- Both therapeutic approaches for transcatheter device closure of VSD were immediately safe and effective but retrograde approach is less likely to have complication compared to antegrade procedure. Patients must be accurately selected before choosing VSD device closure approach; operator skills and experience still have a large impact on success rate for this procedure. ***Phil Heart Center J 2021;24 (2):29-40.***

Key Words: Ventricular septal defect ■ VSD device closure ■ retrograde approach ■ antegrade approach

Ventricular septal defect (VSD) is the most common type of congenital heart abnormality approximately 40% of congenital heart defects.[1] Perimembranous VSD, which is the most common and involves the membranous septum and the adjacent portion of the muscular septum, accounts for about 70% of cases.[2] In 1856, Dushane and Kirklin at Mayo Clinic perform the first successful closure of VSD using cardiopulmonary bypass.[3] Open-heart surgery is considered safe and effective treatment for VSD, however it still carries risks, such as complete atrioventricular block, residual shunt, postpericardiotomy syndrome, and wound infection, etc.[1]

In 1988, the first report of catheter-based approach of VSD has been shown to be an alternative to surgical closure with acceptable mortality and morbidity.[4-11] Transcatheter closure of VSD has become an acceptable alternative to surgical closure of muscular, traumatic, and postoperative residual and post infarct VSDs. However, transcatheter closure of perimembranous VSD is controversial due to unacceptably high rate of post-procedural and late-onset heart block accounting for 1% up to 22%. Recent reports on this treatment for perimembranous VSD have been limited to small series with insufficient follow-up. One study done by

2st place, Oral Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Babie Catherine R. Causapin.*** 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

Butera et al.[8] which percutaneous closure of both muscular and perimembranous VSDs were done on 140 patients whom concluded that it is safe but in young children with perimembrabous VSD occurrence of complete AV block is a major concern. Yang et al.[2] concluded that safety and successful outcome with low morbidity and mortality of transcatheter perimembranous VSD still depends on the operator skill and experience.

Their study also had a favourable long-term result and concluded that transcatheter approach provides a less-invasive alternative that may become the first choice in selected patients.

In a local study done by Valdez, B. et al, comparison of the clinical outcome and cost of transcatheter device occlusion and surgical closure of isolated ventricular septal defect among 62 patients (surgical = 31 and device = 31) was done. This study supported the continued use of transcatheter occlusion as a treatment of isolated VSD in terms of procedural cost-effectiveness against surgical procedure ($p<0.001$).[12] In a large institutional study on outcomes and complications after transcatheter closure of a perimembranous-type ventricular septal defect in 890 cases in Taiwan by Jun Liu, et al, the incidence of serious complication was 1.12% (10/890), including third-degree atrioventricular block, severe tricuspid valve regurgitation, cerebral infarction in the basal ganglia area, and femoral artery thrombosis. There were no reported deaths and they concluded that transcatheter closure of perimembranous VSDs in selected patients was effective and safe.[2]

Transcatheter closure of perimembranous and muscular VSDs are still widely used in many center with a low mortality and morbidity rate; regardless of its approval status in the US and many countries in Europe. In other Asian countries, many children are waiting to be treated; and which transcatheter approach is attractive for patients, family and physicians, particularly with soft indication for closure. The advantage of avoiding cardiopulmonary bypass, reducing the psychological impact, pain are some the positive points for choosing transcatheter approach rather than the surgical option. Due to the complexity and proximity of the septal defect to adjacent structures, especially aortic valves; closure of this defect percutaneously is challenging. Many types of device have tried to close this defect with varied results.

Evolving technology in the interventional techniques has now made the transcatheter closure of anatomically selected ventricular septal defects feasible with satisfactory results and low morbidity rates.[10] In most centers, the procedure is approached using antegrade or transvenous method by creating an arteriovenous guide wire loop, which is the standard technique for transcatheter VSD device closure. Some studies have described that retrograde method and transarterial approach cannot be performed due to technical difficulties, mostly in adult patients. Recent studies of using variety of Amplatzer occluder devices had been successful with retrograde technique in adolescents and children with congenital VSD. Retrograde technique involves fewer steps and possesses the potential to significantly reduce fluoroscopy and total procedure time in comparison with the conventional methods. In a case series of Pekel et al. presented their experience of the transcatheter VSD closure using transarterial retrograde approach and concluded that it simplifies the procedure, decreases the radiation exposure, and shortens the procedure time.[13] After a thorough literature search, no local study on transcatheter device closure of VSD comparing the two techniques was published.

Early in this institution, most patients with ventricular septal defect that undergo transcatheter technique still use the conventional method (transvenous antegrade approach). Only ten years ago, transcatheter closure using implantable devices has been introduced and is recently gaining popularity. When explaining the therapeutic options to the patients or the parents with VSD, outcome goals and complications or adverse events should be fully discussed. Since transcatheter device closure of VSD is an evolving technology, data on effectiveness, cost and mid-term outcome comparing these two techniques in transcathether closure of ventricular septal defect are currently lacking; hence this research was formulated.

OBJECTIVES

The general objective is to compare the clinical outcome of transcatheter device closure of ventricular septal defect using antegrade and retrograde approaches among patients of this institution. While its specific objectives are: (1) to compare clinical characteristics of patients underwent antegrade and retrograde group; (2) to compare procedural data of patients underwent antegrade and retrograde group; (3) to determine clinical outcome of antegrade technique on VSD closure; and (4) to determine clinical outcome of retrograde technique on VSD closure.

METHODS

Patients: From January 2013 to July 2018, we retrospectively collected data on 81 patients who underwent transcatheter device closure of VSD at our institution. Seventy-two of these 72 subjects were diagnosed with isolated VSD that underwent transcatheter closure. Patients were assessed by the standard transthoracic echocardiographic protocol. The study was conducted in compliance with the ethical principle set forth in the Declaration of Helsinki. The study was also reviewed and approved by the Institutional Ethics Review Board (IERB).

Sample Size Calculation: Sample size computed for this study was n = 72 at 95% confidence level, maximum tolerable error of 5% and assumed prevalence of 31 cases who underwent transcatheter closure of VSDs among children in the paper of Valdez et al.[12]

Inclusion and exclusion criteria: The criteria for inclusion in this study were:

1. Age > 1 year old and weight > 7kg
2. Pre and post-procedure Transthoracic Echocardiography done at our institution
3. Pre and post-procedure chest radiography and 15 Lead ECG done at our institution
4. Fulfill all the echocardiography criteria:
   a. Presence of ventricular septal defect in 2 different views
   b. Defect diameter on the left ventricular side < 12mm
   c. Aortic rim > 5mm
   d. No significant aortic valve prolapsed nor regurgitation

The criteria for exclusion in this study were:

1. Pelvic vein or inferior vena cava thrombosis
2. Other cardiac anomaly that require surgical or transcatheter intervention
3. Patients who have pulmonary vascular resistance >8woods unit

Subjects were labeled into 2 groups: those who underwent transcatheter VSD closure using antegrade or arteriovenous (AV) loop and retrograde or transarterial approach.

Occluder Devices - Two local brands of device are available in our institution: Lifetech Scientific and Cocoon. The availability of the devices at operation day will be the main factor in the choice of devices.

Procedures - Percutaneous closure of a VSD is performed under general anesthesia with sedation. Patients are given heparin 100 IU/kg, hydrocortisone 5mg/kg and antibiotic intravenously. The procedure is performed under fluoroscopic control. Procedures for apical VSD (*Figure 1*) using antegrade technique; and perimembranous VSD (*Figure 2*) using retrograde technique have been previously reported in detailed.[13,14]

Study Maneuver

a. A retrospective review of the charts of all pediatric patients who underwent transcatheter device closure of VSD from January 2014 to July 2018 was done. Data were extracted from Medical Records of the hospital; and patients were identified by discharge diagnosis from the CV laboratory databases. Patients who underwent transcatheter VSD closure were grouped according to the approach used during the procedure.

b. Charts were reviewed and the following information were obtained:

i. Demographic Information
1. Age of the patient
2. Gender
3. Weight
4. Modified Ross Classification

Modified Ross Heart Failure Classification in Children	
I	Asymptomatic
II	Mild tachypnea or diaphoresis with feeding in infants Dyspnea on exertion in older children
III	Marked tachypnea or diaphoresis with feeding in infants Marked dyspnea on exertion Prolonged feeding times with growth failure
IV	Symptoms such as tachypnea, retractions, grunting, or diaphoresis at rest

ii. Electrocardiographic Data
1. Heart rate
2. PR interval
3. Rhythm
4. ST-T wave (normal, elevation, depression)

iii. Echocardiographic Data
1. Maximum diameter Ventricular septal defect (mm)
2. Presence of Left Ventricular enlargement
3. Presence of Left Atrial enlargement
4. Pulmonary artery pressure (mmHg)

iv. Procedural Data
1. Fluoroscopy time
2. Procedure time
3. Mean pulmonary artery pressure (mmHg)
4. VSD size (mm)
5. Device used

c. Charts were reviewed for the outcome.
1. Principal Efficacy

i. Acute procedure success: the number of patients where the two techniques were attempted, those who successfully close the ventricular septal defect.

ii. Pre-discharge efficacy (24-hrs efficacy): complete closure at pre-discharge (maximum 24 hours)

iii. Hospital stay

iv. Follow-up Periods:
1. 2D echo follow-up (complete closure of VSD)
a. 1-month efficacy: complete closure at 1-month follow- up
b. 3-month efficacy: complete closure at 3-month follow-up
2. Principal Safety
i. Serious adverse event: any event causing death
ii. Major adverse event: any event causing organ failure or dysfunction (e.g. stroke emboli) or any damage to other structure inside the heart, device embolization required surgical removal, and
iii. Minor adverse event: device embolization required percutaneous removal, mild to moderate regurgitation of the valve (especially tricuspid and aorta) related to the procedures, hemolysis, hematoma of the groin, loss of peripheral pulse, cardiac arrhythmia requiring cardioversion or medication during procedures, blood loss required transfusion and residual shunt.
iv. Any adverse event: any event not classified above.

Follow-up Period **-** The follow-up variables includes clinical examination; electrocardiography and echocardiography at 1 month and 3-month follow up.

Data Analysis **-** We used SPSS 16.0 for Windows (SPSS, Inc., Chicago, IL, USA) for the statistical analysis. The quantitative variables were summarized and presented as mean and standard deviation, while qualitative variables will be tabulated and presented as frequency and percent distribution.

Homogeneity of characteristics between the 2 groups was tested using the t-test for the quantitative variables and Fisher's exact test for qualitative variables. Comparison of outcome between the 2 groups was determined and tested using independent *T*-test for the fluoroscopic time, procedure time and length of hospital stay while Fisher's exact test for specific outcomes. A p-value less that or equal to 0.05 was considered significant. Furthermore, logistic regression analysis was used to compare the two techniques of transcatheter VSD closure in terms of developing at least 1 complication.

RESULTS

A total of 81 patients who underwent successful transcatheter closure of VSD were reviewed in our institution. Based on the inclusion criteria only 72 patients (88.9%) were included in this study. There were 37 whom underwent antergrade or transvenous (Group A) approach (*Fig. 1)* and 35 whom underwent retrograde or transarterial (Group B) approach (*Fig. 2)*. The mean age of patient in Group A was 9.89 years ± 4.68 and in Group B was 12.03 years ± 5.03; which was not statistically significant. There were 37 male

and 35 female patients. The weight and height of the patients between the two groups were statistically significant (p-value 0.001 and <0.001); Group A had 25% with z-score of -2 (wasted and stunted) while Group B had 100% with z-score of -1 to 0 (normal). In this study, group B had higher body surface area (BSA) at 1.19 ± 0.37 compared with group A with BSA of 1.00 ± 0.39 (p-value 0.041). Functional Class using Modified Ross Classification was not significant with p-value 0.061. Diagnostic data such as types and sizes of VSD as well as presence of LA enlargement and pulmonary arterial hypertension were not significant for both groups with p-values above 0.05. The most common VSD type for both groups was the perimembranous type with 28 (77%) patients in Group A and 33 (94%) patients in Group B. Twenty-seven (72.97%) of patients from Group A manifested with LV enlargement compared with Group B with 11 (31.43%); which was statistically significant (p-value 0.000). Significant shunting (QpQs ratio) was also observed more with Group A (1-1.6:1) compared with Group B (1-1.2:1). Electrocardiograhic data such as PR interval and rhythm were not statistically significant (p-values >0.05). Heart rate of Group B (74.37 + 13.9) was noted to be lower in comparison with Group A (84 ± 14.85) with p-value of 0.004. Demographic and diagnostic data are summarized in Table 1.

The median fluoroscopic time was 21.3 minutes (13.43–27.3 minutes) in Group A and 15.34 minutes (10.87–24.07 minutes) in Group B; which was not significant (p-value 0.086). The mean procedure time was 38.6 minutes (26.9 – 45.6 minutes) in Group A and 25.7 minutes (18.6–33.7 minutes) in Group B;which was significant (p-value 0.000). Most of the pulmonary arterial (PA) pressure measured were normal for both groups and was not significant (p-value 0.079). According to ventriculography, the median measured of VSD size for Group A was 0.6cm (0.4–1.5cm) and Group B was 0.4cm (0.3–0.5cm), which was significant (p-value 0.001). There were several device occluders used during the study period with Lifetech Multifunctional occluder (MFO) (Group A 2, 5.41% and Group B 35,100%) as the majority device used. Procedural data was summarized in Table 2.

The median follow-up was 24 months (4 – 55.3 months). Acute procedure success was not significant. Antegrade technique had 100% success rate while retrograde technique had 97% success rate (34 out of 35). This case was a 6-year-old male diagnosed case of VSD perimembranous who had embolization and was retrieved percutaneously. His technique was converted to antegrade approach and was successfully occluded. Pre-discharge complete closure was seen in 27 (73%) patients for Group A and 8% of residual shunts diminished 3 months after the intervention. In comparison with Group B, immediate closure was seen in 27 (77%) patients and all residual shunts diminished 3 months after the intervention. Comparison of immediate or pre-discharged complete closure of the defect was not significant (p value 0.683). The median hospital stay for both group were at 3 days (Group A, 3-4days and Group, B 3-3days). Most of the patients on Group A had stayed more than 3 days while Group B patients had stayed 3 days at the hospital. Comparison of hospital stay between two groups was significant at p value of <0.001. In our study, residual shunt was considered with a presence of left-to-right shunt across the interventricular septum on color Doppler flow mapping. On a 3-month follow-up, it was noted that 89%n (33 out of 37 cases) on Group A had residual shunts while Group B had 100% complete closure; which was significant (p-value 0.012). Comparison of principal efficacy for both groups was summarized in Table 3.

In pre-procedure echocardiography, there were 53% of patients with left ventricular (LV) enlargement and 40% with left atrial (LA) enlargement. Noted a significant improvement (p-value <0.001) with chamber sizes post-transcatheter closure of VSD (*Table 4*). Two patients whom still with LV enlargement still had residual shunt after transcatheter closure via antegrade approach.

A total of 12 adverse events (16.7%) were reported in patients who underwent VSD device closure. No serious and major adverse events were observed in this study. In Group A, 10 minor adverse events were observed: Device embolization (n = 1), new or increased valve regurgitation (n = 3), hematoma of the groin (n = 1), cardiac

arrhythmia (n = 1); and residual shunt (n = 4). In Group B, 2 minor adverse events were observed: embolization and cardiac arrhythmia. Complications were summarized in Table 5. Odds ratio was used and showed that patients in Group A had 6.11 times more likely to have complication compared to Group B. (*Table 6*).

Figure 1. Antegrade or transvenous closure of perimembranous VSD. (a) Left ventriculography showed a perimembranous VSD tubular type, the shunt jet is long and the diameter in both sides of the septum is the same. (b) Terumo exchange wire is snared in the pulmonary artery or SVC and exteriorized out of the femoral vein to establish an arteriovenous guidewire circuit.(c) Ventriculography before the release of the occluder (Lifetech Multifunctional Occluder (MFO) size 10mm/8mm) was done showing a total occlusion of the defect. (d) Still image showing the occluder in place after the release.

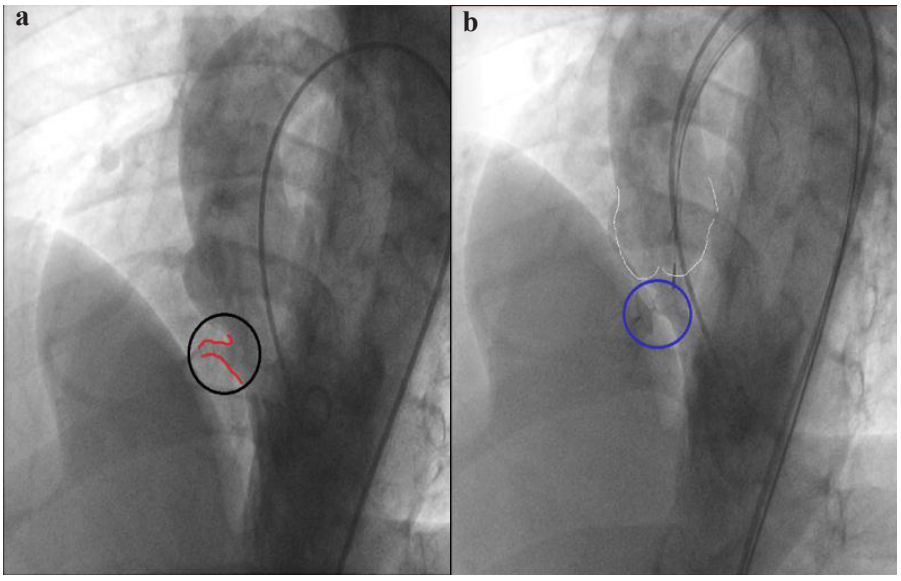

Figure 2. Retrograde or transarterial closure of perimembranous VSD. (a) Left ventriculography showed a perimembranous VSD conical type, the shunt jet is wide on the LV side of the septum and narrow on the RV side. (b) Ventriculography before the release of the occluder with the delivery cable on the arterial side (femoral artery – descending aorta – ascending aorta – LV) was done showing a total occlusion of the defect.

Table 1. Baseline demographic and diagnostic of the patients underwent transcatheter procedure according to technique used.

	Antegrade (n=37)	Retrograde (n=35)	P-Value
	Frequency (%); Median (IQR)	Mean ± SD;	
Demographic Profile			
Age	9.89 ± 4.68	12.03 ± 5.03	0.066
Sex Male Female	 22 (59.46) 15 (40.54)	 18 (51.43) 17 (48.57)	0.493
Weight z-score	 -1 (-2 to 0)	 0 (-1 to 0)	**0.001**
Height z-score	 -1 (-2 to 0)	 0 (0 to 0)	**<0.001**
BSA	1.00 ± 0.39	1.19 ± 0.37	**0.041**
Modified Ross Functional Class I II	 31 (83.78) 6 (16.22)	 33 (97.06) 1 (2.94)	0.061
Echocardiographic Parameters			
VSD, type Muscular Perimembranous Apical Multiple	 7 (18.92) 28 (75.68) 1 (2.70) 1 (2.70)	 2 (5.71) 33 (94.29) 0 (0) 0 (0)	0.051
VSD Size cm	0.5 (0.40 to 0.70)	0.45 (0.38 to 0.50)	0.062
LV enlargement Yes	 17 (45.95)	 12 (34.29)	0.313
PA Pressure Normal Mild Moderate Severe	 30 (81.08) 2 (5.41) 4 (10.81) 1 (2.70)	 33 (94.29) 2 (5.71) 0 (0) 0(0)	0.165
QpQs Ratio	1.2:1 (1 to 1.6:1)	1:1 (1 to 1.2:1)	**0.002**
Electrocardiographic Parameters			
HR	84 ± 14.85	74.37 ± 13.9	**0.004**
PR interval	0.12 ± 0.02	0.12 ± 0.02	0.723
Rhythm Sinus Abnormal	 36 (97.30) 1 (2.70)	 35 (100) 0 (0)	0.959

Table 2. Procedural Data

	Antegrade (n=37)	Retrograde (n=35)	P-Value
	Frequency (%); Mean + SD; Median (IQR)		
Fluoroscopic time (min)	21.3 (13.43 to 27.3)	12.03 ± 5.03	0.086
Procedure time (min)	38.6 (26.9 to 45.6)	25.7 (18.6 to 33.7)	**<0.001**
VSD Size cm	0.6 (0.4 to 1.5)	0.4 (0.3 to 0.5)	**0.001**
PA Pressure			
Normal	32 (86.49)	35 (100)	**0.079**
Mild	4 (10.81)	0 (0)	
Moderate	1 (2.70)	0 (0)	
VSD Device Size cm	0.6 (0.6 to 1.8)	0.6 (0.5 to 0.8)	**0.123**
Device Occluder Used			
PDA ductal			
Lifetech	2 (5.41)	0 (0)	
Cocoon	1 (2.70)	0 (0)	
VSD symmetrical			<0.001
Lifetech	18 (48.65)	0 (0)	
Cocoon	5 (13.51)	0 (0)	
VSD muscular			
Lifetech	9 (24.32)	0 (0)	
Lifetech MFO	2 (5.41)	35 (100)	

Table 3. Principal Efficacy

	Antegrade (n=37)	Retrograde (n=35)	P-Value
	Frequency (%); Mean + SD; Median (IQR)		
Acute Procedure success	37 (100)	34 (97.14)	0.486
Pre-discharge complete closure	27 (72.97)	27 (77.14)	**0.683**
Hospital Stay	3 (3 to 4)	3 (3 to 3)	**<0.001**
Complete Closure on 2D Echo			
1 month follow-up	29 (78.38)	30 (85.71)	0.419
3 month follow-up	33 (89.12)	35 (100)	**0.012**

Table 4. LV and LA enlargement in 2D Echo (n=72)

	Pre procedure	Post procedure	P-Value
	Frequency (%)		
With LV enlargement	38 (52.78)	2 (2.78)	**<0.001**
With LA enlargemen	29 (40.28)	1 (1.39)	**<0.001**

Table 5. Complications after VSD device closure according to technique

COMPLICATIONS	Antegrade n = 10	Retrograde n = 2
Serious adverse event (Death)	0	0
Major adverse events		
Thromboembolism	0	0
Device Embolization required surgical removal	0	0
Complete Heart Block	0	0
New onset valvular regurgitation that required surgical repair	0	0
Minor adverse event		
Device Embolization required percutaneous removal	1	1
New or increased (mild to moderate) regurgitation of the valve	3	0
Hemolysis	0	0
Hematoma of the groin	1	0
Loss of peripheral pulse	0	0
Cardiac arrhythmia (LBBB,RBBB)	1	1
Blood transfusion becauseof blood loss	0	0
Residual shunt	4	0
Others (fever, rash)	0	0

Table 6. Comparison of the outcome according to technique used (n=72)

	With complication (n=12)	Without complication (n=60)	Odds ratio (95% CI)	P-value
	Frequency (%)			
Antegrade	10 (83.33)	27 (45)	6.11 (1.23 to 30.3)	**0.027**
Retrograde	2 (16.67)	33 (55)	**0.16 (0.03 to 0.81)**	

DISCUSSION

Ventricular septal defect represents the most common type of congenital heart malformation, accounting for up to 40% of congenital heart defects and it is more frequent in Asian countries.[8] Our previous local study and literature from other countries showed that both surgery closure, and transcatheter closure using the antegrade technique have excellent results in closing VSDs. Meanwhile, this local study also showed that transcatheter closure has the advantage of reduced psychological impact, less pain, and discomfort due to the procedure, shorter hospital stay, no need for admission to an intensive care unit, faster time to normal activities.[12] Different devices had been used to close ventricular septal defects, and with evolving technology improved devices made it possible to use it on transcatheter closure using the retrograde technique. However, studies with transcatheter closure of VSD using retrograde technique have been lacking. This study was designed to compare the clinical outcome of transcatheter device closure of ventricular septal defect using antegrade and retrograde techniques.

Demographic profile and Diagnostic data of patients:

Based on WHO child growth assessment, it was observed in this study that more patients in Group A (p value 0.001) were wasted at below Z score -1. Stunted growth for Group A was also noted (Z-score -2 to 0, p-value <0.001). This observation may be explained by the larger ventricular septal defect size on echocardiography (0.4cm to 0.7cm) in younger patients for group A (9.89 years ± 4.68); although age and defect size were not significant in these study. In added effect of large VSD defect in group A, expected LV enlargement and shunt significance (Qp:Qs ratio) were observed with Group A

compared with Group B. In Group A, faster heart rate was also observed due to younger population and significance of shunt (Qp:qs ratio) in this group. In this study, it was observed that Group A patients belong to a younger group with significant shunt and weighed less compared to Group B. This may be explained that in able to successfully perform transcather closure of ventricular septal defect, weight, age and size of the defect of the patient were factors on selecting the technique to be used. With the large ventricular septal defect, expected larger devices and sheath to be used hence antegrade approach will be a better technique for younger and wasted patients to avoid vascular injury with retrograde technique.

Efficacy of transcather device closure of ventricular septal defect:

We have presented 72 patients who underwent transcather VSD closure with 37 patients via antegrade approach and 35 patients via retrograde approach. The meadian follow-up was 24 months. In this study, we considered effectiveness in terms of procedural success, complete defect closure (pre-discharge, 1-month and 3-month follow-up) and hospital stay. Transcatheter closure of VSD via retrograde approach shows a shorter hospital stay and 100% complete closure of the defect in 3 month follow-up. However, the present study also demonstrates an excellent immediate outcome and follow-up results for both techniques; supported by the significant improvement on chamber sizes.

Safety of transcatheter device closure of ventricular septal defect:

In our study, complications of transcatheter closure of VSD using both techniqhes were rare. Among all 12 complications (minor adverse events 16.7% of the study population), no serious and major adverse event occurred; which is comparable with the study of Butera et al. (14.7% complication rate) on a percutaneous closure of ventricular septal defects in children aged less than 12 years old.

In our retrospective study suggested that complications (10 of 12) are 6.11 times more likely to occur with patients undergoing antegrade technique. Most cases of minor adverse events: residual shunts (4 of 12) and new or increased valve regurgitation (3 of 12) were observed with antegrade technique. The creation of arteriovenous loop with antegrade technique might explain the new tricuspid regurgitation in 3 cases, in the early period of the study. Other minor adverse events observed in this study include device embolization, hematoma of the groin and cardiac arrhythmia. Both cases of cardiac arrhythmia were resolved within 24 hours and no recurrence during follow-up. Outcome from this study is rather diverse from earlier studies.[2,6,8] Generally, in this study manageable adverse events were recorded and did not outweigh the benefits of transcatheter closure of VSD using both techniques.

Technical consideration of transcatheter closure of ventricular septal defect:

Transcatheter closure of ventricular septal defect has many important technical considerations due to the involvement of adjacent structures (aortic valve, tricuspid tendineae, AV node, conduction bundle) and variations of VSD type (tubular, conical, window and aneurysmal type). First, the inclusion criteria for transcatheter closure of muscular and perimembranous VSD should be strict. Large VSD defined as more than 2/3 the size of the aortic valve annulus, VSD with severe pulmonary hypertension, severe aortic valve regurgitation and small infants with weight less than 7 kg should be referred to open heart surgery and excluded from transcatheter intervention. Due to this strict criteria that the success rate of transcatheter VSD closure in both groups were high. As previously discussed, VSD size determined during angiography was crucial in selecting the appropriate approach in transcatheter closure of VSD. Most of patients underwent VSD device closure with antegrade approach was observed with a larger median ventricular septal defect size of 0.6 cm (0.4–1.5cm).

Second, the most crucial step on transcatheter VSD device closure is passing of the guidewire catheter across the defect. In our study, we had used two types of guide catheters that were useful in passing the defect: Judkins right and cut pigtail catheter with the use of hydrophilic 0.032” or 0.035”x260cm Terumo long guidewire.

Third, the technique selection in this study was one of the important technical considerations. Antegrade technique requires a creation of arteriovenous wire loop for line stabilization through which the device can be advanced. Unlike retrograde technique that directly advanced the delivery system without AV loop to the defect from the LV side and deployed the RV disc of the occlude first. This technique simplifies the step compared to the antegrade technique; hence also avoids the factors associated with the advancement failure of the device via the venous route. It was observed in this study that retrograde approach shortened the procedural time, high rate of successful deployment (97.1%), and lower rate of complications (5.7%). This outcome is similar with the previous reported series and case reports.[13,14,15]

Fourth, device selection was another important technical consideration. Multiple devices were used during this study, however the availability of the device was the main decisive factor on which device to be used; in early study period. The availability of the multifunctional occluder device (MFO) Lifetech™ heralded the transcatheter closure of VSD via retrograde technique. In our study, most perimembranous VSD could be successfully closed with retrograde approach using multifunctional occluder device (MFO) Lifetech™ requiring a French 5–7mm delivery sheath.

Lastly, in previous studies.[2,4,6,7] transesophageal echocardiography (TEE) is the imaging modality that is mostly used for guidance on transcatheter VSD closure. During the early years of the study period, angiography was the sole imaging modality that guide us through the transcatheter closure because TEE extends the procedural time. However in the later years of the study period, usage of transthoracic echocardiography (TTE) combined with angiography remarkably guide us on device closure of VSD.

STUDY LIMITATION

Although our study demonstrated a significant advantage of transcatheter VSD closure using retrograde approach, it nevertheless had some limitation. First, this was a single-center, non-randomized study and our experience may not be universally representative. Second, these techniques can only be carried out safely and complications managed in the proper way by very experienced hands. Third, although both of the techniques of VSD closure appear to be safe in the mid-term follow-up, it is not known whether they are safe in the very long-term, whereas the long-term safety and efficacy of surgical closure are well documented.

CONCLUSION

The transcatheter VSD closure using both approaches were immediately safe and effective. In the presence of favorable characteristic of patients and anatomic considerations, retrograde technique is less likely to have complications; and shortened procedure time compared to antegrade technique. The only limitation in pediatric patients is the size of the delivery sheath. Smaller size of delivery sheath is required for the safe placement of the device using the retrograde technique to avoid vascular injury.

The results of this study suggest that retrograde approach may be implemented successfully in transcatheter closure of VSD. This study suggests that transcatheter VSD closure must be initiated using the retrograde approach; and may switched to antegrade approach if with unfavourable anatomic conditions.

REFERENCES

1. Minette MS, Sahn DJ. Ventricular septal defects Circulation. 2006 Nov 14;114(20):2190-7.
2. Yang J, Yang L, Wan Y, Zuo J, Zhang J, Chen W, et al. Transcatheter device closure of perimembranous ventricular septal defects: mid-term outcomes Eur Heart J. 2010 Sep;31(18):2238-45.
3. McDaniel NL, Gutgesell HP. Moss and Adams' heart disease in infants, children, and adolescents including the fetus and young adult. Philadelphia, Pa: Lippincott Williams and Wilkins; 2001.
4. Lock JE, Block PC, McKay RG, Baim DS, Keane JF et al. Transcatheter closure of ventricular septal defects Circulation. 1988 Aug;78(2):361-8. defects. Circulation 1988;78:361–368.

5. Bridges ND, Perry SB, Keane JF, Goldstein SA, Mandell V, Mayer Jr JE, et al. Preoperative trans catheter closure of congenital muscular ventricular septal defects. N Engl J Med. 1991 May 9;324(19):1312-7.
6. Kalra GS, Verma PK, Dhall A, Singh S, Arora R. Transcatheter device closure of ventricular septal defects: immediate results and intermediate-term follow-up. Am Heart J. 1999 Aug;138(2 Pt 1):339-44.
7. Pedra, CA, Pedra SRF, Esteves CA, Pontes Jr C, Braga SLN, Arrieta SR, et al. Percutaneous closure of perimembranous ventricular septal defects with the Amplatzer device: technical and morphological considerations. Catheter Cardiovasc Interv. 2004 Mar; 61 (3):403-10.
8. Butera G, Carminati M, Chessa M, Piazza L, Abella R, Negura DG, et al. Percutaneous closure of ventricular septal defects in children aged <12: early and mid-term results. Eur Heart J. 2006 Dec;27(23):2889-95.
9. Holzer R, de Giovanni J, Walsh KP, Tometzki A, Goh Th, Hakim F, et al. Transcatheter closure of perimembranous ventricular septal defects using the amplatzer membranous VSD occluder: immediate and midterm results of an international registry. Catheter Cardiovasc Interv. 2006 Oct;68(4):620-8.
10. Thanopoulos BVD, Rigby ML, Karanasios E, Stefanadis C, Blom N, Ottemkamp J, Zarayelyan A. Transcatheter closure of perimembranous ventricular septal defects in infants and children using the Amplatzer perimembranous ventricular septal defect occluder. Am J Cardiol. 2007 Apr 1;99(7):984-9.
11. Xunmin C, Shisen J, Jianbin G, Haidong W, Lijun W. Comparison of results and complications of surgical and Amplatzer device closure of perimembranous ventricular septal defects. Int Cardiol. 2007 Aug 9; 120 (1):28-31.
12. Valdez B, Reganion JG, Villareal JG. Comparison of the clinical outcome and cost of transcatheter occlusion and surgical closure of isolated ventricular septal Defect. Phil Heart Center J. 2016;21:41-46.
13. Pekel N, Ercan E, Özpelit ME, Özyurtlu F, Yılmaz A, Topaloğlu C, et al. Directly ventricular septal defect closure without using arteriovenous wire loop: our adult case series using transarterial retrograde approach. Anatol J Cardiol. 2017 Jun;17(6):461-468.
14. Muthusamy K. Retrograde closure of perimembranous ventricular septal defect using muscular ventricular septal occluder: a single-center experience of a novel technique. Pediatr Cardiol. 2015 Jan;36(1):106-10.
15. Koneti NR, Penumatsa RR, Kanchi V, Arramraj SK, Jaishankar S, Bhupathiraju S. Retrograde transcatheter closure of ventricular septal defects in children using the Amplatzer Duct Occluder II. Catheter Cardiovasc Interv. 2011 Feb 1;77(2):252-9.
16. Jameel AA, Arfi AA, Arif H, Amjad K, Omar GM. Retrograde approach for device closure of muscular ventricular septal defects in children and adolescents, using the Amplatzer muscular ventricular septal defect occluder. Pediatr Cardiol. Nov-Dec 2006;27(6):720-8.

Factors Associated with Reperfusion Lung Injury After Total Correction of Tetralogy of Fallot

Claudio Q. Gayeta Jr, MD; Bianca Sanz, MD; Juan Reganion, MD; Sarah Zampaga, MD

Background **---** Reperfusion lung injury (RLI) is one of the most common complications after Tetralogy of Fallot (TOF) correction that leads to prolonged hospitalization and significant morbidity. This study investigates on different factors that may be associated with RLI after TOF correction.

Method **---** All patients with TOF who underwent TOF correction from January 2015 to December 2016 in a tertiary cardiovascular referral center were included. Baseline characteristics, echocardiographic and intra-operative findings along with their post-operative course were reviewed. Serial chest radiographs were reviewed and each lung were given a pulmonary edema score prior to and after surgery to determine presence of RLI. Statistical analysis was performed in STATA SE version 13. Factors associated with reperfusion lung injury were determined using logistic logarithm analysis. The level of significance was set at 5%.

Results **---** RLI was present in 41 of 114 (36%) patients after TOF correction. Factors for the development of RLI included female sex which increases its occurrence with an odds ratio of 2.9 (95% CI 1.29-6.55, p=0.01). Intraoperative use of propofol is a protective factor with an odds ratio of 0.24 (95% CI 0.07-0.85, p=0.027). We did not identify significant association between the occurrence of RLI and the factors that reflect the degree of pulmonary stenosis.

Conclusion **---** RLI is common after TOF correction. Female sex increases the risk of its occurrence while intraoperative use of propofol is a protective factor. ***Phil Heart Center J 2021;24 (2):41-48.***

Key Words: ■Tetralogy of Fallot ■ TOF correction ■ reperfusion lung injury

Tetralogy of Fallot (TOF) is the most common form of cyanotic congenital heart disease. In a meta-analysis done in 2002, which included 41 studies about TOF, the best estimate of its incidence is 577 cases per million live births.[1]

Since the first successful correction of TOF in 1954 by Lillehei and associates in a 10-year-old boy,[2] this condition was studied extensively and its surgical correction was quickly replicated in other conditions. TOF correction nowadays is done through a transatrial incision for closure of ventricular septal defect and relief of obstruction to the right ventricular outflow tract[3] while on cardiopulmonary bypass.

Reperfusion lung injury in the setting of pulmonary artery angioplasty for relief of right ventricular outflow obstruction is a well recognized entity.[4] It typically manifests as a transient pulmonary edema that is localized to an area of increased perfusion of lung tissue that results in impaired gas exchange. It has been thought that this injury is due to increased blood flow to areas of the lung that has been chronically underperfused.[5] Pulmonary injury after cardiopulmonary bypass has led to prolonged hospitalization, intubation and increased cost of hospital stay.[6]

In a study done in 2012 by Maskatia and associates, they reported a 65% incidence of reperfusion injury in patients with TOF – pulmonary valve atresia with major aortopulmonary collateral arteries after unifocalization procedure. They reported that the risk factors

3rd place, Oral Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Claudio Q. Gayeta.*** Department of Pediatric Cardiology. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** 2021 ISSN 0018-9034

development of pulmonary reperfusion injury velopment of pulmonary reperfusion injury include bilateral unifocalization and the severity of stenosis in collateral arteries.[7]

Reperfusion lung injury after TOF correction has not been studied. The aims of this study are to describe the incidence, clinical profile and risk factors for the development of reperfusion lung injury after TOF correction. Based on the results reported by Maskatia and associates, it is hypothesized that post-operative reperfusion lung injury is more likely to develop in TOF cases with more severe pulmonary stenosis, thereby with lower baseline oxygen saturation, higher hematocrit and with history of recurrent admissions for phlebotomy. TOF correction done at an advanced age probably has higher risk of developing reperfusion injury since the lungs has been more chronically underperfused. Furthermore, it is hypothesized that prior palliative shunting procedures done to augment pulmonary blood flow will reduce the incidence of reperfusion lung injury provided that the shunt remains patent.

METHODS

This study was conducted in strict compliance with the ethical principles presented in the Declaration of Helsinki. Prior to the conduction of the study, the protocol was reviewed and approved by the Philippine Heart Center Institutional Ethics Review Board (PHC-IERB). The investigator requested that acquiring of informed consent be waived since it is difficult to obtain individual authorization from all the study subjects. The risk to the privacy of the subjects was minimal. No sensitive information was obtained. The anonymity of the subjects was ensured by the investigator.

This is a a retrospective cohort study done at the Philippine Heart Center from January 2015 to December 2016. Included in the study were all pediatric patients age 0-18 years old with TOF who underwent total correction from January 2015 to December 2016 at a tertiary cardiovascular referral center. While excluded were patients with other medical problems such as pneumonia and acute respiratory disease syndrome and and incomplete medical records.

***Sample Size*:** Using Epi Info Version 7, the minimum sample size requirement is at least 87 based on a 65% incidence (42 of 65 patients) of reperfusion lung injury which among patients with TOF - pulmonary valve atresia with major aortopulmonary collateral arteries who underwent unifocalization procedures[7] with margin of error at 10% and confidence level at 95%.

Identification of Study Variables

- Age
- Sex
- Nutritional status
- Prior palliative shunting procedures
- History of recurrent phlebotomy
- Hypercyanotic spell
- Maintenance medication
- Pre-operative oxygen saturation
- Baseline Hematocrit
- 2D Echocardiography findings
- Intraoperative findings
- Intraoperative anesthesia used
- Bypass and cross-clamp time

***Study Maneuver*:** The list of patients with TOF who underwent total correction from January 2015 to December 2016 was obtained from the database and the medical records section. The medical records of the included patients were obtained to determine the following variables:

1. *Demographic data:* age, sex, nutritional status, prior shunting procedures, others
2. *Clinical and laboratory data:* history of recurrent phlebotomy, maintenance medications, hypercyanotic episodes, pre-operative oxygen saturation, and baseline hematocrit.
3. *2D echocardiographic findings:* sizes of the main and branch pulmonary arteries, degree of obstruction to right ventricular outflow tract, presence of other sources of pulmonary blood supply, and function of both ventricles.
4. *Intraoperative findings:* type of repair, cross-clamping time, bypass time.

The chest radiographs of included patients were reviewed by radiologists to determine who among the subjects developed reperfusion injury. The radiologist involved in the study was blinded of the clinical history and subsequent hospital course of the patients. Only the name, age and hospital number of all included patients were given. Chest radiographs done on pre-operative, post-operative days 0 to 2, and 2 weeks post-operative or at discharge from the hospital were assessed. The radiographs were scored using a pulmonary edema scoring system used in a previous study which assessed pulmonary reperfusion injury in patients who underwent lung transplantation.[8] The scoring system proceeded as follows:

1. Each lung was scored on a scale of 0 to 3. The degree of edema on each lung was assessed using a 4-point scale:
   - 0 For normal lung
   - 1 With minimal opacity not obscuring lung vessels.
   - 2 With opacity partially obscuring lung vessels.
   - 3 With opacity completely obscuring lung vessels

2. The average score of the 2 lungs was the final edema score.

The presence of reperfusion lung injury was defined as a change in pulmonary opacity appearing immediately after TOF correction that resolved within 2 weeks or before discharge and is not associated with pulmonary hemorrhage, pneumonia, or atelectasis. A change in edema score of 2 or more was used to define reperfusion lung injury.

Those patients with pulmonary edema but with clinical course that is more compatible with pneumonia (presence of fever, copious secretions per endotracheal tube, productive cough, increased CRP, and prolonged duration of pulmonary opacity) were excluded. Patients with a pre-operative radiograph with an edema score of more than 1 were not included. This is to exclude patients with other causes of pulmonary opacity.

Statistical Analysis: Data analysis was performed in STATA SE version 13. Quantitative variables were summarized as mean and standard deviation, while qualitative variables were tabulated as frequency and percent. Factors associated with reperfusion lung injury were determined using logistic logarithm analysis. The level of significance was set at 5%.

RESULTS

A total of 130 records of patients with Tetralogy of Fallot who underwent total correction were retrieved and reviewed. Four were excluded because of incomplete data record, most of which do not have intraoperative anesthesia monitoring sheet. Another 8 patients were not included because of lack of baseline work-up of either 2D echocardiography (3 patients) or chest radiograph (5 patients). Five patients were further excluded because of different diagnosis (double outlet right ventricle with pulmonary stenosis). This gives a total of 114 patients that were eventually included in the study. Out of these study subjects, 36% (n=41) developed reperfusion lung injury. The true incidence falls between 27.3% to 45.5% with a 95% confidence interval as shown in Table 1.

Table 2 shows the association of various demographic factors and the occurrence of RLI in patients who underwent TOF correction. The age and nutritional status of the patient at the time of surgery do not significantly increase the occurrence of RLI. Having a prior shunting procedure increases the odds of developing RLI by 3.69 but this is not statistically significant. Female patients are significantly more likely to develop RLI compared with their male counterparts with an odds ratio of 2.91 (p=0.009).

The association of clinical and laboratory data with the development of RLI is shown in Table 3. All variables used did not show statistically significant association with occurrence of RLI. However, data trend shows that having a history of recurrent phlebotomy and hypercyanotic spell tend to increase the risk of developing RLI. On the other hand, pre-operative use of propranolol and having a higher baseline oxygen saturation tend to have a lower odds of developing reperfusion injury.

Pre-operative echocardiographic sizes of the main and branch pulmonary arteries did not have statistically significant association with the occurrence of RLI as shown in Table 4. However, data shows that smaller right and left pulmonary artery sizes tend to increase the odds of developing reperfusion injury. The severity of RVOT obstruction also did not have significant association with development of RLI.

The presence of another source of pulmonary blood flow other than the main and the branch pulmonary arteries (collaterals and PDA) carries a higher risk of developing RLI (OR = 1.82) but this is not statistically significant. In contrast, increasing Mc Goon's value tends to lower down the risk of having RLI but this also did not reach statistical significance. The association of RV and LV function on the occurrence of RLI was not established as all of the included patients had good RV and LV systolic function prior to surgery.

Table 5 shows that no particular type of RVOT repair showed a statistically significant association with developing RLI. However, MPA and RVOT augmentation may potentially increase the likelihood of developing RLI. Cross-clamp and bypass duration both do not show statistically significant effect on the occurrence of RLI but trends show that prolonging the duration of bypass and cross-clamp has a higher odds of developing RLI.

Out of all the anesthesia being used during the operation, only propofol showed statistically significant association in lowering the occurrence of reperfusion lung injury with an odds ratio of 0.24 denoting that those who use propofol are 4.17 times less likely to have reperfusion lung injury (p=0.03).

Table 1. Incidence of Reperfusion Lung Injury Among Patients Who Underwent TOF Correction

	n	% With RLI	95% CI
With reperfusion lung injury	41	36	27.3% to 45.5%
Without reperfusion lung injury	73		
Total	114		

Table 2. Association of Demographic Factors With Presence of Reperfusion Lung Injury in Patients Who Underwent TOF Correction

Demographic Variables	With RLI (n=41) n,%	Without RLI (n=73) n,%	Odds Ratio	95% CI	p value
Age at TOF					
Less than 5 Years	25, (61)	43, (58.9)	0.9173	0.42 to 2.00	0.829
5 Years and Above	16, (39)	30, (41.1)			
Sex					
Female	20, (48.8)	18, (24.7)	2.9101	1.29 to 6.55	0.010
Male	21,(51.2)	55, (75.3)			
Nutritional Status (Weight for Age)					
Z-Score >+2	1,(2.4)	0, (0.0)		Reference	
Z-score 0 to +2	6, (14.6)	8, (11.0)			
Z-Score 0 to -2	9, (22)	32, (43.8)	0.3214	0.09 to 1.13	0.076
Z-Score <-2	25, (61)	33, (45.2)	0.8658	0.28 to 2.71	0.804
Prior Shunting Procedures					
Present	2, (4.9)	1, (1.4)	3.6923	0.32 to 42.02	0.292
None	39,(95.1)	72, (98.6)			

Table 3. Association of Clinical and Laboratory Findings With Presence of Reperfusion Lung Injury in Patients Who Underwent TOF Correction.

Clinical and Laboratory Findings	With RLI (n=41) n,%	Without RLI (n=73) n,%	Odds Ratio	95% CI	p value
Phlebotomy					
Recurrent	3, (7.3)	3, (4.1)	1.84	0.35 to 9.58	0.468
None	38, (92.7)	70, (95.9)			
Hypercyanotic Spell					
Recurrent	13, (31.7)	18, (24.7)	1.42	0.61 to 3.31	0.418
None	28, (68.3)	55, (75.3)			
Propranolol					
Not maintained	7, (17.1)	20, (27.4)	0.55	0.21 to 1.43	0.217
Maintained	34, (82.9)	53, (72.6)			
Oxygen Saturation					
<60%	3, (7.3)	4, (5.5)		Reference	
60-80%	27, (65.9)	37, (50.7)	0.9730	0.20 to 4.71	0.973
>80%	11, (26.8)	32, (43.8)	0.4583	0.09 to 2.38	0.353
Preoperative Hematocrit					
<60%	27, (65.9)	48, (65.8)	1.0000	0.45 to 2.25	0.991
60-80%	14, (34.1)	25, (34.2)			
>80%	0, (0)	0, (0)	-	-	-

Table 4. Association of Pre-operative Echocardiographic Findings with Presence of Reperfusion Lung Injury in Patients Who Underwent TOF correction

Echocardiographic Variables	With RLI (n=41) n,%	Without RLI (n=73) ,%	Odds Ratio	95% CI	p Value
MPA Size					
Z-Score +2	0, (0))	0,(0)		Reference	
Z-score 0 to +2	2, (4.9)	2, (2.7)			
Z-Score 0 to-2	10, (24.4)	18, (24.7)	0.56	0.07 to 4.57	0.585
Z-Score <-2	29, (70.7)	53, (72.6)	0.55	0.07 to 4.09	0.557
RPA Size					
Z-Score >+2	1, (2.4)	0, (0)		Reference	
Z-Score 0 to +2	6, (14.6)	12, (16.4			
Z-Score 0 to-2	26, (63.4)	49, (67.1)	0.91	0.32 to 2.59	0.859
Z-Score <-2	8, (19.5)	12, (16.4)	1.14	0.31 to 4.16	0.840
LPA Size					
Z-Score >+2	1, (2.4)	1, (1.4)		Reference	
Z-Score 0 to +2	13, (31.7)	28, (38.4)			
Z-Score 0 to-2	22, (53.7)	37, (50.7)	1.23	0.54 to 2.82	0.622
Z-Score <-2	5, (12.2)	7, (9.6)	1.14	0.40 to 5.50	0.559
RVOT Obstruction					
Mild	0, (0)	1, (1.4)			
Moderate	2, (4.9)	3, (4.1)	0.88	0.15to 5.05	0.15 to 5.05 0.890
Severe	39, (95.1)	69, (94.5)			
Other Sources of PBF					
Present	10, (24.4)	11, (15.1)	1.82	0.70 to 4.74	0.222
Absent	31, (75.6)	62, (84.9)			
Right Ventricular Function					
Good (RVEF≥36)	0, (0)	0, (0)	-	-	-
Poor (RVEF<36)	41, (100)	73, (100)	-	-	-
Mc Goon's					
<1	1, (2.4)	0, (0)		Reference	
1.0 to 1.5	11, (26.8)	15, (20.5)			
1.6 to 2.0	23, (56.1)	37, (50.7)	0.78	0.31 to 1.95	0.591
>2.0	6, (14.6)	21, (28.8)	0.36	0.11 to 1.17	0.088

Table 5. Association of Intraoperative Findings with Presence of Reperfusion Lung Injury in Patients Who Underwent TOF correction

Echocardiographic Variables	With RLI (n=41) n,%	Without RLI (n=73) n,%	Odds Ratio	95% CI	p value
Type of RVOT Repair					
Transannular patch	25, (61)	52, (71.2)	0.63	0.28 to 1.41	0.263
Infundibulectomy	38, (92.7)	69, (94.5)	0.73	0.16 to 3.45	0.696
MPA Augmentation	8, (19.5)	8, (11)	1.97	0.68 to 5.72	0.213
RVOT Augmentation	7, (17.1)	8, (11)	1.67	0.56 to 5.01	0.358
Commissurotomy	0, (0)	1, (1.4)	-	-	-
LPA Augmentation	1, (2.4)	2, (2.7)	-	-	-
Pulmonary Valvotomy	0, (0)	2, (2.7)	-	-	-
Pulmonary Valve Reconstruction (Monocuspal)	0, (0)	1, (1.4)	-	-	-
RPA Augmentation	1, (2.4)	0, (0)	-	-	-
RV to PA Conduit	0, (0)	1, (1.4)	-	-	-
Cross-Clamp Time					
<1 hour	1, (2.4)	2, (2.7)		Reference	
1-2 hours	31, (75.6)	55, (75.3)	1.13	0.10 to 12.94	0.923
>2 hours	9, (22)	16, (21.9)	1.13	0.09 to 14.20	0.928
Bypass Time					
<2 hours	15, (36.6)	32, (43.8)		Reference	
2-3 hours	20, (48.8)	32, (43.8)	1.33	0.58 to 3.06	0.497
>3 hours	6, (14.6)	9, (12.3)	1.42	0.43 to 4.73	0.566
Anesthesia Used Intraoperatively					
Sevoflurane	40, (97.6)	70, (95.9)	1.71	0.17 to 17.04	0.646
Midazolam	39, (95.1)	73, (100)	-	-	0.997
Fentanyl	41, (100)	71, (97.3)	-	-	0.998
Rocuronium	40, (97.6)	71, (97.3)	1.13	0.10 to 12.82	0.923
Propofol	33, (80.5)	69, (94.5)	0.24	0.07 to 0.85	0.027
Ketamine	0, (0)	2, (2.7)	-	-	0.998
Atracurium	4, (9.8)	3, (4.1)	2.52	0.54 to 11.87	0.242
Isoflurane	1, (2.4)	3, (4.1)	0.58	0.06 to 5.80	0.646
Morphine	0, (0)	1, (1.4)	-	-	0.998
Oxycodone	0, (0)	1, (1.4)	-	-	0.998

DISCUSSION

This study is a retrospective review of patients who underwent total correction of TOF to determine the incidence and the factors associated with RLI. We found that 41 out of 114 (36%) study subjects developed RLI. Only female sex is associated with significant increase in the risk of developing RLI while intraoperative use of propofol significantly decreases the odds of having reperfusion injury. The mechanism by which these factors affect the development of RLI still has to be determined. Other factors being investigated failed to show significant association with development of RLI.

Our results contradict the findings of Maskatia and co-workers who strongly correlated the development of RLI with the degree of pulmonary stenosis.[7] Clinical, laboratory, and echocardio-

graphic findings consistent with higher degree of pulmonary stenosis failed to demonstrate significant increase in the occurrence of RLI. In the same way, factors consistent with milder degree of pulmonary stenosis also did not show significantly lower risk of developing RLI. Intraoperative factors like the type of repair of right ventricular outflow obstruction and bypass and cross clamp durations also failed to demonstrate significant association with RLI occurrence.

Our study suggests that reperfusion injury is not a direct reflection of the degree of pulmonary stenosis and is not solely due to increased blood flow in chronically underperfused lung. Though the degree of pulmonary stenosis may still play an important role in developing RLI, as shown in our data trends, we hypothesize that there are other more important factors that come into play. Post-operative management of fluids as well as early and aggressive use of diuretics could have affected the occurrence of RLI. Most of the patients included in the study were given furosemide and other diuretics early in the post-operative period. This could have changed the course of patients that were supposed to develop reperfusion injury.

The extensiveness of dissection and lung trauma due to retractions intraoperatively could have contributed to post-operative radiographic picture of reperfusion injury. Mechanical ventilator management in the post-operative period could also have affected our data. Changing ventilator settings can produce dramatic variations in the appearance of pulmonary vasculatures in technically identical radiographs, especially the positive end-expiratory pressure.[9]

This study has several limitations given that it is a retrospective study design. The diagnosis of RLI is based on chest radiographic findings alone and we did not use molecular markers for reperfusion. Other pathology could have caused the radiographic picture of RLI that could have affected our results. The scoring system that we used in determining the presence of pulmonary edema has not been validated. The factors that we analyzed in the study were limited. There may be other clinical, laboratory, echocardiographic, medical, hemodynamic, intraoperative and post operative factors that could have contributed to RLI.

We suggest that future similar studies focusing on the factors contributing to RLI to use more specific molecular markers to definitely diagnose reperfusion injury in addition to chest radiographic findings. We also suggest that post operative fluid management be investigated as well. Larger study subject is also recommended since the trend of our data shows that perhaps the degree of pulmonary stenosis may contribute to the development of RLI but did not reach statistical significance.

CONCLUSION

Reperfusion lung injury is common in the setting of total correction of TOF with an incidence of 36% in our cohort. Female sex and intraoperative use of propofol are the factors that were recognized to increase or decrease the occurrence of RLI, respectively. We failed to demonstrate significant association between RLI and other laboratory, echocardiographic, and intraoperative factors. The cause of RLI in patients after TOF correction is likely multifactorial. Further study regarding RLI is needed.

REFERENCES

1. Hoffman JIE, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002;39:1890-1900.
2. Kirklin JW, Blackstone EH, Kirklin JK, et al. Surgical results and protocols in the surgical spectrum of tetralogy of Fallot. Ann Surg. 1983;198:251-265.
3. Guolin S, Xuefeng W, Jinjin C, Ruiyan M, Fuping L, Lin C, Yingbin X. Primary repair of tetralogy of Fallot in infants: Transatrial/transpulmonary or transventricular approach. Asian J Surg. 2013;36:137-143.
4. Bergersen LJ, Perry SB, Lock JE. Effect of cutting balloon angioplasty on resistant pulmonary artery stenosis. Am J Cardiol. 2003;91:185-9.
5. Kreutzer J, Perry SB, Jonas RA, Mayer JE, Castaneda AR, Lock JE. Tetralogy of Fallot with diminutive pulmonary arteries: pre-operative pulmonary valve dilatation and transcatheter rehabilitation of pulmonary arteries. J Am Coll Cardiol. 1996;27:1741-7.

6. Kreutzer J, Perry SB, Jonas RA, Mayer JE, Castaneda AR, Lock JE. Tetralogy of Fallot with diminutive pulmonary arteries: pre-operative pulmonary valve dilatation and transcatheter rehabilitation of pulmonary arteries. J Am Coll Cardiol. 1996;27:1741-7.
7. Su, ZK, Sun Y, Yang YM, Zhang HB, Xu ZW. Lung function after deep hypothermic cardiopulmonary bypass in infants. Asian Cardiovasc Thorac Ann. 2003;11:328-31.
8. Maskatia SA, Feinstein JA, Newman B, Hanley FL, Roth SJ. Pulmonary reperfusion injury after the unifocalization procedure for tetralogy of Fallot, pulmonary atresia, and major aortopulmonary collateral arteries. J Thorac Cardiovasc Surg. 2012;144:184-9.
9. Anderson DC, Glazer HS, Semenkovich JW, Pilgram TK, Trulock EP, Cooper JD, et al. Lung transplant edema: chest radiography after lung transplantation – the first 10 days. Radiology. 1995;195:275-81.
Zimmerman JE, Goodman LR, Shahvaru MB. Effect of mechanical ventilation and positive end-expiratory pressure (PEEP) on chest radiograph. AJR Am J Roentgenol. 1979 Nov;133(5):811-5.

Scoring System to Predict Good Outcome among Patients Who Underwent Total Correction for Tetralogy of Fallot at The Philippine Heart Center

Elugevina C. Domingo, MD; Ma. Bernadette A. Azcueta, MD

Background--- Surgery for Tetralogy of Fallot is the definitive treatment for this condition. Over the years, it has become a safe procedure with good results. However, post-operative complications continue to affect selected patients. This study aimed to develop a scoring system that will predict a good outcome for patients undergoing total correction of TOF.

Methods --- A retrospective review of medical records of all patients who underwent TOF correction from January 2006 to December 2015 was done. Pre-operative variables included in the study were age, gender, nutritional status, level of hematocrit, oxygen saturation, history of phlebotomy, LV end diastolic diameter, Nakata index, McGoon's ratio, RPA and LPA sizes and PV annulus. These risk factors were associated with post-op complications namely death, pneumonia, reperfusion injury, pleural/pericardial effusion, hemorrhage and septicemia.

Results --- Sixty three (34%) out of 183 children developed post-operative complications, with pneumonia (22.2%) being the most frequent complication. Among the clinical and echocardiographic variables analyzed, only three variables were independently predictive of a good outcome, namely LVEDD >/= -2 (beta-coefficient 3.92, OR at 95% CI 14 to 172, P=<0.001), McGoon's ratio (beta-coefficient 4.43, OR at 95% CI 30 to 229, P=<0.001) and LPA (beta-coefficient 4.93, OR at 95% CI 44 to 431, P=<0.001). ROC analysis arrived at best minimum cut-off score of 1, with sensitivity of 95%, specificity of 92% and accuracy of 94%.

Conclusion --- This scoring system can be a simple and straightforward tool in stratifying pediatric patients who will undergo surgical correction for TOF. ***Phil Heart Center J 2021;24(2):49-55.***

Key Words: ■ Tetralogy of Fallot ■ scoring system ■ risk stratification ■ post-operative complication

Tetralogy of Fallot remains to be the most common cyanotic heart disease affecting children today. It is a disease comprised of four lesions: pulmonary stenosis, right ventricular hypertrophy, over riding of the aorta and ventricular septal defect. It has an incidence of 1 per 3600 and accounts for 3.5% of all infants born with congenital heart disease.[1] Definitive treatment is through surgery alone. There are varying opinions regarding the optimal time of repair for patients with Tetralogy of Fallot. For many years, the protocol at the Hospital for Sick Children in Toronto was to repair children with TOF at an age of 18months.[2] Another study done by Hirsch et al reviewed the post operative success of neonates who underwent repair. The study concluded that the complete repair of TOF in the neonate is associated with excellent intermediate-term survival.[3]

The success of TOF correction depends on several factors. The more frequently cited factors affecting the outcome of surgery in several studies include age, surgical technique, pulmonary artery sizes, pulmonic valve annulus, to name a few. Saygi et al in their research Factors affecting perioperative mortality in Tetralogy of Fallot mentioned several variables that may directly/indirectly affect the result of the surgical intervention done on patients. They

Finalist, Oral Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Elugevina C. Domingo.*** 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

mentioned McGoon's index, pulmonary artery sizes as determinants of the outcome, with outcomes being measured through complications, days on mechanical ventilator, mortality, etc.[4] Locally, Gudani et al studied the Nakata Index vs McGoon's ratio to predict the outcome following total correction among patients who underwent TOF correction.

It is the purpose of the study to formulate a scoring system that will predict a good surgical outcome for patients undergoing Tetralogy of Fallot correction. This will be beneficial for clinicians in planning the timing of surgery among their patients. This will be the first study to be done on this topic.

METHODS

The protocol of this research was presented, reviewed and approved by the Institutional Ethics Review Board (IERB). Due to the difficulty of obtaining individual authorization from the subjects of the study, the investigator requested for the waiver of informed consent.

Study Design: This is a retrospective cohort study on TOF patients between January 2006 to December 2015.

Study Population: This study included all pediatric patients aged 1 to 19 years old who were diagnosed with Tetralogy of Fallot who underwent total correction from January 2006 to December 2015 in a tertiary cardiovascular center.

Included in the study are pediatric patients diagnosed with TOF who underwent total correction within the period of January 2006 to December 2015 while excluded are patients who underwent palliative surgery prior to the admission for total correction.

DATA COLLECTION

A comprehensive list of surgical patients and procedures done during the specified period was obtained from the Medical Records and Pediatric Cardiology Surgical Intensive Care database. All patients who underwent TOF correction within the time period of the study were listed and included. This list was then submitted to the Medical Records Section for chart review and recording of pertinent data. Additional data were gathered from a fully integrated medical clinic workflow software system in the hospital (MEDtrak). A data collection sheet was created where information gathered can be written.

Primary Outcome Measures: Good outcome defined as the absence of mortality, complications like reperfusion injury and prolonged hospital stay.

Sample Size for Logistic Regression Using Odd's Ratio: A minimum sample size of 167 subjects is required for this study. Using NCSS-PASS 2013 software, the minimum sample size requirement was computed based on a set of R-squared of 0.10 for 12 independent variables to be tested in a multivariate regression analysis with alpha level of 5% and of power of 80%.

Statistical Analysis: Data encoding was done using Microsoft Excel. 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 between patients with good and bad outcome, respectively. Odds ratio and corresponding 95% confidence intervals from binary logistic regression was computed to determine significant predictors of good outcome. Significant individual predictors was fitted into multiple logistic regression model to come up with equation to predict good outcome, then the beta coefficient of each predictor was used as values for building the calculator for the outcome. Lastly, receiver operating characteristic and area under the curve analysis was used to determine the clinically meaningful cut off to predict the outcome using the calculator from multiple logistic regression analysis. All statis-

tical tests were two tailed test. Shapiro-Wilk was used to test the normality of the continuous variables. Missing variables was neither replaced nor estimated. Null hypotheses was rejected at 0.05 α-level of significance. STATA 13.1 was used for data analysis.

RESULTS

A total of 183 pediatric patients with TOF underwent total correction from 2006 to 2015 in our institution (*Table 1*). There were more slightly more males (55%) than females (45%). Almost half of the subjects (45.4%) who were operated on belonged to the 1-3 years old age group.

Clinical and echocardiographic pre-operative variables are shown in Table 2a with their respective p-values. No significant difference was noted with regards to hematocrit level (p=0.014), oxygen saturation (p=0.0566) and history of phlebotomy (p=0.002). The rest of the clinical and echocardiographic pre-operative variables all showed significance with p-values at <0.001. Table 2b summarized the outcomes for these patients, with 63 subjects (34%) having post-operative complications and a median hospital stay of 10.

Table 3 shows the result of the univariate analysis done on all the clinical and echocardiographic variables in the study. Among the clinical variables analyzed, the following variables may independently predict a good outcome post-corrections: LVEDD ≥ -2 (beta-coefficient 3.92, OR at 95% CI 14 to 172, P ≤ 0.001); Nakata Index (beta-coefficient 1.76, OR at 95% CI 2.7-12.4, P ≤ 0.001); McGoon's ratio (beta-coefficient 4.43, OR at 95% CI 30 to 229, P ≤ 0.001) ; RPA (beta-coefficient 3.27, OR at 95% CI 11.6 to 59, P ≤ 0.001); LPA (beta-coefficient 4.93, OR at 95% CI 44 to 431, P ≤0.001) and PV annulus ≥ -2 (beta-coefficient 1.75, OR at 95% CI 2.78 to 11.9, P ≤ 0.001).

Table 4 shows the result of the multivariate analysis done among the variables known to independently predict good outcome. Three variables were identified to predict good outcome post-TOF surgery. Listed are the adjusted beta-coeffcients with the corresponding score for each variable.

The final proposed scoring system is summarized in Table 5. The lowest achievable score is -4 while the highest is 4. The proposed risk stratification using the scoring system is seen in Table 6.

The receiver operating curve was used to determine the accuracy of the scoring system. It was noted that at a cut point of >/= 1 (at least a combination of two predictor variables), the accuracy of predicting a good outcome is 94%.

Table 1. Demographic Profile Associated with Outcome among TOF patients.

	Good outcome (n=120)	Poor outome (n=63)	Total (n=183)	p value
	Frequency (%)			
Age				0.036
1-3	55 (45.83)	28 (44.44)	83 (45.36)	
3-6	40 (33.33)	16 (25.40)	56 (30.60)	
6-12	24 (20)	13 (20.63)	37 (20.22)	
>12	1 (0.83)	6 (9.52)	7 (3.83)	
Sex				0.580
Male	68 (56.67)	33 (52.38)	101 (55.19)	
Female	52 (43.33)	30 (47.62)	82 (44.81)	

Table 2a. Clinical and Echocardiographic Pre-operative Variables Associated with Outcome Among TOF Patients.

Clinical Indicators	Good outcome (n=120)	Poor outome (n=63)	Total (n=183)	p value
	Frequency (%); Mean + SD; Median (IQR)			
Nutritional status	-1 (-2 to-1)	-2 (-3 to-1)	-1 (-2 to-1)	<0.001
None to mild	82 (68.33)	18 (28.57)	100 (54.64)	<0.001
Moderate	25 (20.83)	22 (34.92)	47 (25.68)	
Severe	13 (10.83)	23 (36.51)	36 (19.67)	
Hematocrit	58.56 + 6.85	61.30 + 7.65	59.50 + 7.23	0.014
< 50	6 (5)	5 (7.94)	11 (6.01)	0.007
50 to 65	90 (75)	33 (52.38)	123 (67.21)	
> 65	24 (20)	25 (39.68)	49 (26.78)	
O2 saturation	68.4 + 6.63	69 + 6.86	68.61 + 6.70	0.566
< 75	95 (79.17)	50 (79.37)	145 (79.23)	0.975
≥ 75	25 (20.83)	13 (20.63)	38 (20.77)	
Left ventricular dimension				
LVEDD	-2 (-3 to-1)	-4 (-5 to-4)	-2.8 (-4 to-2)	<0.001
>-2	86 (71.67)	3 (4.76)	89 (48.63)	<0.001
≤-2	34 (28.33)	60 (95.24)	94 (51.37)	
Nakata Index	188 (156 to 257)	132 (88 to 158)	169 (113 to 213)	<0.001
< 100 (0)	13 (10.83)	26 (41.27)	39 (21.31)	<0.001
≥ 100 (1)	107 (89.17)	37 (58.73)	144 (78.69)	
McGoons	1.9 (1.75 to 2)	1.4 (1.3 to 1.4)	1.8 (1.4 to 2)	<0.001
≥ 1.5 (1)	112 (93.33)	9 (14.29)	121 (66.12)	<0.001
< 1.5 (0)	8 (6.67)	54 (85.71)	62 (33.88)	
RPA	-1 (-2 to-1)	-3 (-3 to-3)	-2 (-3 to-1)	<0.001
<-2 (0)	13 (10.83)	48 (76.19)	61 (33.33)	<0.001
≥-2 (1)	107 (89.17)	15 (23.81)	122 (66.67)	
LPA	0 (-1 to 0)	-3 (-3 to-3)	-1 (-3 to 0)	<0.001
<-2 (0)	5 (4.17)	54 (85.71)	59 (32.24)	<0.001
≥-2 (1)	115 (95.83)	9 (14.29)	124 (67.76)	
PV annulus	-1 (-3 to-1)	-3 (-4 to-2)	-2 (-3 to-1)	<0.001
≤-2 (0)	51 (42.50)	51 (80.95)	102 (55.74)	<0.001
>-2 (1)	69 (57.50)	12 (19.05)	81 (44.26)	
PHLEBOTOMY	42 (35)	37 (58.73)	79 (43.17)	0.002

Table 2b. Outcomes

	Frequency (%); Median (IQR)
With complications	63 (34.41)
Length of stay	10 (10 to 18)

Table 3. Univariate Analysis of the Variables Predictive of the Outcome

Variables	Beta-coefficient	Crude Odds ratio (95% CI)	P Value
Nutritional status			
None to mild	(reference)	(reference)	-
Moderate	-1.38	0.25 (0.12 to 0.4)	<0.001
Severe	-2.08	0.12 (0.05 to 0.29)	<0.001
Hematocrit			
< 50	(reference)	(reference)	-
50 to 65	0.82	2.27 (0.65 to 7.95)	0.199
> 65	-0.22	0.8 (0.22 to 2.97)	0.739
O2 saturation			
< 75 (1)	(reference)	(reference)	-
≥ 75 (2)	0.01	11.01 (0.48 to 2.15)	0.975
Left ventricular dimension			
LVEDD			
>-2 (0)	3.92	50.6 (14 to 172)	<0.001
≤-2 (1)	(reference)	(reference)	-
Nakata Index			
< 100 (0)	(reference)	(reference)	-
≥ 100 (1)	1.76	5.78 (2.7 to 12.41)	<0.001
McGoons			
≥ 1.5 (1)	4.43	84 (30 to 229)	<0.001
< 1.5 (0)	(reference)	(reference)	-
RPA			
<-2 (0)	(reference)	(reference)	-
≥-2 (1)	3.27	26.34 (11.6 to 59)	<0.001
LPA			
<-2 (0)	(reference)	(reference)	-
≥-2 (1)	4.93	138 (44 to 431)	<0.001
PV annulus			
≤-2 (0)	(reference)	(reference)	-
>-2 (1)	1.75	5.75 (2.78 to 11.9)	<0.001
With phlebotomy	-0.97	0.38 (0.20 to 0.71)	0.002

Table 4. Multivariate Analysis of the Variables Predictive of the Good Outcome.

Variables	Adjusted Beta-coefficient	P Value	Score
LVEDD >-2	2.16	0.007	2
McGoons > 1.5	2.89	<0.001	3
LPA >-2	3.16	<0.001	3
Constant	-3.73	-	-4

Table 5. Proposed Scoring System to Predict Good Outcome Post TOF-correction.

PREDICTOR	SCORE	ASSIGNED SCORE RANGE
LVEDD		0 to 2
LVEDD >/=-2	2	
LVEDD <-2	0	
McGoon's Ratio		0 to 3
>/= 1.5	3	
< 1.5	0	
LPA		0 to 3
>/=-2	3	
<-2	0	
Constant		- 4

Highest Possible Score = LVEDD >/= -2 (2) + McGoon's Ratio >/= 1.5 (3) + LPA >/= -2 (3) – Constant (4) = 4

Lowest Possible Score = LVEDD < -2 (0) + McGoon's Ratio <1.5 (0) + LPA <-2 (0) – Constant (4) = -4

Table 6. Diagnostic Accuracy of Scoring System to Predict Good Outcome

Cut point	Sensitivity	Specificity	LR+	LR-	Accuracy
> 1	95%	92.06%	11.97	0.05	93.99%

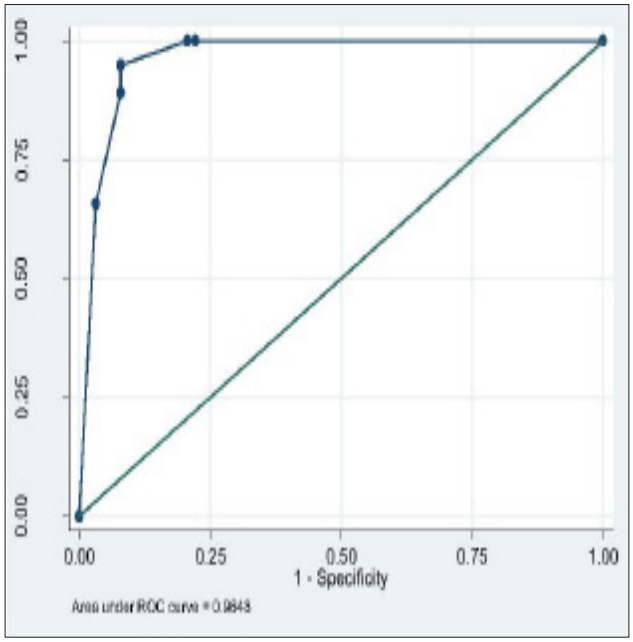

Figure 1. ROC analysis of the Scoring System Using the Three Variables in Predicting Good Outcome of TOF Surgery among Pediatric Patients, Philippines Heart Center January 2006 to December 2015.

DISCUSSION

In 1945, the first surgical palliation for Tetralogy of Fallot was performed by Blalock and Taussig. Since then, primary corrective repair has been noted to be done safely across all ages with post-operative complications still noted to occur. To help improve outcomes, this study was carried out to determine pre-operative clinical and echocardiographic variables that may help predict a good surgical outcome. In recent years, several pre-operative characteristics were identified to be predictive of good outcome including adequacy of pulmonary artery sizes, pulmonary valve annulus and left ventricular end-diastolic diameter. Even age at one point became crucial as to the success of surgical correction until several researches were published claiming that even neonates could go undergo successful TOF surgery with minimal complications. However, in a study by Ooi et al, although early surgery may be done in infants less than three months old, these patients are more likely to experience post-operative complications like prolonged ventilator support.[6] In our setting where resources are meager, despite the promising results of earlier surgery, patient tend to be operated on at a much later time.

In this study, although not significant, majority of the patients who were operated on between 1 to 6 years old showed good outcomes in almost 80% of the cases. Although without statistical significance, data on nutritional status showed that patients who were moderately and severely wasted were more likely to experience bad outcomes. In this study, significant variables included left ventricular end diastolic diameter, pulmonary valve annulus, Nakata Index, McGoons ratio and RPA and LPA sizes based on the Z-score normogram, with both the Nakata Index and McGoon's being dependent on pulmonary artery diameters. In a study of Park et al, the most common cause for re-operation was pulmonary artery stenosis.[7] However, conflicting evidences as to the efficacy of Nakata Index in predicting operative survival in earlier years have led physicians to prevent from using it and turn instead to McGoon's ratio and absolute pulmonary artery sizes. Other indicators such as history of phlebotomy and level of hematocrit pre-operative did not seem to influence a good outcome.

As a result of this study, three objective pre-operative variables could provide a simple and quick pre-operative assessment of patients being considered for surgical correction. McGoon's and LPA size support previous findings that adequate pulmonary artery sizes were critical in the success of any TOF surgery. This was supported by findings of Kirklin et al where it was noted that underdevelopment of the pulmonary arteries increased the risk of surgical mortality in TOF.[8] Left ventricular end diastolic diameter post surgery because it reflects the capacity of the left ventricle to handle the volume that is now being delivered to it from the right side. The pre-operative physiology of TOF is characterized by reduced pulmonary blood flow hence an untrained LV.[9] The unprepared LV may then go into dysfunction once correction is done. In this study, an LV end diastolic diameter measurement of =/> -2 is a an indicator of good outcome. Under the Receiver Operator Curve, at least any two of these variables may be used to predict a good outcome for all patients pre-operatively, with a minimum score of 1 providing 94% accuracy.

CONCLUSION

Surgical correction for Tetralogy of Fallot has yielded good results over the years. However, patients with this condition still face serious post-operatie complication. This study was able to identify several clinical and echocardiographic variables which showed significant relationships to a good outcome post-TOF surgery. Although not modifiable, these variables may provide data as to the right timing for a successful correction. Furthermore, a validation study must be done to test the accuracy of the variables identified in this research.

REFERENCES

1. Shinebourne E, Babu-Narayan S, Carvalho J. Tetralogy of fallot: from fetus to adult. Heart 2006 Sep; 92(9): 1353-1359
2. Arsdell G, Maharaj G, Tom J, Rao V, Coles J. What is the optimal age for repair of Tetralogy of Fallot. Circulation. 2000;102.
3. Hirsch J, Mosca R, Bove E. Complete repair of tetralogy of fallot in the neonate. Annals of surgery. 2000 Oct; 232(4): 508-514.
4. Saygi M, Ergul Y, Tola H, Ozyilmaz I, Ozluric E. Factors affecting perioperative mortality in tetralogy of Fallot. Pediatr Int. 2015 Oct;57(5):832-9
5. Egbe, A, Mittnacht A, Nguyen K, Joashi U. Risk factors for morbidity in infants undergoing tetralogy of fallot repair. Ann pediatr cadiol. 2014 Jan-Apr; 7(1): 13-18.
6. Ooi A, Moorjani N, Baliulis G, Keeton B, Salmon A et al. Medium term outcome for infant repair in tetralogy of fallot: indicators for timing of surgery. Eur J Cardiothoracic Surg. 2006 Dec; 30(6):917-922.
7. Park C, Lee J, Lim H, Kim W, Kim Y. The long-term result of total repair for tetralogy of fallot. Eur J Cardiothoracic Surg. 2010 Sep; 38(3):311-317.
8. Kirklin JW, Blackstone EH, Jonas RA et al. Morphologic and surgical determinants of outcome events after repair of tetralogy of fallot. A two-institution study. J. Thoracic. Cardiovascular Surg. 1992; 103:706-23.
9. Zervan K, Male C, Benesch T, Salzer-Muhar U. Ventricular interaction in children after repair of tetralogy of fallot: a longitudinal echocardiographic study. Eur J Echocardiogr. 2009 July; 10(5):641-646.PHC

Cardiovascular Surgery and Anesthesia

Factors Associated with Unfavorable Early Outcomes in Patients with D-Transposition of the Great Arteries Undergoing Arterial Switch Operation

Princess Pearl L. Lopez, MD; Florian R Nuevo, MD; Renato Pacis, MD

Background **---** Arterial Switch Operation (ASO) remains to be a formidable operative procedure with a high mortality rate. The main objective of this study was to determine the pre-operative, intra-operative and post-operative variables associated with early unfavorable outcomes, with the hope that we can identify significant contributory factors that can eventually be improved upon.

Methods **---** This is a retrospective review of 60 ASO patients in a tertiary hospital between January 2013 to December 2017. The variables were gathered by manual chart review. Data were analyzed for their association to unfavorable early outcomes.

Results **---** A total of 60 patients were included; mean age is 5.9 months. Forty-five out of 60 patients (75%) had early unfavorable outcomes, with a mortality rate of 48%; only 15 out of 60 patients (25%) had favorable outcomes. Age (p=0.098), gender (p=1.000), weight (p=0.087), length of hospital stay (p=0.092) and ICU stay (p=0.334), inotropic score (p=0.335), first 24-hr bleeding volume (p=0.521) and urine output (p=0.349) did not differ between patients with unfavorable and favorable outcomes. Variables associated with unfavorable early outcomes are prolonged bypass and ischemic time (p=0.005), prolonged interval time from intubation to cutting time (p=0.007), low post-bypass MAP (p=0.027), prolonged postop ventilation time (p=0.005). For every hour increase in bypass time, this increases the odds of having unfavorable outcome by 97% [OR = 1.97; 95% CI: 1.09 to 3.54]. For every hour increase in the intubation to cutting time, this increases the odds of having unfavorable outcome by a factor of 12.25 [95% CI: 2.00 to 75.00].

Discussion **---** Prolonged bypass time, ischemic time, intubation to cutting time are significant factors that contribute to early unfavorable outcome of patients. ***Phil Heart Center J 2021;24(2):56-63.***

Key Words: ■ Arterial Switch Operation ■ d-TGA ■ unfavorable outcomes

The arterial switch operation (ASO) has evolved from a pioneering neonatal procedure to a reproducible technique allowing anatomic repair of transposition of the great arteries (TGA).[2] Outcomes in the modern era are excellent, conferring at least 90% twenty year survival to those children treated at experienced medical centers. Advances in prenatal diagnosis, neonatal care, surgical intervention in the first days of life, surgical techniques, anesthetic man agement, perfusion strategies, postoperative care, and long - term cardiology surveillance have afforded an overall excellent quality of life to perioperative survivors of the ASO.[12]

Previous risk factor analysis have identified "complex d-TGA" and "simple d-TGA with VSD" as risk factors for mortality, but additional details are needed for accurate pre-operative risk stratification, operative planning, and family counseling. Central to surgical planning decisions is the ability to distinguish between patients who have uncorrectable anatomy and those whose anatomy provides technical difficulty and consequent morbidity associated with longer cardiopulmonary bypass and circulatory arrest times. [3,4]

Finalist, Poster Presentation - Original Paper. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Princess Pearl L. Lopez.*** Department of Cardiovascular Surgery and Anesthesia. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

Multiple studies have implicated that the most common cause of early mortality was coronary events related myocardial ischemia: Pretre and his colleagues (6% early mortality),[6] Prandstetter and co (1.75%)[7] Fricke and co (2.8%)[8] and 2.2% early mortality in shim and his associates.[9] Age of operation is also considered a factor. But in a study done by Mekkawy, there was no statistical significance correlating bad outcome with different age groups who underwent ASO.[5] Prolonged ischemic time is also a significant predictor for unfavorable outcome. Lastly, combined preoperative and intraoperative use of gluco-corticoids in neonatal cardiac surgery does not favorably affect early clinical outcomes and may exacerbate perioperative renal dysfunction.[10]

The objective of this study was to determine the pre-operative, intra-operative and post-operative variables associated with unfavorable early outcomes in ASO, with the hope that we can identify significant contributory factors that we can eventually improve upon.

METHODS

This is a retrospective cohort study, approved by the Institutional Review Board with waiver of the informed written consent. All patients diagnosed with d-TGA who underwent ASO between January 2013 to December 2017 were included. All other patients who underwent ASO for other congenital anomalies, such as DORV and those who underwent double switch procedure were excluded. Patients who died intra-operatively were excluded as well.

All medical charts of the 60 patients were reviewed including echocardiography, cardiac catheterization data and operative reports. A data collection sheet was created to systematically gather the pre-operative, intra-operative and post-operative variables as we manually do our chart review.

We defined these events as "unfavorable early outcomes": (1) highest inotropic score in the first 48 hours, (2) bleeding in the first 24 hours/kg in ml, (3) need for ECMO, (4) capillary leak syndrome, (5) reoperation, (6) infection, (7) interval time to secondary sternal closure (in days), (8) post-operative ventilation time (in days), (9) length of ICU stay (in days) and (10) length of hospital stay (in days).

Sample Size: A minimum sample size of 62 patients was required for this study. This value gives 80% power to detect an effect size of 1.08841 at 0.05 α-level of significance. The 7.2 odds ratio of early mortality among infants was based on a study by Blume ED et al. in 1999.[3]

Statistical Analysis: Mean and standard deviation were used to summarize data in quantitative form. Median and interquartile range (IQR) was used in the inotropic score. Counts and percentages were used in categorical variables. Independent *T*-test was used to compare the demographic profile, such as age and weight of two groups of patients while Fisher's exact test was used in gender. Mann-Whitney test was used to compare the inotropic score of patients with improved and unfavorable outcome.

Binary logistic regression was used to identify the factors leading to unfavorable outcome of patients. All the statistical tests were performed in SPSS ver. 20.0. P-values less than 0.05 were considered significant.

RESULTS

The preoperative, operative and postoperative data gathered were summarized in Table 1, Table 2, Table 3, respectively.

A total of 60 patients were included in the study, with a mean age of 5.9 months (range, 1 month to 7 years). Thirty-six (60%) are male and 24 (40%) are females. Their mean weight is 4.1 kg (range, 2.5 to 22), with mean duration of 27.1 days (range, 6 days to 3 months) and 7.6 days (range, 0 days to 1 month) in the hospital and ICU, respectively. (*Table 1)*

The mean age (p=0.098), weight (p=0.087), length of hospital (p=0.092) and ICU stay (p=0.334) did not differ between patients with unfavorable and favorable early outcomes. Gender (p=1.000) was not also significant.

None among the palliative interventions, preoperative steroids, and echocardiography findings were found to significantly differ with the early outcomes of patients.

Both the balloon atrial septosomy (p=0.346) and preoperative prostaglandin infusion (p=0. 662) did not show any significant difference on the outcome of patients. The coronary artery pattern was found to be a significant factor in favorable early outcome of patients (p=0.005). (*Table 1)*

With respect to anesthesia parameters, (*Table2*), the interval time from time of intubation to cutting time (p=0.002) was found to have a significance in affecting early outcome which showed that a prolonged interval time from intubation to cutting time showed unfavorable outcome.

Furthermore, the mean intubation to cutting time duration of patients with unfavorable early outcome is significantly longer (p=0.002), indicating that patients with unfavorable early outcome, at an average, had longer duration of intubation to cutting time by 0.5 hours [95% CI: 0.2 to 0.9].

Among the perfusion parameters, the bypass time and ischemic duration of those patients with unfavorable early outcomes are significantly longer (p=0.005) as compared to patients with favorable outcome.

This indicates that patients with unfavorable early outcome had longer duration of bypass time by 1.3 hours and ischemic time by 1.5 hours [95% CI: 0.4 to 2.1].

Additionally, the mean intubation to cutting time duration of patients with unfavorable early outcome is significantly longer (p=0.002), indicating that patients with unfavorable early outcome, at an average, had longer duration of intubation to cutting time by 0.5 hours [95% CI: 0.2 to 0.9].

Patients with unfavorable early outcome had significantly lower post-bypass MAP compared to patients with favorable outcome (p=0.019), which indicates that patients with unfavorable early outcome, at an average, had post-bypass MAP lower by 8.9 [95% CI: 1.5 to 16.2]

The inotropic score of patients with improved and with unfavorable outcome did not differ (p=0.335). Additionally, first 24-hr bleeding volume (p=0.521) and urine output (p=0.349) were not evident to be significant factors in the outcome of patients; ventilation time also did not show any significance as a predictor of unfavorable outcome (p=0.727) (*Table 3)*.

Among the 60 patients, 16 patients (26%) experienced morbidity. Table 4 Out of these, twelve patients (75%) experienced infection; 2 patients died, and 4 patients had community acquired pneumonia. Three of those had pseudomonas aeruginosa infection, one had stenotropomonas malthophila, and 4 had necrotising fascitis. Specific infections of the other three patients were not reported.

Eight (50%) patients experienced delayed sternal closure; 1 patient died. Seven patients (46%) had capillary leak syndrome, such as pulmonary edema (2 patients), hemorrhage and subdural hematoma (2 patient), massive bleeding (1 patient), edematous and bleeding of nose (1 patient), and minimal pericardial effusions (1 patient); out of these, 5 patients died.

Four (25%) had to undergo reoperation due to profuse bleeding (2 patients), mediastinal exploration due to blood clots on the posterior mediastinum, and abdominal distention; 3 of these patients died.

In summary, the bypass duration (p=0.024), intubation to cutting time duration (p=0.007) and post-bypass MAP (p=0.027) were the significant factors that contributed to unfavorable outcome of patients. This shows that for every hour increase in the duration of bypass, the odds of having unfavorable outcome will increase by 97% [OR = 1.97; 95% CI: 1.09 to 3.54]. An hour increase in the intubation to cutting time increases the odds of having unfavorable outcome by a factor of 12.25 [95% CI: 2.00 to 75.00]. On the contrary, 1 mmHg increase in the post-bypass MAP decreases the odds of having unfavorable outcome by 8% [OR = 0.92; 95% CI: 0.85 to 0.99].

Table 1. Baseline Characteristic of the patients

Demographics & Clinical Profile Number of PAtients	All (n=61)	Early Outcome		p-value
		Unfavorable (n=45)	Favorable (n=16)	
		Median (IQR)		
Age (years)	0.83(0.08 to 12)	0.67 (0.17 to 12)	1.92 (0.08 to 9)	0.391
<15 days	11(25%)	6(22.2%)	5(29.4%)	
15 to 30 days	20(45.5%)	23(48.2%)	7(41.2%)	
>30 daysto 1 year old	10(22.7%)	14(29.6%)	2(11.8%)	
> 1 year	3(6.8%)	0(0%)	3(17.7%)	
Gender: Male	36(60%)	22(50%)	14(31.8%)	1.000
Weight (Kg)	3.2(3 to 3.9)	3.2(2 to 3.7)	3.5(3.2 to 4.6)	0.140
Length of hospital stay (days)	25(14 to 32)	25(14 to 32)	29(20 to 37)	0.259
Length of ICU stay (days)	5(4 to 10)	5(4 to 10)	5(4 to 18)	0.691
Palliative Intervention				
Balloon Atrial Septosomy	18(40.9%)	13(48.2%)	5(29.4%)	0.346
Prostaglandin	38(86.4%)	24(88.9%)	14(82.4%)	0.662
Coronary Pattern:Different	32 (72.7%)	16(59.3%)	16(94.1%)	0.005
Echo Findings				
LV mass (g)	23(20 to 30)	23(20 to 28)	25(21 to 45)	0.335
VSD characteristic				0.431
Subaortic Large	1(2.3%)	1(3.7%)	0(0%)	
Pulmonic	1(2.3%)	0(0%)	1(5.9%)	
Muscular	4(9.1%)	4(14.8%)	0(0%)	
Perimembranous	12(27.3%)	7(25.9%)	5(29.4%)	
None	18(40.9%)	11(40.7%)	7(41.2%)	
IVS	14(31.8%)	9(33.3%)	5(29.4%)	1.000
ASD	5(11.4%)	3(11.1%)	2(11.8%)	1.000
PS	3(6.8%)	1(3.7%)	2(11.8%)	0.549
Pulmonary Artery Stenosis	1(2.3%)	1(3.7%)	0(0%)	1.000
TV Regurgitation	1(2.3%)	0(0%)	1(5.9%)	0.386
LVOTO OR PS	17(38.6%)	11(40.7%)	6(35.3%)	0.761
PDA length (cm)	03.(0.3 to 0.37)	0.3(0.3 to 0.37)	0.40(0.25 to 0.50)	0.130
PFO (cm)	0.36(0.25 to 0.41)	0.4(0.25 to 0.4)	0.34(0.24 to 0.45)	0.755
Coarctation of Aorta	1(2.3%)	1	0	1.000
Presence of Interruped Arch	0(0%)	0(0%)	0(0%)	-

Values Expressed as mean ± SD, or counts (%).

Table 2. Intra-operative findings

Parameters Number of Patients	All (n=61)	Early Outcome Unfavorable (n=45)	Early Outcome Favorable (n=16)	p-value
		Frequency (%) Median (IQR)		
Perfusion Parameters				
Pre-bypass urine output (cc)	5 (2 to 6)	5 (2 to 5)	5 (2 to 10)	0.298
Post-bypass urine output (cc)	13.5 (7 to 40)	10 (6 to 36)	35 (25 to 100)	0.009
Bypass Duration (hours)	4.4 ± 1.6	4.9 ± 1.8	3.6 ± 1.1	0.005
Ischemic Duration (hrs)	2.9 ± 1.1	3.1 ± 1.2	1.6 ± 0.8	0.005
Total Cardioplegia	410 (180 to 600)	390 (180 to 600)	450 (180 to 700)	0.680
No. of Plegia Doses	4 (3 to 6)	4 (3 to 6)	5 (4 to 6)	0.317
No. of rebypass episodes	0 (0 to 1)	0 (0 to 1)	0	0.625
No. of reclamping episodes	18 (36)	17 (37.78)	1(20)	0.642
Lowest temperature (°c)	28 (28 to 32)	28 (28 to 32)	28 (28 to 28)	0.371
Anesthesia Airway Management				
Pre-op Oxygen saturation (%)	73.2 ± 11.2	71.0 ± 12.4	76.4 ± 8.4	0.129
Combined Induction Technique	40 (90.9%)	25 (92.6%)	15(88.2%)	0.634
received intubated	9 (20.5%)	7 (25.9%)	2(11.8%)	0.445
intubation to Cutting Time (hrs)	1.3 ± 0.6	1.5 ± 0.6	1.0 ± 0.4	0.002
Heart Rate				
Pre-bypass heart rate	151.2 ± 22.6	155.2 ± 20.1	144.9 ± 25.5	0.145
Post-bypass heart rate	130.0 ± 30.0	125.8 ± 33.1	136.4 ± 24.1	0.264
Pre-bypass MAP	61.2 ± 12.0	61.5 ± 11.7	60.8 ± 12.8	0.861
Post-bypass MAP	50.8 ± 12.3	47.3 ± 12.9	56.2 ± 9.4	0.019
Hematocrit				
Pre-bypass hematocrit	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.082
Post-bypass Hematocrit	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.0	0.336
Drugs Anesthetic				
Sevoflurane (%)	1.2 ± 0.6	1.2 ± 0.7	1.3 ± 0.5	0.578
Midazolam Dose (mg)	0.9 ± 0.7	1.0 ± 0.8	0.8 ± 0.7	0.553
Fentanyl Dose (cc)	2.0 ± 0.7	2.0 ± 0.6	2.1 ± 0.8	0.571
Rocuronium (mg)	4.2 ± 3.7	3.4 ± 1.3	5.6 ± 5.7	0.159

Values Expressed as mean ± SD, or counts (%).
p-values are based on Independent t-test or Fisher's test.

Table 3. Post-operative data

ICU Parameters Number of Patients	All (n=61)	Early Outcome Unfavorable (n=45)	Early Outcome Favorable (n=16)	p-value
		Median (IQR)		
*Inotropic Score	17.0(10.0 - 29.0)	22.5(9.8 - 29.3)	16.0(10.0 - 23.7)	0.335
First 24-hours bleading volume (cc)	40(27 to 70)	40(30 to 76)	40(25 to 70)	0.513
Ventilation Time(days)	3(2 to 5)	3(2 to 5)	3(2.7)	0.727
First 24-hours urine output (cc)	138(75 to 220)	138(72.5 to 220)	140(94 to 300)	0.620

Values expressed as mean ± SD or median (IQR)
* Mann-Whitney Test for introtopic
p-values are based on binary logistic regression

Table 4. Morbidity experienced post-operatively

Morbidity	Number of Patients
Delayed sternal closure	8 (50%)
Infection	12 (75%)
Capillary leak syndrome	7(45%)
Reoperation	4 (25%)

Table 5.Early Outcome of patients

Outcome	Number of Patients
With presence of;	
Mortality	29 (48.0%)
Morbidity	16 (26.7%)
Favorable	15 (25.3%)

DISCUSSION

The apparent improvement in the outcome of patients undergoing arterial switch operations in the modern era, albeit continued differences in morbidity and mortality rates, encouraged us to do a review study in our own institution. We wanted to determine the different perioperative factors that can affect early post-operative outcome.

This five-year review of the ASO operations done in our Institution revealed that the significant factors which contributed to unfavorable early outcome of patients included the following, namely (1) bypass duration (p=0.024), (2) intubation to cutting time duration (p=0.007) and (3) a low post-bypass mean arterial pressure (MAP) (p=0.027). The only significant factor (p=0.005) associated with a favorable early outcome of patients was the coronary artery pattern, that is, those patients with coronary arteries arising from different ostia.

The mean age (p=0.098), gender (p=1.000) weight (p=0.087), length of hospital (p=0.092) and ICU stay (p=0.334) did not differ between patients with unfavorable and favorable outcomes. This was consistent with a study done by Mekkawy et al.[5] In another study by Ismail et al.,[14] arterial switch operation can still be tolerated beyond the first month of life in patients with intact ventricular septum (IVS) provided that the left ventricle (LV) remains well conditioned. Also, Kang et al [15] in their study showed no difference in outcome in terms of in-hospital mortality (5.5% versus 3.8%) or need for mechanical circulatory support (3.6% versus 5.7%)' between early and late arterial switch groups.

Palliative interventions, both the balloon atrial septostomy (BAS) (p=0.346) and Prostaglandin (p=0.662) and 2D-Echo findings showed no statistical significance in the outcome of patients.

A new and interesting finding in this review is the significant effect of a prolonged interval time between intubation to cutting time (p=0.002) among patients with unfavorable early outcome. This interval time reflected the time spent from induction, laryngoscopy/intubation, successful placement of central venous access and arterial lines, asepsis and antisepsis and draping, until the surgeon is ready to start the procedure.

Concerning ischemic and bypass time, we found that there was strong statistical significance of having unfavorable outcome with prolongation of the ischemic time (p=0.005) and statistical significant tendency towards having unfavorable outcome with increased bypass time (p=0.005). These results are consistent with what was found in other studies done by Blume et al[3] and Stoica et al.[16]

RECOMMENDATIONS AND LIMITATIONS OF THE STUDY

This review has shown that our process of patient selection and preparation for ASO procedures have no significant influence anymore on patient outcome. Rather, we have reaffirmed that the proficiency in surgical and anesthesia care can significantly affect unfavorable early outcomes in ASO. May this observation encourage more skills laboratory workshops to hone pertinent surgical and anesthesia skills in the care of TGA patients.

We also hope that the data registry on ASO procedures continue and include parameters that can monitor and reflect improvement on the skills and its effect on patient outcome.

The authors acknowledge the difficulty of doing a manual review of each chart. We found that the problems of non-standardized reporting, non-legible writing, and incomplete or missing data could have affected the data gathered and hence, the results of the statistical analysis made in this study.

CONCLUSION

Low birth weight, age at operation, pre-operative corticosteroids, palliative intervetions preoperatively carry no added benefit for the patients. However, longer bypass and ischemic time, prolonged postoperative ventilation time have consistently been identified as a risk for unfavorable outcome. Furthermore, the new observation that a prolonged interval time from intubation to cutting time is associated with unfavorable early outcome should be taken into consideration. Thus, it is quite interesting to note that perioperative factors observed to be associated with unfavorable early outcomes are reflective of the proficiency in the skills of surgeons and anesthesiologists.

Therefore, it becomes very essential that the physicians involved in the perioperative care of TGA patients (transposition of the great arteries) must have undergone the necessary training and should have the capacities to provide proper supervision and assistance to the fellows-in training, so as to ascertain better or favorable patient outcomes.

REFERENCES

1. Arterial switch operation for transposition of great arteries. [online] Available at: http://pediatricct.surgery.ucsf.edu/conditions--procedures/arterial-switch-operation.aspx [Accessed 12 Sep. 2018].
2. Stoica S, Carpenter E, Campbell D, Mitchell M, da Cruz E, Ivy D, et al. Morbidity of the arterial switch operation Ann Thorac Surg. 2012 Jun;93(6):1977-83.
3. Blume ED, Altmann K, Mayer JE, Colan SD, Gauvreau K, Geva T. Evolution of risk factors influencing early mortality of the arterial switch operation. J Am Coll Cardiol. 1999 May;33(6):1702-9.
4. Hutter PA, Bennink GB, Ay L, Raes IB, Hitchcock, JF, Meijboom EJ. Influence of coronary anatomy and reimplantation on the long-term outcome of the arterial switch. Eur J Cardiothorac Surg. 2000 Aug;18(2):207-13.
5. Mekkawy A, Ghoneim A, El-Haddad O, Photiadis J, Elminshawy A. Predictors of early outcome of arterial switch operation in patients with D-TGA. J Egyptian Society of Cardio-Thoracic Surgery. 2017 Mar; 25(1):52-57.
6. Prêtre R, Tamisier P, Bonhoeffer P, Mauriat P, Pouard P, Sidi D, Vouhé P. Results of the arterial switch operation in neonates with transposed great arteries. Lancet. 2001 Jun 9;357(9271):1826-30.
7. Prandstetter C, Hofer A, Lechner E, Mair R, Sames-Dolzer E, Tulzer G. Early and mid-term outcome of the arterial switch operation in 114 consecutive patients: a single centre experience. Clin Res Cardiol. 2007 Oct; 96(10):723-9.
8. Fricke TA, d'Udekem Y, Richardson M, Thuys C, Dronavalli M, Ramsay JM, et al. Outcomes of the arterial switch operation for transposition of the great arteries: 25 years of experience. Ann Thorac Surg. 2012 Jul;94(1):139-45.
9. Man-shik S, Tae-Gook J, Yang JH, Park PW, Kang IS, Huh J, Young Song JY. Current expectations of the arterial switch operation in a small volume center: a 20-year, single-center experience J Cardiothorac Surg. 2016 Feb 24;11:34.
10. Graham EM, Atz AM, Butts RJ, Baker NL, Zyblewski SC. Standardized preoperative corticosteroid treatment in neonates undergoing cardiac surgery: results from a randomized trialJ Thorac Cardiovasc Surg. 2011 Dec;142(6):1523-9.
11. Naguib N, Tobias JD, Hall MW, Cismowski MJ, Miao Y, Barry N. The role of different anesthetic techniques in altering the stress response during cardiac surgery in children: a prospective, double-blinded, and randomized study. Pediatr Crit Care Med. 2013 Jun;14(5):481-90.
12. Latham GJ, Joffe DC, Eisses MJ, Richards MJ, Geiduschek JM. Anesthetic considerations and management of transposition of the great arteries. Semin Cardiothorac Vasc Anesth. 2015 Sep;19(3):233-42.

13. Chinn S. A simple method for converting an odds ratio to effect size for use in meta-analysis. Statistics in Medicine 2000; 19(1): http://www.aliquote.org/pub/odds_meta.pdf (accessed 3 July 2017).
14. Kabbani MS, Najm HK, Abusuliman RM, Elbarbary M. Early outcome for the primary arterial switch operation beyond the age of 3 weeks. Pediatr Cardiol. 2010 Jul;31(5):663-7.
15. Kang N, de Leval MR, Elliot M, Tsang V, Kocyildirim E, Sehic I, Foran J, Sullivan I. Extending the boundaries of the primary arterial switch operation in patients with transposition of the great arteries and intact ventricular septum. Circulation. 2004 Sep 14;110(11 Suppl 1):II123-7.
16. Stoica S, Carpenter E, Campbell D, Mitchell M, da Cruz E, Ivy D, Lacour-Gayet F. Morbidity of the arterial switch operation. Ann Thorac Surg. 2012 Jun;93(6):1977-83.

The First Minimally-Invasive Tricuspid Valve Annuloplasty for Ebstein's Anomaly in an Adult Filipino: a case report

Ana Katrina C. Longos, MD, Aimee Victoria B. Dalisay, MD, Raul D. Jara, MD

Introduction **---** Ebstein's Anomaly is a rare congenital heart condition with a varied clinical course ranging from intrauterine death to asymptomatic survival to late adulthood depending on the severity of the tricuspid valve deformity and dysfunction. Surgical intervention when warranted was previously done only through open surgical repair. To date in the Philippines, there are no published data on repair of the tricuspid valve in Ebstein's Anomaly via minimally invasive surgery.

Case **---** A 29-year old Filipina was seen in our institution due to decreasing functional capacity. She initially complained of easy fatigability and palpitations during her sixth month of pregnancy three years ago. She was then diagnosed to have Ebstein's Anomaly with concomitant secundum type atrial septal defect. She underwent minimally invasive surgery with tricuspid valve annuloplasty and atrial septal defect closure on July 2, 2018. Patient had an unremarkable post-operative course and was discharged 4 days after the surgery.

Discussion --- Our patient had a Celermajer Grade of 1, cardiothoracic ratio less than 60%, no right ventricular outflow tract obstruction and presentation was during adulthood. In our patient, these factors portended a favorable outcome with surgical intervention. Benefits of minimally invasive surgery seen in our patient were: reduced surgical trauma, minimal blood loss, shorter intensive care unit and hospital length of stay, and a more rapid return to functional activity.[9,18]

Conclusion **---** Ebstein's Anomaly is a rare congenital heart condition and the usual management is tricuspid valve repair or replacement. This is the first documented repair done via minimally invasive surgery in the Philippines. ***Phil Heart Center J 2021;24(2):64-69.***

Key Words: ■ adult Ebstein's Anomaly ■ minimally invasive surgery ■ tricuspid valve annuloplasty

Ebstein's anomaly is a rare congenital heart condition initially discovered by Wilhem Ebstein in 1886.[1] The common feature of the anomaly consists of apical displacement of the septal tricuspid valve leaflet in conjunction with leaflet dysplasia[2] and it occurs in approximately 1 in 20,000 live births and accounts for 0.3 to 0.7% of all cases of congenital heart disease.[3] It is also associated with other cardiac malformations; most commonly an interatrial communication in 80-94% of cases as either an atrial septal defect or patent foramen ovale.[4] The clinical course depends on the severity of the tricuspid valve deformity and dysfunction and ranges from intrauterine death to asymptomatic survival to late adulthood.[4-5]

The diagnosis is usually made by echocardiography with the following findings: apical displacement of the septal leaflet of the tricuspid valve by 8 mm/m^2 or more combined with the elongated sail-like appearance of the anterior leaflet.[3,6]

The management of Ebstein's anomaly ranges from medical management for mild forms to catheter ablation for patients with arrhythmias to surgical intervention.[5] Surgical intervention is given a class IC recommendation by the European Society of Cardiology for patients with more than moderate tricuspid regurgitation and symptoms (New York Heart Classification (NYHA) class > II or arrhythmias) or deterio-

Winner, Poster Presentation - Case Report. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Ana Katrina C. Longos.*** 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

rating exercise capacity.[7] In the study by Jara et al. involving a total of 28 patients with Ebstein's anomaly over the course of 20 years, it showed that tricuspid valve repair was done in 75% of the patients while 25% had tricuspid valve replacement and these were all done via open surgical approach.[8] Recent trends toward minimally invasive surgery have gained ground, due to its potential benefits such as: reduced surgical trauma, minimal blood loss, less re-operation for bleeding. Furthermore, pain, shorter hospital stay and rapid return to functional activity are cited as benefits.[9] To date in the Philippines, there is no published data on repair of the tricuspid valve in Ebstein's anomaly via minimally invasive surgery.

Case: A 29-year old, female, Filipino, with no known co-morbidities, born via normal spontaneous delivery to a healthy mother was seen in our institution due to complaints of decreasing functional capacity. Her mother had no complications during the pregnancy and had no history of lithium intake. Patient's symptoms started three years ago during the sixth month of her first pregnancy when she noted easy fatigability and palpitations. She sought consult where a 2D echocardiogram revealed Ebstein's anomaly. No medications were given and she was advised for close follow-up. She however still had persistence of the symptoms after the pregnancy and sought a second opinion. Another echocardiogram was done, this time with bubble contrast and the presence of an atrial septal defect was detected. She was then given Ivabradine 5mg tab once daily due to the palpitations.

The persistence of easy fatigability, palpitations, exertional dyspnea and occasional bipedal edema prompted consult and subsequent admission in our institution. On physical examination, patient was normotensive with blood pressure of 120/70 mmHg on the right arm and 110/70mmHg on the left arm, with heart rate of 68 beats per minute, afebrile, not in respiratory distress with normoxemia at room air with normal body mass index of 20.08 kg/m^2. Additional physical examination findings were: absence of cyanosis, absence of neck vein engorgement, vesicular breath sounds, adynamic precordium with apex beat at 5th left intercostal space, midclavicular line, with S1 > S2 at the apex, S2 > S1 at the base, with a grade 2/6 holosystolic murmur best heard at the lower left parasternal border increasing with inspiration with a right ventricular heave. There was no organomegaly, no bipedal edema, no clubbing of the nails. The electrocardiogram (*Figure 1*) revealed sinus tachycardia with normal axis, incomplete right bundle branch block with secondary ST-T wave changes.

Chest radiograph (*Figure 2*) showed normal to slightly increased pulmonary vascularity, cardiomegaly with right ventricular prominence and slightly prominent main pulmonary artery.

The 2-dimensional echocardiogram (*Figures 3-4*) revealed the following findings: apical displacement of the septal tricuspid leaflet by 14.8mm/m^2, atrial septal defect, secundum type with a predominantly left to right shunt. The right atrium, right ventricle and tricuspid valve annulus were all dilated. There was moderate tricuspid regurgitation, trivial mitral regurgitation and mild pulmonary hypertension.

Patient was appraised on surgical repair due to deteriorating exercise capacity. She had reservations on the prolonged recovery time of open surgical repair, hence minimally invasive surgery was offered. She underwent minimally invasive surgery with tricuspid valve annuloplasty utilizing Medtronic Contour 3D size 26 and atrial septal defect closure with total bypass time of 3 hours and 49 minutes and total ischemic time of 2 hours and 12 minutes. The operation was done via access through the right common femoral artery and right common femoral vein with incisions also done at the right inframammary area and at the right chest area. Post-operative transesophageal echocardiography (*Figures 5-6*) showed no residual shunt across the mid-interatrial septum, increased echogenecity noted at the tricuspid annular plane consistent with an annuloplasty ring with computed tricuspid valve area of 2.6 cm^2 by pressure-halftime with mean gradient of 1.4mmHg and tricuspid valve annulus of 2.4cm.

Patient had an unremarkable post-operative course and was discharged 4 days after the surgery. She showed improved functional capacity with no recurrence of palpitations nor easy fatigability on follow-up.

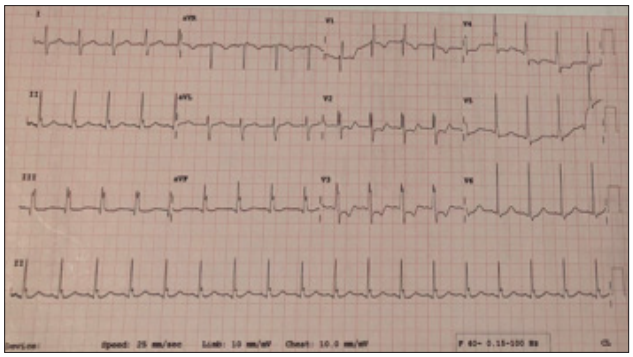

Figure 1. 12 lead electrocardiogram showing sinus tachycardia with normal axis of +84 degrees, incomplete right bundle branch block with secondary ST-T wave changes.

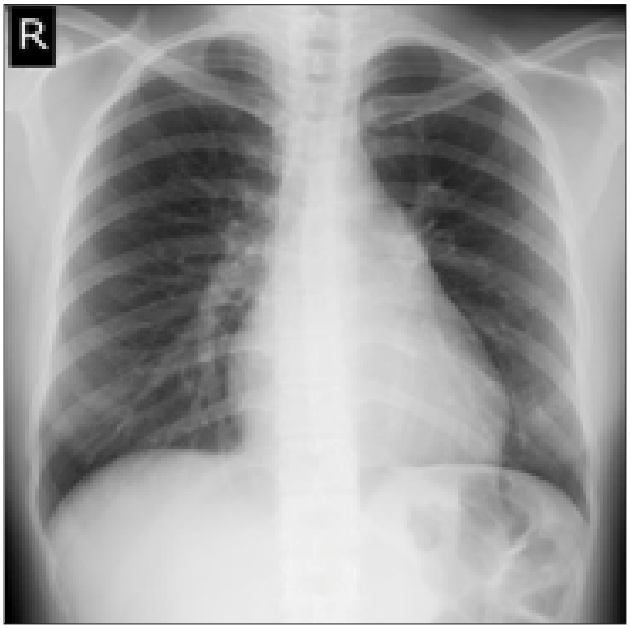

Figure 2. Chest radiograph showing cardiomegaly, slightly increased pulmonary vascularity and slightly prominent main pulmonary artery.

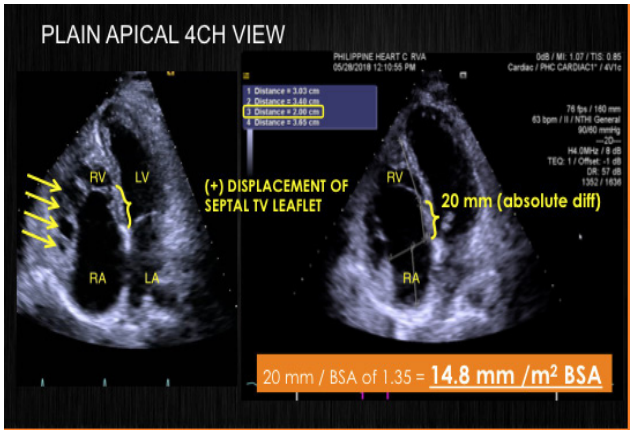

Figure 3. An apical 4 chamber view 2 dimensional echocardiogram showing apical displacement of the septal tricuspid valve leaflet by 14.8mm/m²

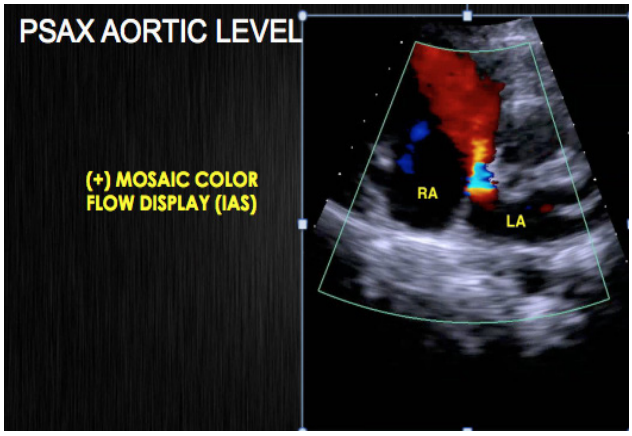

Figure 4. A parasternal short axis view 2 dimensional echocardiogram at the level of the aortic valve showing mosaic color flow display across the mid interatrial septum (IAS)

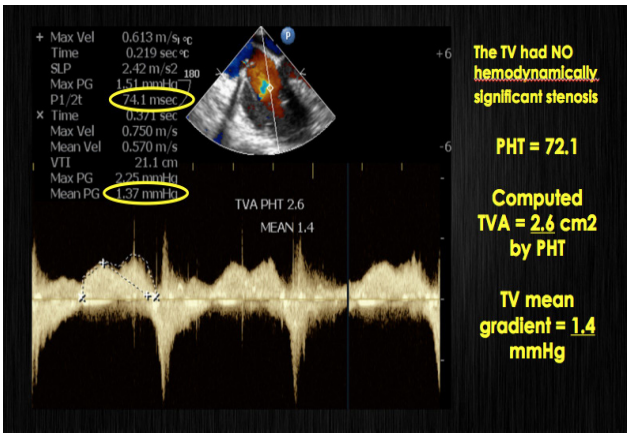

Figure 5. Post-operative transesophageal echocardiogram showing no hemodynamically significant tricuspid stenosis with computed tricuspid valve area (TVA) of 2.6 cm² by pressure half time (PHT) with a tricuspid valve mean gradient of 1.4 mmHg

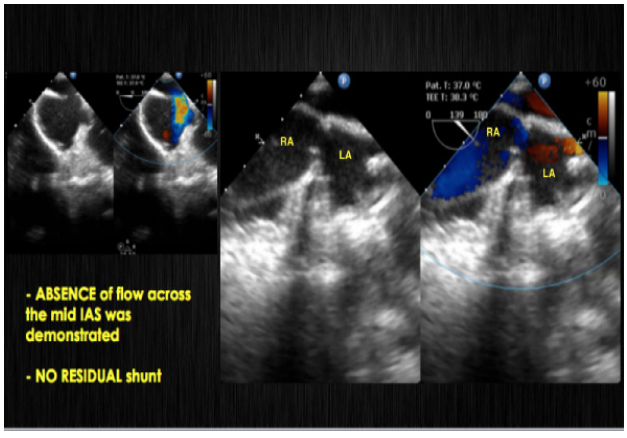

Figure 6. Post-operative transesophageal echocardiogram showing no residual shunt across the interatrial septum (IAS)

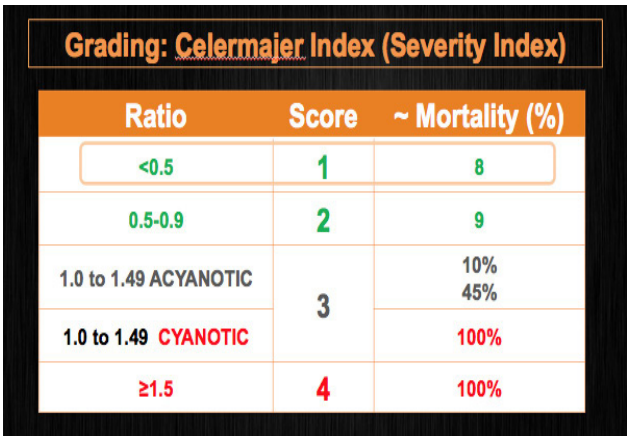

Figure 7. Celermajer Index showing the ratio and corresponding mortality rates

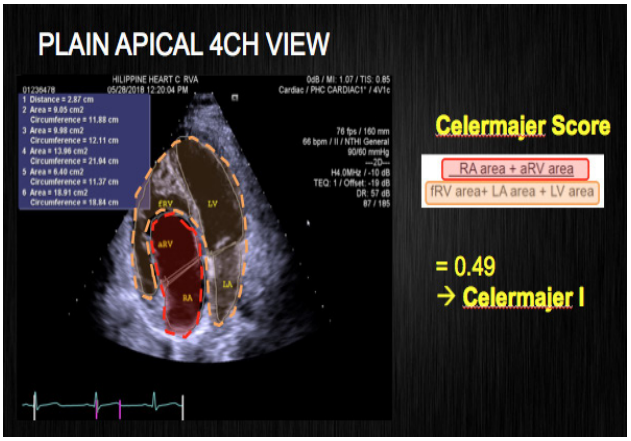

Figure 8. Celermajer Score of the patient

DISCUSSION

Ebstein's anomaly is a rare congenital heart condition occurring approximately 1 in 20,000 live births and accounting for 0.3 to 0.7% of all cases of congenital heart disease.[3] The clinical course depends on the severity of the tricuspid valve deformity and dysfunction and ranges from intrauterine death to asymptomatic survival to late adulthood.[4-5] Patients usually present with cyanosis, right-sided heart failure, arrhythmias and sudden cardiac death and it is dependent on age at presentation and degree of hemodynamic disturbance.[10] Adults usually present more with arrhythmias and decreasing exercise tolerance[11] as seen in our patient who has been acyanotic since birth but has only recently complained of easy fatigability, palpitations and exertional dyspnea. The main hemodynamic abnormality producing symptoms in Ebstein's malformationis the severity of the tricuspid regurgitation.[12] The tricuspid regurgitation in this case was only moderate and the shunt was from left to right. Hence, this patient had no cyanosis and only had complaints of easy fatigability and exertional dyspnea.

The diagnosis is usually made by echocardiography with the following findings: apical displacement of the septal leaflet of the tricuspid valve by 8 mm/m^2 or more combined with the elongated sail-like appearance of the anterior leaflet.[6] The patient had an apical displacement of the septal tricuspid leaflet of 20mm/m^2 (14mm/m^2 when adjusted to body surface area), which clinched our diagnosis for Ebstein's anomaly. An atrial septal defect was also noted on the echocardiogram and this is seen in 80-94% of cases.[4] The downward displacement of the septal tricuspid valve leaflet is associated with discontinuity of the central fibrous body and septal atrioventricular ring, thus creating a potential substrate for accessory atrioventricular connections and ventricular pre-excitation making the patient at risk of sudden death.[12] The patient had a normal PR interval but was noted to have incomplete right bundle branch block that is seen in 75-95% of cases in subjects without pre-excitation.[13] On chest radiograph, the patient was noted to have only mild cardiomegaly, slightly increased pulmonary vascularity and slightly prominent main pulmonary artery. A study by Attenhofer-Jost [14] noted that the cardiac silhouette may vary from almost normal to the typical Ebstein's anomaly configuration consisting of a globe-shaped heart with a narrow waist.

The displacement of the septal leaflet leads to division of the right side of the heart into three morphologic components: the right atrium proper; the inlet portion of the right ventricle which is the atrialized right ventricle; and the trabecular and outlet portion, which is the functional right ventricle.[12] Celermajer used this in 1992 to formulate an echocardiographic scoring system to describe the severity of the disease and to help guide the operative management (*Figure 7*). Our patient had a Celermajer grade of 1 with a ratio of 0.49 (*Figure 8*). The lowest mortality rate of 8% for Celermajer grade I is also associated with better surgical outcomes.[11]

The management of Ebstein's anomaly ranges from medical management for mild forms to catheter ablation for patients with arrhythmias to surgical intervention.[5] According to Driscoll, et al [15], surgery brings about a significant improvement in exercise tolerance in patients with an atrial septal defect as what was also seen in our patient. Surgical intervention is given a class IC recommendation by the European Society of Cardiology for patients with more than moderate tricuspid regurgitation and symptoms (New York Heart Classification (NYHA) class > II or arrhythmias) or deteriorating exercise capacity.[7] Valve repair is the preferred primary approach in most centers as seen in a study by Boston et al [16] and Li, et al.[17] They also found out in their study that if there is failure of the delamination of more than 50% of the anterior leaflet or if the leading edge of the leaflet has hyphenated or linear attachment to the right ventricle and when a durable repair may not be obtainable, valve replacement is then preferred. They showed similar freedoms from reoperation for recurrent tricuspid valve problems at 10 years.[16] A study done by Jara et al. documenting the early and late outcome of surgery in Ebstein's anomaly for the past 20 years (1992-2012) in Philippine tertiary centers showed that tricuspid valve surgery as a management strategy for Ebstein's anomaly had a preoperative mortality as high as 14% but the long-term survival of post-operative patients approximated that of 94%. Their study also showed that tricuspid valve repair was done in 75% of the patients while 25% had tricuspid valve replacement and these were all done via open surgical approach [8]. When compared to a standard median sternotomy approach, the potential benefits of minimally invasive valve surgery include: reduced surgical trauma, minimal blood loss, reduced rate of re-operation for bleeding, and pain; a shorter intensive care unit and hospital length of stay, as well as a more rapid return to functional activity. Isolated tricuspid valve repair has been associated with mortality rates of 8.2–9.5% while mortality rates with re-operative isolated tricuspid valve surgery have ranged from 13.2–37%.[9,18]

Univariate analysis by Celermajer, et al[11] showed that a significant risk of death was associated with Celermajer grade 4, cardiothoracic ratio >60%, associated right ventricular outflow tract obstruction and presentation in fetal life. Our patient had a Celemajer grade of 1, cardiothoracic ratio was less than 60%, there was no right ventricular outflow tract obstruction and presentation was during adulthood. In our patient, these factors portended a favorable outcome with surgical intervention.

CONCLUSION

Ebstein's anomaly is a rare congenital heart condition, and the usual management is tricuspid valve repair or replacement. To our knowledge, this is the first documented repair done via minimally invasive surgery in the Philippines.

REFERENCES

1. Ebstein W. Ueber einen sehr seltenen Fall von Insufficienz der Valvula tricuspidalis, bedingt durch eine angeborene hochgradige Missbildung derselben. Arch Anat Physiol. 1866; 238–255.
2. Zipes D, Libby P, Bonow R, Mann D, Tomaselli G, Braunwald E. Braunwald's heart disease. 11th ed. Philadelphia, PA: Elsevier Saunders, 2018.
3. Perloff J, Marelli A. Perloff's clinical recognition of congenital heart disease. 6th ed. Philadelphia, PA: Elsevier Saunders, 2011
4. Watson H. Natural history of Ebstein's anomaly of tricuspid valve in childhood and adolescence. An international co-operative study of 505 cases. Br Heart J. 1974 May;36(5):417-27.
5. Morray B. Preoperative Physiology, Imaging, and Management of Ebstein's Anomaly of the Tricuspid Valve. Semin Cardiothorac Vasc Anesth. 2016, 20(1):74-81.
6. Jara R, Anonuevo J. Philippine General Hospital adult congenital heart disease PATCHED. 2nd ed. UP-Manila: Section of Cardiology, 2016.
7. Baumgartner H, Bonhoeffer P, De Groot NMS, de Haan F, Deanfield JE, Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC), et al. ESC Guidelines for the management of grown-up congenital heart disease. Eur Heart J. 2010 Dec;31(23):2915-57.
8. Jara R, Javier A, Chiong L, Lasco J. Early and late outcome of surgery for Ebstein anomaly: a 20 year experience in Philippine tertiary centers. Philipp J Cardiol. 2013, 41 (1): 17-22.
9. Lamelas J. Minimal access tricuspid valve surgery. Ann Cardiothorac Surg. 2017 May;6(3):283-286

10. Attenhofer Jost C, Connolly H, Edwards W, Hayes D, Warnes CA, Danielson GK. Ebstein's anomaly – review of a multifaceted congenital cardiac malformation. Swiss Med Wkly 2005; 135: 269–281.
11. Celermajer DS, Bull C, Till JA, Cullen S, Vassillikos VP, Sullivan ID, et al. Ebstein's anomaly: presentation and outcome from fetus to adult. J Am Coll Cardiol 1994; 23: 170-6.
12. Frescura C, Angelini A, Daliento L and Thiene G. Morphological aspects of Ebstein's anomaly in adults. Thorac Cardiovasc Surg. 2000; 48(4): 203-208.
13. Kastor JA, Goldreyer BN, Josephson ME, Perloff JK, Scharf DL, Manchester JH, et al. Electrophysiologic characteristics of Ebstein's anomaly of the tricuspid valve. Circulation. 1975 Dec;52(6):987–995.
14. Attenhofer Jost C, Connolly HM, Dearani JA, Edwards WD, Danielson GK. Ebstein's anomaly. Circulation. 2007 Jan; 115(2): 277–285.
15. Driscoll DJ, Mottram CD, Danielson GK. Spectrum of exercise intolerance in 45 patients with Ebstein's anomaly and observations on exercise tolerance in 11 patients after surgical repair. J Am Coll Cardiol 1988 Apr;11(4):831–6.
16. Boston US, Dearani JA, O'Leary W, Driscoll DJ, Danielson GK. Tricuspid valve repair for Ebstein's anomaly in young children: a 30-year experience. Ann Thorac Surg. 2006 Feb;81(2):690-5; discussion 695-6.
17. Li B, Sun HS, Pan SW, Xu JP. Outcomes of Ebstein's anomaly patients treated with tricuspid valvuloplasty or tricuspid valve replacement: experience of a single center. Chin Med J 2018 May;131(9):1067-74.
18. Schmitto JD, Mokashi SA, Cohn LH. Minimally-invasive valve surgery. J Am Coll Cardiol 2010 Aug 3 56(6):455-62.

Unusual Organ Combination of Double Primary Malignancy, A Rare Biatrial High-Grade Myofibroblastic Sarcoma and Colonic Adenocarcinoma: a case report

Niña Carissa L. Alegado, MD; Desilu Aliza P. Lazaro, MD; Vince Ryan V. Muñoz, MD

Introduction **---**A double primary malignancy is a phenomenon that is now being increasingly recognized. However, the combination of a primary malignancy intercurrent with the heart and colon is extremely rare.

Case Presentation **---** This report highlights the case of a 50-year old Filipino female who presented with heart failure symptoms. A two dimensional echocardiogram revealed a biatrial mass attached to the interatrial septum. On the third hospital day, the patient underwent complete resection of the biatrial mass. The histopathologic findings and immunohistochemical staining were compatible with a high-grade myofibroblastic sarcoma.

A metastatic work up revealed a colonic mass on CT scan and confirmed with a colonoscopy. The patient opted to defer colonic surgery and was sent home with Warfarin. Two months later, the patient sought admission in another hospital for lower gastrointestinal bleeding. During the same admission, she underwent transverse hemicolectomy with complete excision of the colonic mass. Histopathologic findings revealed a low grade adenocarcinoma. The patient was later seen by an oncologist and initiation of Gemcitarabine was contemplated. Two weeks after surgery however, the patient was readmitted due to sudden onset of severe dyspnea after self- discontinuation of warfarin. She eventually expired with a consideration of massive pulmonary embolism.

Conclusion **---** Due to the disease's rarity, treatment development has proved to be elusive such that proper documentation of such cases is an important element to further research. ***Phil Heart Center J 2021;24(2):70-75.***

Key Words: ■ double primary malignancy ■ primary cardiac tumor

A double primary malignancy is not an uncommon phenomenon since its discovery a hundred years back. In reported autopsy series, multiple primary cancers originated in the same organs of the same system rather than unrelated organs.[1,2] While colonic malignancy ranks 3rd as the most common malignancy in the world,[3] extracolonic primary cancer is reported most frequently in the skin, stomach, breast, urinary bladder and prostate.[4,5,6] A concomitantly occurring primary colonic malignancy and a biatrial cardiac malignancy in a single patient, however, is a rarity in medical literature. In addition, a cardiac mass histologically classified as a high-grade myofibrobastic sarcoma has an extremely rare incidence, thus prompting us to publish the case.

CASE PRESENTATION

A 50 year old Filipino female was transferred to our institution due to progressive cough, dyspnea and bipedal edema for two months. The symptoms were non-resolving despite completion of multiple courses of antibiotics. The patient was non-hypertensive and non-diabetic but was previously admitted a year prior for stroke with residual right-sided weakness. The patient had no family history of cancer. Her physical examination at the emergency room showed a cachectic patient with stable vital signs except for tachycardia. There was no neck vein distention, but her chest and lung findings revealed decreased breath sounds bilaterally. Her heart was not enlarged with the PMI noted

Finalist, Poster Presentation - Case Report. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Nina Carissa L. Alegado.*** 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

at the 5th ICS left mid clavicular line, with note of thrills, but no murmur. The extremities had grade 2 bipedal edema with residual right-sided weakness in both upper and lower extremities. The blood chemistries and bleeding parameters were normal. The chest radiograph showed minimal bilateral pleural effusion with no pneumonic infiltrates. Her ECG showed sinus tachycardia within normal limits.

A transthoracic two-dimensional echocardiogram revealed a biatrial heterogenous echogenic masses with well delineated borders and broad attachment to the interatrial septum (*Figure 1A*). The left atrial mass measured 4.3x 3.8 cm with an area of 13 cm^2. The inferior pole of the mass crosses the mitral valve and prolapses into the ventricle during diastole causing an obstruction of the left ventricular inflow tract (*Figure 1B*). The right atrial mass measured 2.3x 2.1 cm with an area of 5.2 cm^2 (*Figure 1C*). The overall systolic function was normal with an EF 69% by Simpson's with mild mitral regurgitation and localized minimal pericardial effusion with no tamponade physiology. Coronary angiography revealed normal coronaries. The patient underwent resection of both atrial masses as well as a mitral valve annuloplasty. Post-surgical intraoperative transesophageal echocardiography done showed a trivial mitral regurgitation, with a mean gradient of 2.2, mild tricuspid regurgitation. No residual mass was noted attached to interatrial septum (*Figure 2B*).

Gross histologic examination of the resected masses showed irregular white to cream-white piecemeal excision specimens that were noted to be rubbery to firm (*Figure 3*).

Microscopic sections showed a vague fascicular pattern of smooth muscle bundles in a well vascularized connective tissue. The atypical spindle cells are elongated with hyperchromatic nuclei, inconspicuous nucleoli, eosinophilic or occasional fibrillar cytoplasm, and indistinct cell membranes with many abnormal mitosis seen. Necrosis was rare. Immunohistochemical studies of both specimens showed reactivity of the neoplastic cells to vimentin, smooth muscle actin and desmin; with non-reactivity to calponin and S100. The proliferation index is >90% using p53 and Ki-67. Differential diagnoses included high-grade myofibroblastic sarcoma and leiomyosarcoma. However, further immunohistochemical study using h-Caldesmon, a specific marker for smooth muscle tumors, showed non-reactivity thus totally ruling out leiomyosarcoma. The specimen was also examined by two independent pathologists who both concurred with the diagnosis of a high-grade myofibroblastic sarcoma (*Figure 4*).

Metastatic work up showed a plain cranial CT scan with chronic right basal ganglia infarct. The contrast chest CT scan showed two non-specific mediastinal lymph nodes and a small bilateral pleural effusion while contrast CT scan of the whole abdomen showed a circumferential wall thickening in the proximal transverse colon (*Figure 5A*). A colonoscopy confirmed the presence of a polypoid friable lesion occupying more than 80% of the lumen of transverse colon preventing further insertion of the scope (*Figure 5B*). Multiple biopsies were taken which were histopathologically consistent with a well differentiated adenocarcinoma. The patient was advised surgical intervention but opted to discharge and defer colonic surgery in the meantime. The patient was sent home on Warfarin and was advised follow up for protime monitoring with poor compliance. Two months later, she was admitted in another hospital for lower gastrointestinal bleeding for which she underwent transverse colectomy with end-to-end anastomosis, completely excising a 5.5x 3.0 x 3.0 cm brown tan, firm and fungating mass with serpiginous borders obstructing the lumen. The histopathologic study revealed a low grade adenocarcinoma. She was subsequently discharged after being seen by an oncologist with plan for Gemcitarabine treatment. However, the patient was readmitted two weeks post-discharge due to sudden onset severe dyspnea. History revealed self-discontinuation of warfarin. The patient eventually expired. A massive pulmonary embolism was considered.

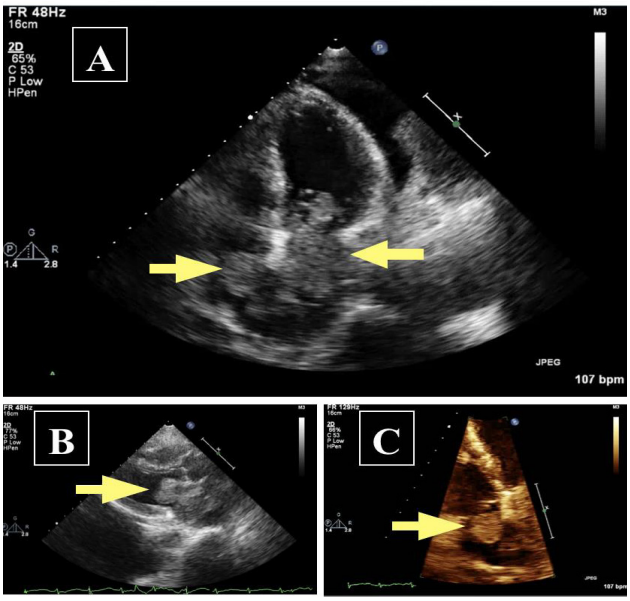

Figure 1. Echocardiography. (A) Four chamber view showing the biatral mass (yellow arrow) with minimal pericardial effusion without tamponade. (B) PLAX view showing the left artial mass (yellow arrow) with inferior pole of the mass crossing the mitral valve and prolasping into the ventricle during diastole causing obstruction of the left ventricular inflow tract. (C) Two chamber view showing the right artial mass (yellow arrow).

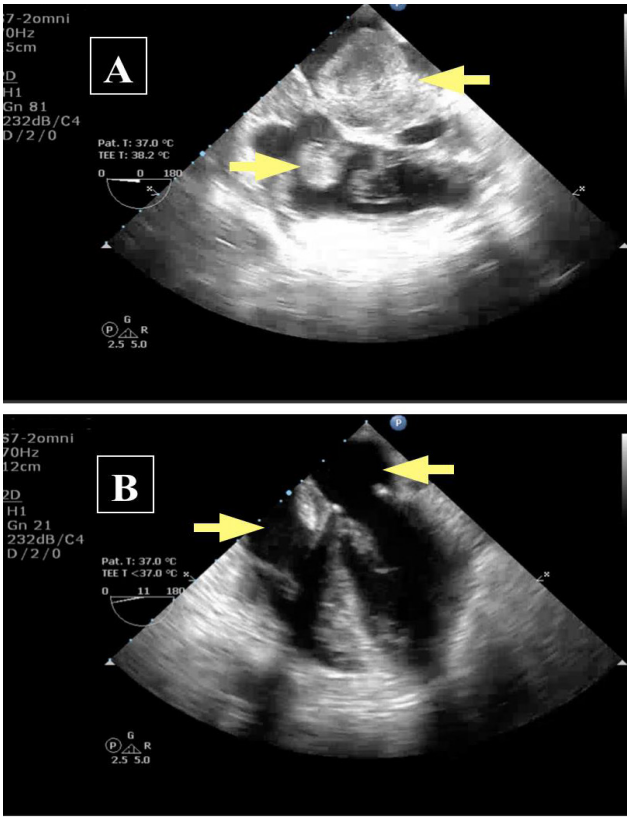

Figure 2. Intra-operative transesophageal echocardiogram (A) Mid-esophageal view showing the biatrial mass prior to surgical resection (yellow arrow) (B) Mid-esophageal view showing complete surgical resection of the mass (Yellow arrow).

Figure 3. (A) Left atrial mass (debulking)- piecemeal; irregular, white to cream, rubbery to firm; 6.0 x 5.0 x 5.0 cm. (B) Right atrial mass (excision)- piecemeal; irregular, white to cream, rubbery to firm; 5.0 x 5.0 x 3.0 cm.

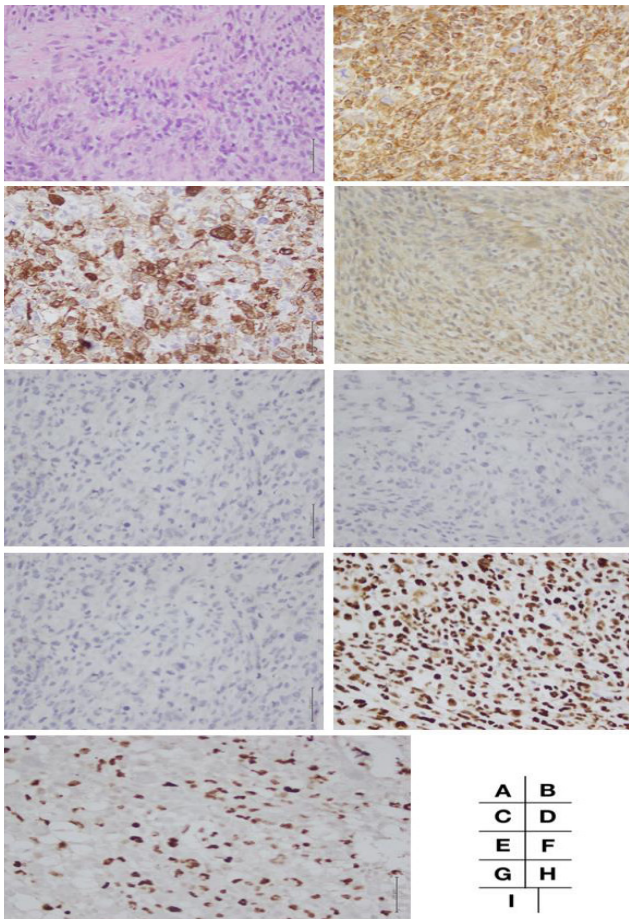

Figure 4. Histologic study and immunohistochemical stains (A) H and E 400x. Vague tasticular pattern of smooth muscle bundles in a well vascularized connective tissue. The atypical spindle cells are elongated with hyperchromatic nuclei, inconspicuous nucleoli, eosinophilic or ocassional fibrillar cytoplasm, and indistinct cell membraines. many abnormal mitosis identified. Necrosis is rare. (B) Vimentin-positive (C) SMA-positive (D) Desmin-positive (E) Calpolin-negative (F) S100-negative (G) H-Caldesmon-negative (H) P53- 90% proliferation (I) Ki67- >90% proliferation

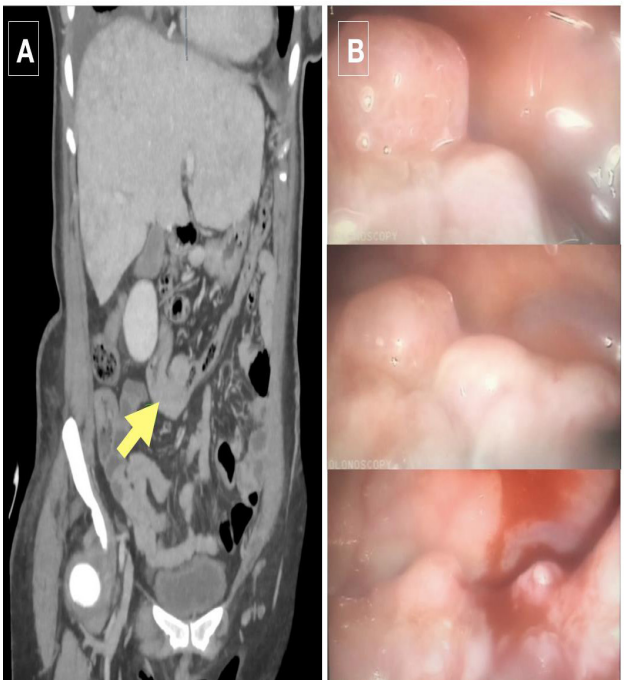

Figure 5. (A) Coronal view of abdominal CT scan showing circumferential wall thickening in proximal transverse colon (yellow arrow). (B) Colonoscopy Findings at the level of transverse colon showing presense of a polyloid friable lesion with minimal bleeding after biopsy.

DISCUSSION

Double primary malignancy in a single patient was first described 100 years back by Billroth.[1] Since then, this phenomenon has been increasingly recognized due to better diagnostic and treatment protocols leading to an overall increase in the life expectancy of cancer survivors.[1] Epidemiologic data reported the frequency of multiple primary malignancies ranging from 2-17%.[7]

The diagnosis of a second lesion, whether it is a true-primary or a distant-metastasis is difficult to decide. Hence, the Warren and Gates criteria (1932) was used which proposes that a diagnosis of multiple primary malignancies requires the following: (1) each tumor should present a definite picture of malignancy; (2) each tumor should be histologically distinct; and (3) the possibility that one is a metastasis of the other must be excluded.[1,4,7,8,9] Once a double primary malignancy is established, it can be further categorized based on the interval between tumor diagnosis. Synchronous malignancies are second tumors occurring either simultaneously, or within six months after the first malignancy. While metachronous malignancies are secondary tumors that have developed after six months or more from the first malignancy.[8] Synchronous tumors occur uncommonly with the most common tumors arising from the breast.[1]

Primary cardiac tumors are rare[10] with a reported surgery and autopsy incidence of 0.3 to 0.7% while metastatic cardiac tumors are 30 times more common.[11] The vast majority of primary cardiac tumors are benign with myxoma being the most common, seen in 75% of cases. Only 10- 25% of cardiac tumors are malignant, and of these, 75% are sarcomas.[12] Malignant primary cardiac tumors are usually found in the right atrium and are most commonly angiosarcomas. In reported cases of left atrial mass, the most common tumors are pleomorphic sarcoma and leiomyosarcoma.[11] Biatrial tumor is an extremely rare phenomenon, mostly documented through case reports and series.[13]

This is a case of a post-cardioembolic stroke patient who eventually developed heart failure symptoms. Work-up revealed a biatrial mass which emerged to be a high-grade myofibroblastic sarcoma and the discovery of a well-differentiated colonic adenocarcinoma. To the best of our knowledge, this is the first reported case of a synchronous double primary malignancy of the heart and colon with the said histopathologic biopsy.

Myofibroblastic sarcoma (MS) represents a distinct malignant mesenchymal neoplasm composed of myofibroblasts different from fibrosarcoma and leiomyosarcoma.[14,15] They may arise in soft tissue or bone in adults and children and occur mainly in subcutaneous tissues of the head, neck, and extremities.[15, 16, 17] In literature, a case of high-grade myofibroblastic sarcoma of cardiac origin was reported presenting with hemorrhagic pericardial effusion with the tumor arising from the pericardium.[18]

Most MS are low grade yet a less differentiated high-grade variant exists. High-grade MS is hypercellular, has less collagen production, may exhibit necrosis, and demonstrates hyper-

chromasia and increased mitotic activity. The cells of MS express smooth muscle actin and calponin and lack h-caldesmon.[15, 19, 20] The rarity of the disease and its low grade features make an accurate diagnosis difficult in most cases.[19] In the latest WHO Classification of Tumors, there is yet to be a consensus as to the definition of intermediate and high-grade myofibroblastic sarcoma with less reproducible characteristics.[21]

Even on its own, high-grade myofibroblastic sarcomas is already an extremely rare tumor of the heart. And a high-grade myelofibroblastic sarcoma occurring concomitantly with a primary adenocarcinoma of the colon is remarkably noteworthy.

To date, this is the first documented case of a high-grade myofibroblastic sarcoma presenting as a biatral mass with a synchronously occurring well-differentiated colonic adenocarcinoma. Diagnosis is established through histopathology and immunohistochemical staining. Mainstay treatment follows guidelines targeting each of the malignancies separately. Hence, an ideal single chemotherapeutic agent remains to be the goal to minimize adverse effects and financial burden of multiple chemotherapeutic drugs. However, due to the disease's rarity, the development of this treatment has proved to be elusive such that proper documentation of such cases is an important element to further research.

REFERENCES

1. Preetam Acharya, Anand Ramakrishna, Tanuj Kanchan, and Rahul Magazine. Case Report. Dual Primary Malignancy: A Rare Organ Combination. Hindawi Publishing Corporation. Case Reports in Pulmonology. Volume 2014, Article ID 760631, 3 pages http://dx.doi.org/10.1155/2014/760631
2. S. Watanabe, T. Kodama, Y. Shimosato et al., "Multiple primary cancers in 5,456 autopsy cases in the National Cancer Center of Japan," Journal of the National Cancer Institute, vol. 72, no. 5, pp. 1021–1027, 1984.
3. Division of Cancer Prevention and control, Centers for Disease Control and Prevention. Colorectal Cancer Statistics. June 2012.
4. TUNG-KWANG LEE, M.D., MICHAEL BARRINGER, M.D., RICHARD T. MYERS, M.D., F.A.C.S., J. MICHAEL STERCHI, M.D., F.A.C.S. Multiple Primary Carcinomas of the Colon and Associated Extracolonic Primary Malignant Tumors. Lippincott Company. Volume 195. Number 4
5. Moertel CG. Multiple primary malignant neoplasms-their Incidence and significance. Recent Results Cancer Res 1966; 7:76-88.
6. Polk HC Jr, Spratt JS Jr, Butcher HR Jr. Frequency of Multiple Primary Malignant neoplasms associated with colorectal Carcinoma. Am J Surg 1965;109;71-75.
7. Alexia Vogt, Sabine Schmid, Karl Heinimann, Harald Frick, Christian Herrmann, Thomas Cerny,1 Aurelius Omlin1,2 Multiple primary tumours: challenges and approaches, a review. ESMO Open 2017;2:e000172. doi:10.1136/esmoopen-2017-000172
8. Puneet Kumar Bagri, Daleep Singh, Mukesh Kumar Singhal, Guman Singh, Gaurav Mathur, Shankar Lal Jakhar, et al. Double Primary Malignancies: A Clinical & Pathological Analysis Report from a Regional Cancer Institute in India. Iranian Journal of Cancer Prevention. Vol 7, No 2, Spring 2014
9. Warren S, Gates O. Multiple primary malignant tumors: A survey of the literature and statistical study. Am J Cancer. 1932; 16:1358-414.
10. Ladich E, Virmani R. Tumors of the Cardisovascular System: Heart and blood vessels. In: Buja L.M., Butany J. eds. Cardiovascular Oathology. 4th Ed. Elsevier; 2016; 735-72.
11. Monika J. Leja, MD, Dipan J. Shah, MD, Michael J. Reardon, MD. Primary Cardiac Tumors. Cancer and the Heart. Texas Heart Institute Journal. Volume 38, Number 3, 2011
12. Paul J. Zhang, MD, John S. Brooks, MD, John R. Goldblum, MD, Brian Yoder, DO, PhD, Raja Seethala, MD. Primary cardiac sarcomas: a clinicopathologic analysis of a series with follow-up information in 17 patients and emphasis on long-term survival. Human Pathology. 2008 September ; 39(9): 1385–1395. doi:10.1016/j.humpath.2008.01.019.
13. Cristina Basso, Stefania Rizzo, Marialuisa Valente, Gaetano Thiene. Prevalence and pathology of primary cardiac tumours. Cardiovascular Medicine 2012;15(1):18–29
14. Geetha J P, Rashmi M V. The myofibroblastic sarcoma of retroperitoneum: A diagnostic dilemma. Indian J Pathol Microbiol 2015;58:409-10
15. Yuri HOJO, Takuma TSUCHIYA, Ayako SHIRAKI, Kazuhiko SUZUKI, Makoto SHIBUTANI and Kunitoshi MITSUMORI. High-Grade Myofibroblastic Sarcoma of Inguinal Region in a Dog. The Japanese Society of Veterinary Science 74(5): 625–628, 2012. doi: 10.1292/jvms.11-0459
16. Fisher C. Myofibroblastic malignancies. advance anatomy pathology 2004; 11: 190 – 201.
17. Mentzel, T. 2001. Myofibroblastic sarcomas: a brief review of sarcomas showing a myofibroblastic line of differentiation and discussion of the differential diagnosis.

Curr. Diagn. Pathol. Med. 36: 349– 352.

18. Seiji Koga, MD, Satoshi Ikeda, MD, Jungo Urata, MD, Risa Chijiwa, MD, Kuniko Abe, MD, Tomayoshi Hayashi, MD, et al. Primary High-Grade Myofibroblastic Sarcoma Arising From the Pericardium. Circulation Journal Vol.72, February 2008
19. T. Mentzel. Myofibroblastic sarcomas: a brief review of sarcomas showing a myofibroblastic line of differentiation and discussion of the differential diagnosis. MINI-SYMPOSIUM: ADVANCES AND CONTROVERSIES IN SOFT TISSUE SARCOMAS. Current Diagnostic Pathology (2001) 7, 17d24. doi:10.1054/cdip.2000.0057, available online at http://www.idealibrary.com
20. J. Doscher, S. Dubner, D. Miller, R. Kelsch, J. Fantasia. High-Grade Myofibroblastic Sarcoma of the Palate and Maxillary Sinus: Case Report With Literature Review. (2010). Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, 110(6), e24. doi:10.1016/j.tripleo.2010.07.060
21. Fletcher CD, Unni KK, Mertens F. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of Soft Tissue and Bone. 3rd ed. Lyon: IARC Press, 2002: 94-96

Criss-Cross Heart in a 1-Year Old Female: a case report

Anne Bernadette B. Arangcon, MD; Ruzenette Felicitas R. Hernandez, MD

Objective **---** To discuss criss cross heart in a 1 year-old, female as to etiology, embryology, clinical manifestations, surgical and medical management and outcome.
Clinical Features **---** The patient presented with cyanosis when crying associated with tachypnea during feeding, poor weight gain and recurrent respiratory tract infection.
Intervention and Outcome **---** The patient underwent pulmonary artery banding with resolution of the above signs and symptoms. Staged surgical procedure is to be done for this patient.
Conclusion **---** Diagnosis for this kind of cardiac anomaly is through transthoracic echocardiography. Clinical manifestations and management options for patients with criss-cross heart depends upon the associated cardiac anomalies. ***Phil Heart Center J 2021;24(2):76-80.***

Key Words: ■ cyanotic congenital heart disease ■ criss-cross heart ■ 2D echocardiogram ■ pulmonary artery banding

Criss-cross is a rare congenital anomaly of the heart first described by Lev and Rowlatt in 1961. It occurs in <8/1,000,000. A total of 150 cases have been reported to date. It is usually characterized by crossing of the inflow streams of the two ventricles and almost always associated with other severe cardiac diseases.[1]

Case: A 1 year-old, girl, presented to us with tachypnea. History revealed shortness of breath during feedings associated with cyanosis when crying first noted a few days after birth. Interval history showed persistent cyanosis when crying associated with tachypnea during feedings, poor weight gain. The patient also had recurrent admissions for pneumonia. Initial 2D-echocardiography done outside our institution showed Congenital Heart Disease, d-Transposition of Great Arteries with Ventricular Septal Defect and Atrial Septal Defect. The patient was maintained on Digoxin and Furosemide. The patient was referred to our institution for cardiac evaluation but was noted to be tachypneic thus admitted. Pertinent physical examinations findings include cyanosis, crackles on all lung fields, dynamic precordium, apex beat at the 4th ICS left MCL,no thrill, heave or tap, regular cardiac rhythm, s1 normal, s2 split with loud p2, (+) g3/4 systolic ejection murmur at the left upper parasternal border, dusky nailbeds with clubbing. The patient was then admitted as a case of Congenital Heart Disease, cyanotic type with increased blood flow, pediatric Community Acquired Pneumonia, moderate risk. Antibiotics were started. The patient underwent hemodynamic studies on the second hospital day. During the procedure, the patient had ventricular tachycardia followed by bradycardia. One dose of epinephrine was given. The patient was transferred to PICU still intubated and was attached to a mechanical ventilator which was gradually weaned. The patient developed high grade fever and was referred to infectious specialist, sepsis was entertained. Meropenem and Amikacin were given.

The patient also developed focal seizure and was referred to a pediatric neurologist. EEG showed generalized slowing of the back-

Finalists, Poster Presentation - Case Report. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Anne Bernadette B. Arangcon.*** 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

ground activity thus Phenobarbital was started. Cranial CT scan was normal.

On the 4th hospital day, the patient had episode of diaphoresis and desaturation (02 sat 40-50%). 2D echocardiography was done which showed LVEF of 32%. Inotropes were started (Dobutamine and Milrinone). Sildenafil was given.

On the 5th hospital day, ETA culture was positive for *Psedomonas aeruginosa*. Meropenem was continued Ciprofloxacin and Gentamycin with sensitivity based on the antibiogram. The patient gradually improved and was extubated.

On the 16th hospital day, the patient underwent pulmonary artery banding with the following operative findings: The aorta is anterior seen arising from the posterior ventricle. The aorta arises from the anterior ventricle.Right sided RA drains the SVC and IVC. Both Pas are dilated. Pre-banding: systemic BP 63/40, PAP 57/40, sat 83% at fio2 30%. Post banding: systemic BP 84/25 (mean 44 mmHg), PAP 47/24 (mean 33 mmHg), sat 90% at fio2 30%. The patient tolerated the procedure well and was transferred to SICU still intubated and was attached to a mechanical ventilator which was gradually weaned.

There was a development of pulmonary congestion on x-ray as well as increase in infectious parameters. Thus, antibiotics were shifted to Piperacillin-Tazobactam. Furosemide drip was likewise started. Patient was continued to be weaned from ventilator support. However, she self extubated on the 19th hospital day but developed tight air entry with wheezing thus was hooked to NCPAP. The patient was eventually transferred to the PICU on low O2 support and medications.

On the 25th hospital day, the patient was transferred to regular ward with marked improvement of the clinical status. She was eventually discharged improved.

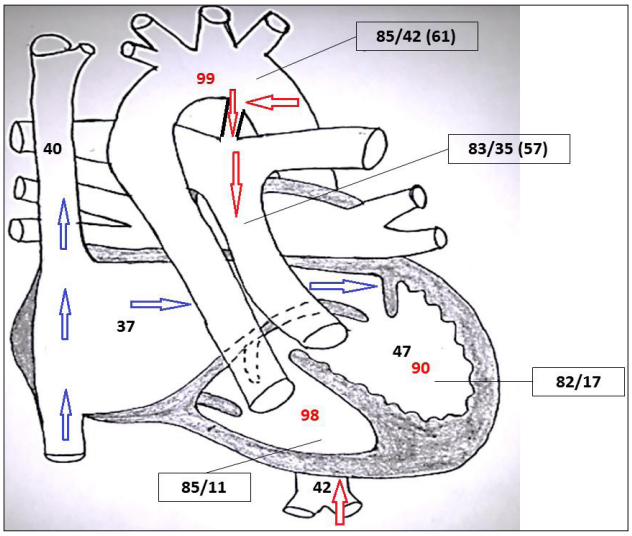

Figure 1a. Hemodynamic study.

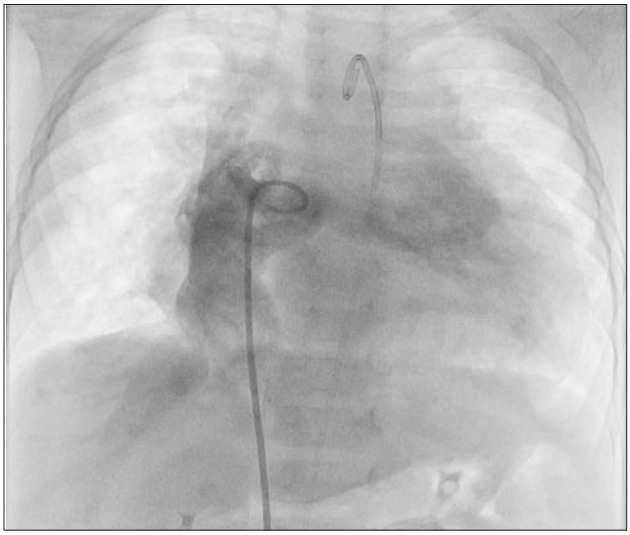

Figure 1b: Right heart catheterization.

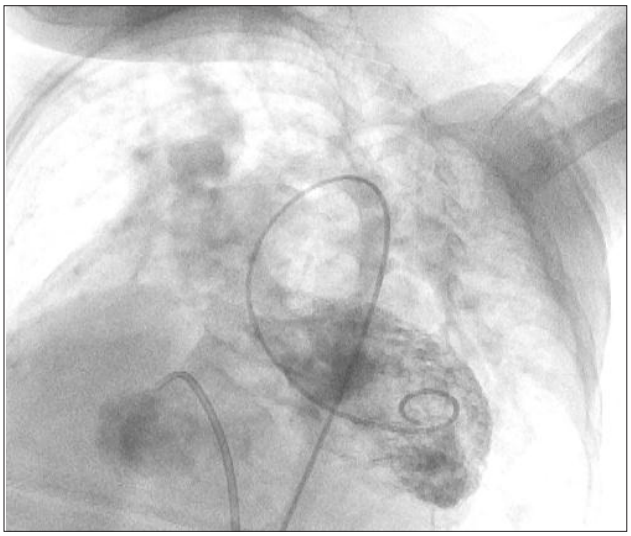

Figure 1c: Left heart catheterization

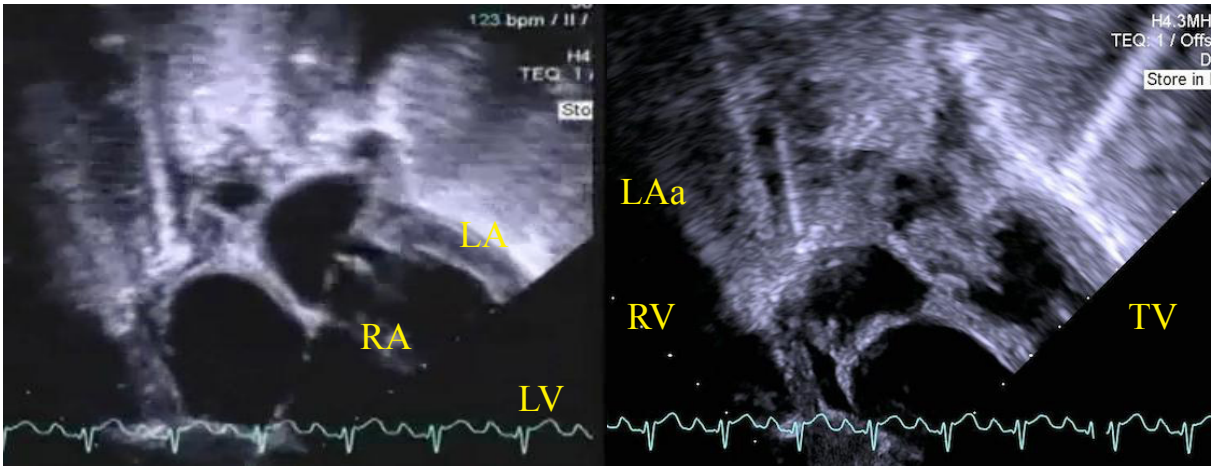

Figure 2. Subcostal View

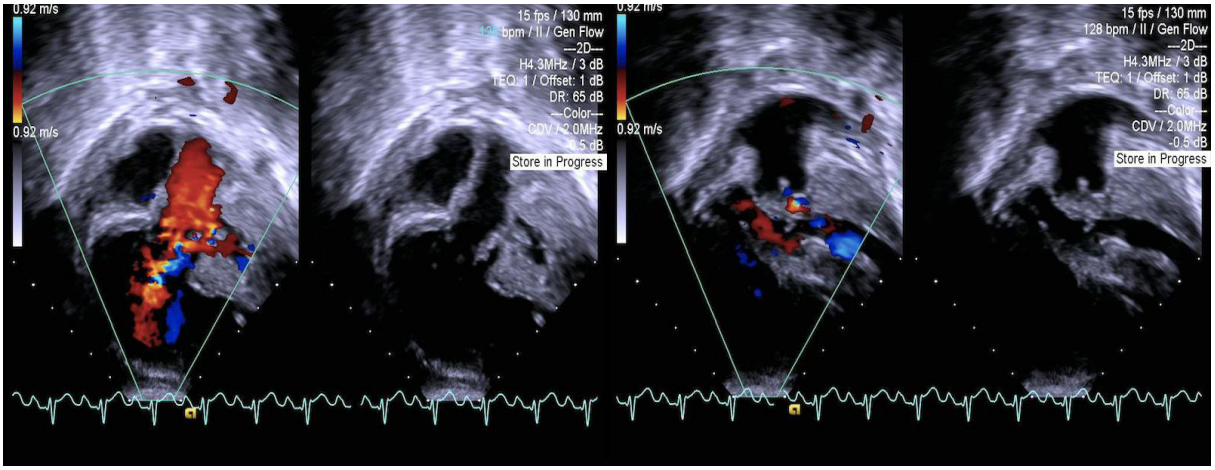

Figure 3. Real time and color study showing the connection of the left-sided left atrium and the right sided left ventricle through the mitral valve and the right sided right atrium to be connected to the left-sided right ventricle through the tricuspid valve.

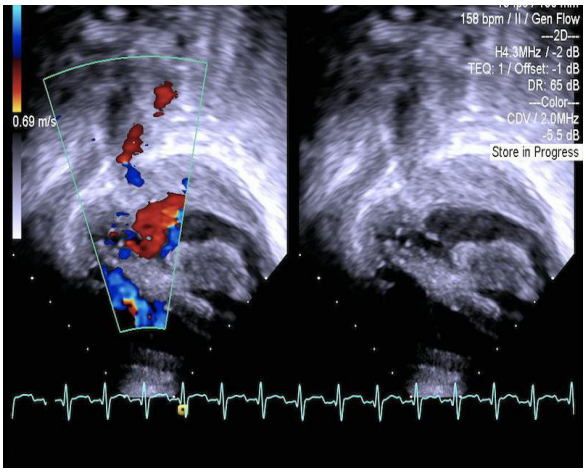

Figure 4. Malposed great arteries

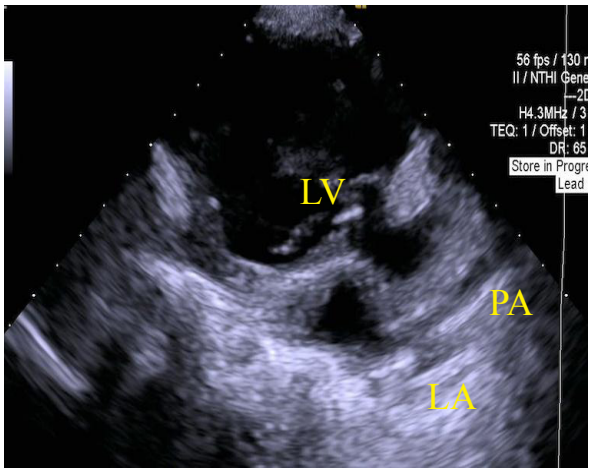

Figure 5. Parasternal long axis view

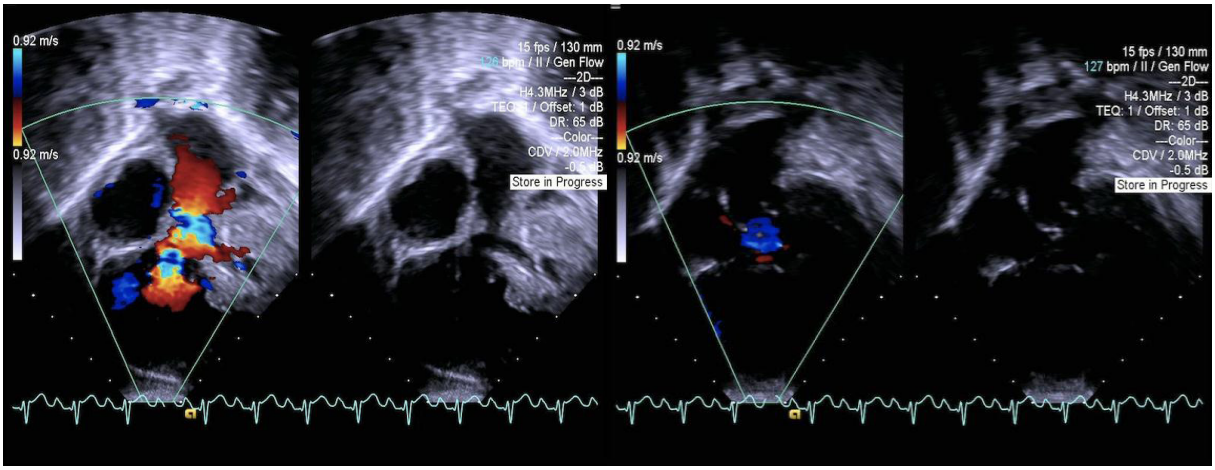

Figure 6. The standard 4 chamber view showing the crossing axes of the two AV valves in adjacent cuts suggesting a criss-cross heart

DISCUSSION

Criss-cross heart is an extremely rare anomaly, constituting less than 0.1% of all the congenital heart diseases. There are no definite develomental mechanisms. One of the proposed mechanisms given by Anderson et al. is a result of clockwise or counter-clockwise post-septational rotation of the heart.[2] The exact etiology has not been clearly understood yet, it seems to be due to abnormal twisting of the apex of the heart, while the base remains relatively fixed. Atrioventricular concordance and ventriculoarterial discordance are seen in 80% of cases.[3] Concordant atrioventricular and discordant ventriculoarterial connections are found in around 80% of cases. Criss-cross heart with concordant atrioventricular connection occurs due to the clockwise twisting of ventricular mass around its long axis. In a criss-cross heart with discordant atrioventricular connection, counter-clockwise twisting of ventricular mass around its long axis occurs.

A ventricular septal defect is seen almost all the time. Other anomalies such as pulmonary stenosis, straddling of atrioventricular valves, tricuspid atresia, double outlet right ventricle, and congenitally corrected transposition are seen.

Presented with a 1 year old, female with history of cyanosis, feeding interruption, frequent respiratory tract infection, and poor weight gain, cyanotic congenital heart disease with increase blood flow was entertained. Right ventricular hypertrophy was noted on chest x-ray thus the following differential diagnoses were considered: (1) d-trasposition of great arteries, (2) total anomalous pulmonary venous return, and (3) hypoplastic left heart syndrome. The clinical manifestations depend upon the associated lesions. Imaging modalities and invasive techniques may be done for the diagnosis of criss-cross heart. Cardiac catheterization in this patient showed left sided coarsely trabeculated right ventricle. Cardiac catheterization may be necessary to obtain pressure and oxymeter data or view additional defects. (*Figure 1*) Cardiac MRI may also be done as a diagnostic tool but this was not done in our patient.

The inability to obtain a characteristic four-chamber view in any plane during transthoracic echocardiography, displaying the crossing of long axes of atrioventricular valves as seen in the subcostal long axis or coronal plane sweep is diagnostic of criss-cross heart.[4]

During echocardiographic examination of this patient, all the four cardiac chambers and the two atrioventricular valves could not be seen in a single plane simultaneously. There was a large secundum atrial septal defect. Inferior vena cava drains to the right sided right atrium and all pulmonary veins drain to the left atrium. There

was a large subarterial ventricular septal defect. The left sided ventricle is coarsely trabeculated and with a moderator band with septophilic atrioventricular valve. The aorta is anterior and to the right of the pulmonary artery which arise from the left sided right ventricle. A patent ductus arteriosus was also noted.

A diagnosis of criss-cross heart with double outlet right ventricle and malposed great arteries was made. Management of criss-cross heart depends upon the associated anomalies. A small right ventricle and pulmonary stenosis may require a staged Fontan repair. In other cases with simple ventricular septal defect or patent ductus arteriosus alone may just require closure of the defects. In case of isolated transposition of great vessels, arterial switch operation may be the only requirement.[5] In this case, pulmonary artery banding was initially done for left ventricular retraining. Staged surgical procedure was planned.

CONCLUSION

A criss-cross heart is a rare and complex anomaly with clinical manifestations that depend on other associated cardiac lesions. Echocardiography is a useful tool in the diagnosis. The inability to obtain a characteristic four-chamber view in any echocardiographic plane is diagnostic for this anomaly in most cases. Management also depends upon the associated anomalies.

REFERENCES

1. Lev M, Rowlatt UF. The pathologic anatomy of mixed levocardia. A review of thirteen cases of atrial or ventricular inversion with or without corrected transposition. Am J Cardiol. 1961 Aug;8:216-63.
2. Shinebourne EA, Gerlis LM. Criss-cross atrioventricular relationships producing paradoxical atrioventricular concordance or discordance. Their significance to nomenclature of congenital heart disease. Circulation. 1974 Jul;50(1):176-80.
3. Muneer PK, Kalathingathodika S, Chakanalil GS, Sony MM. Crisscross heart with dextrocardia and intact interventricular septum. Ann Pediatr Cardiol. 2014 Jan;7(1):70-1.
4. Yang YL, Wang XF, Cheng TO, Xie MX, He LL, Lu XF, et al. Echocardiographic characteristics of the criss-cross heart. Int J Cardiol . 2010 Apr 15;140(2):133-7.
5. Nakada I, Nakamura T, Matsumoto H, Sezaki T. Successful repair of criss-cross heart using modified Fontan operation. Chest. 1983 Mar;83(3):569-70.

Infective Endocarditis Causing Splenic Abscess, Renal Infarcts and Acute Limb Ischemia: a case report

Joy K. Fongayao, MD; Lorenzo Rommel G. Cariño, MD

***Introduction*---** Multiple systemic embolisms to the spleen, kidney and extremities caused by complications of infective endocarditis (IE) in a single patient are rare and have fatal outcomes. Management of complications depends on the emergency and medical condition of patient.

***Case* ---** Presented is a case of a 37 year old male with IE diagnosed initially with splenic abscess with multiple consultations and prolonged antibiotic intake. Percutaneous drainage of the abscess revealed heavy growth of *Streptococcus sanguinis* and blood culture shows growth of Capnocytophagia specie. Laparoscopic splenectomy was done. During hospital stay patient developed Acute Limb Ischemia (ALI) IIB of the right upper extremity and emergency embolectomy was done. Valve repair surgery was performed eventually and patient was discharged improved thereafter.

***Discussion* ---** Reported in this paper is a unique case of IE causing complications of splenic abscesses, renal infracts and ALI with splenic abscess culture of Streptococcus sanguinis and blood culture of Capnocytophagia specie. Embolic complications occur in 20-50% of cases of IE. They can precede the diagnosis of IE in 25-60% of patients. Endocarditis as a result of *Capnocytophaga canimorsus* infection is extremely rare. The incidence of embolization causing ALI is unknown. Approximately 5% of patients with splenic infarction will develop splenic abscess. Current agreement states that IE and splenic abscesses should be treated during the same hospitalization, whether it comes first or after valve operation is still controversial. In our patient, the multiple complications of IE were addressed in same hospitalization stay.

Conclusion* ---** Management of complications of systemic embolism of IE entails a multidisciplinary and individualized approach. Antibiotic therapy, splenectomy, embolectomy and valve surgery on the same hospitalization can have satisfactory outcomes. ***Phil Heart Center J 2021;24(2):81-84.

Key Words: ■ Infective endocarditis ■ Splenic abscess ■ Acute limb ischemia

Infective endocarditis (IE) occurs at a rate of approximately 1–7/100 000 people per year and has a high morbidity and mortality despite advances in antibiotic and surgical treatments. Systemic embolism occurs in 22%–50% of IE patients.[1]

The significance of this study is to present a multidisciplinary and individualized approach in managing patients having IE with complications of multiple systemic embolisms.

Case: A 37-year-old male was admitted in our institution with a history of fever abdominal pain 8 months prior to admission. He was diagnosed to have splenic abscess through abdominal ultrasound and CT scan and was given antibiotics. Subsequent consultations from different physicians resulted with the same diagnosis with prescriptions of oral antibiotics until a 2D echocardiography was done showing severe mitral regurgitation due to torn chordae of mitral valve.

On admission, cardiac auscultation shows grade 3/6 systolic murmur at the apex with radiation to the axilla. Abdomen was soft, with slight tenderness on left upper quadrant area.

Finalist, Poster Presentation - Case Report. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Joy K. Fongayao.*** Department of Cardiovascular Surgery and Anesthesia. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

Abdominal CT scan was done showing splenomegaly with multiple dense lesions considering abscess and bilateral renal infarcts. (*Figures 1-4*) Repeat 2D echocardiography shows thickened mitral valve leaflets with prolapse of A2 segment of anterior leaflet with fluttering echogenic density on the anterior mitral valve with severe mitral regurgitation. (*Figures 5-6*)


Figure 1

Patient was anemic and with electrolyte imbalance, creatinine was normal, with increased ESR and CRP levels. Blood culture shows growth of Capnocytophagia specie on the right arm. Image guided aspiration of the splenic abscess shows heavy growth of *Streptococcus Sanguinis* sensitive only to Vancomycin. Vancomycin IV infusion was started. Patient then underwent laparoscopic splenectomy with intraoperative findings of 15cm x 15cm spleen with necrotic tissues and adhensions.

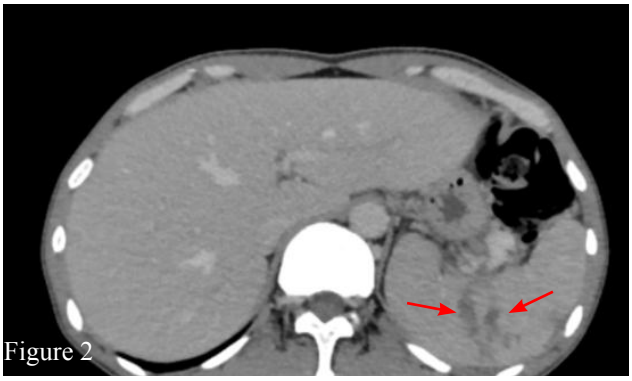
Figure 2

Patient then underwent mitral valve repair (neochordae at A3 and A2), mitral valve annuloplasty using the institution ring size 28, tricuspid valve annuloplasty with institution ring size 28. Intraoperative findings show the mitral leaflet has scattered friable white material, with torn primary chordae at A2 and A3. The posterior mitral valve was retracted at A2. Postoperative TEE shows only trivial mitral and tricuspid regurgitation with ejection fraction of 66%. Patient was subsequently discharged improved after few days of hospitalization.


Figure 3

Figures 1 and 2: Abdominal CT scan - multiple hypodense lesions of the spleen with hypodense rim and minimal peripheral contrast enhancement.

Figure 3 and 4: Abdominal CT scan - peripherally enhancing lesion in the mid cortex of left kidney and hypoenhancement in mid segment of both kidneys consider infarcts.

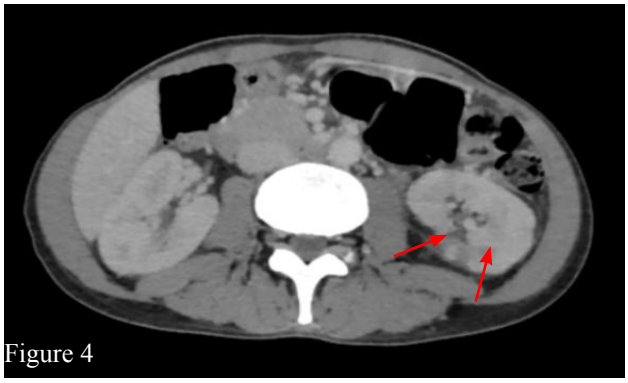
Figure 4

Figures 5 and 6 : 2D Echo; Plax and 4 chambers views showing fluttering echogenic density (vegetation) on the anterior mitral valve leaflet.

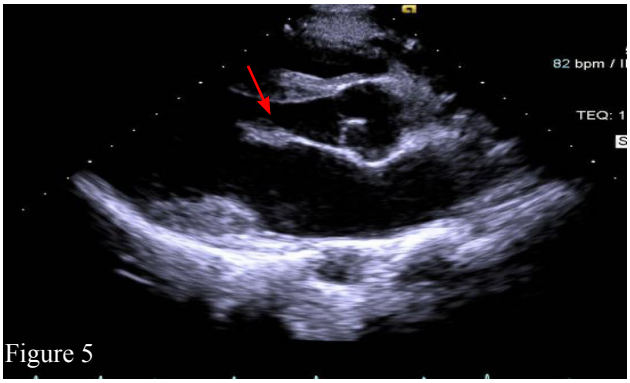

Figure 5

Figure 6

DISCUSSION

Reported in this paper is a unique case of IE causing complications of splenic adscess, renal infarcts and ALI with positive splenic abscess aspirate culture of *Streptococcus sanguinis* and blood culture of Capnocytophagia specie. To my knowledge, a similar case has not been reported previously.

Embolic complications occur in 20-50% of cases of IE, and are associated with increased mortality and morbidity. They can precede the diagnosis of IE in 25 to 60% of patients. More than 50% of embolic events involve the CNS and embolic events to the spleen occur in 19-36% of cases of IE. [2]

The general approach to the treatment of IE is initial clinical stabilization, early acquisition of blood cultures, and definitive medical and surgical treatment.[1]

Approximately 5% of patients with splenic infarction will eventually develop splenic abscess.[3] There is currently general agreement that IE and splenic abscesses should be treated our patient, imaging guided aspiration of abscess during the same hospitalization, whether splenectomy should be performed before, during, or after a valve operation is still controversial.[4] In to identify the causative microorganism was done initially so that appropriate antibiotics will be started. Anemia and electrolyte imbalance were corrected prior to splenectomy.

Endocarditis as a result of *Capnocytophaga Canimorsus* infection is extremely rare, with only 14 cases reported in the literature since 1977. Six of the 15 patients (40%) had been bitten by a dog and another 5 patients (33%) had contact with a dog.[5] Among the *Viridans Streptococci*, *S. sanguinis* is most commonly isolated from infective endocarditis patients.[6] Antibiotic therapy in our patient was based on culture and sensitivity results with 4 weeks of Vancomycin therapy.

Acute limb ischemia is a consequence of peripheral arterial disease and a vascular emergency. The incidence of embolization causing ALI is unknown but in one case series of IE, it occurred in 7 of 90 cases. In another series, 14 of 285 had peripheral acute ischemic syndromes. Emboli can occur before diagnosis, during therapy, or after therapy, most occur within the first 2-4 weeks of antimicrobial therapy and involves lower extremities[7] In our patient, ALI IIb on the right upper extremity occurred more than 2 weeks of Vancomycin therapy.

Septic embolization occurs in at least 30% of patients. One third of these are to the peripheral vasculature. Such emboli are frequently multiple and maybe accompanied by mycotic aneurysms, splenic, cerebral, and renal infarcts. Extent of limb ischemia and degree of cardiac dysfunction dictates the priority of problems. When possible, cardiac valve surgery should proceed before or simultaneously with embolectomy to avoid the morbidity of embolectomy in a hemodynamically unstable patient.[8] The patient presented had stable cardiac functions. Emergency embolectomy was done prior to definitive valve surgery which was performed electively after few days of recovery within the same hospital admission.

CONCLUSION

Management of complications of systemic embolism in IE entails a multidisciplinary and individualized approach based mainly on emergency status of the complication and the patient's medical condition. In this patient appropriate antibiotic therapy, prompt splenectomy and embolectomy then valve repair surgery on the same hospitalization stay can have satisfactory outcomes.

REFERENCES

1. Galyfos G, Giannakakis G, Kerasidis S, Geropapas G, Kastrisios G, Papacharalampous G, et al. Infective endocarditis as a rare cause for acute limb ischemia. World J Emerg Med. 2016;7(3):231-3.
2. Monteiro TS, Correia MG, Golebiovski F, Barbosa GIF, Weksler C, Lamas CC. Asymptomatic and symptomatic embolic events in infective endocarditis: associated factors and clinical impact. Braz J Infect Dis. May-Jun 2017;21(3):240-247.
3. Elasfar A, Albaradai A, Alharfi Z, Alassal M, Ghoneim A, Aighofaili F. Splenic abscess associated with infective endocarditis; case series. J Saudi Heart Assoc. 2015 Jul;27(3):210-5.
4. Blasi S, De Martino A, Levantino M, Pratali S, Anastasio G, Bortolotti U. Splenectomy and valve replacement in patients with infective endocarditis and splenic abscesses. Ann Thorac Surg. 2016 Sep;102(3):e253-e255.
5. Hayani O, Higginson LAJ, Toye B, Burwash IG. Man's best friend? Infective endocarditis due to Capnocytophaga canimorsus. Can J Cardiol. 2009 Apr; 25 (4) :e130-2.
6. Pessinaba S, Kane AD, Ndiaye MB, Mbaye A, Bodian M, Dia MM, Sarr, et al. Vascular complications of infective endocarditis. Med Mal Infect. 2012 May; 42 (5):213-7.
7. Kitts D, Bongard FS, Klein SR. Septic embolism complicating infective endocarditis. J Vasc Surg. 1991 Oct; 14(4):480-5; discussion 485-7.

Cardiovascular Surgery and Anesthesia

Perioperative Management and Anesthesia Considerations in Ectopia Cordis: a case report

Anne Reichel M. Lasquite, MD

Introduction --- Ectopia cordis is define as a heart which is congenitally placed outside the thoracic cavity. The objective of this study is to describe the multidimentional challenges hurdled in the process of anesthesia management and perioperative care.
Case --- Patient is a second of twin, noted to have ectopia cordis with co-existing congenital anomalies of cleft lip and cleft palate and underwent surgical intervention.
Discussion --- The critical areas experienced in this particular patient were (1) airway management, (2) optimum patient monitoring, and (3) pulmonary and hemodynamic stability during anesthesia.
Conclusion --- Anesthesia management for the repair of ectopia cordis remains to be very difficult for the anesthesiologist, and would require the use of both invasive and non-invasive monitoring. ***Phil Heart Center J 2021;24(2):85-89.***

Key Words: ■ Ectopia cordis ■ airway management ■ hemodynamic stability ■ anesthesia management

Ectopia cordis is defined as a heart which is congenitally placed outside the thoracic cavity, either partially or completely.[2,3] It was first noted by the Babylonians, as documented in the cuneiform tablets of Nineveh.[4] The incidence today is 5.5 – 7.9 per million live births. Without surgical intervention, it is incompatible with life.[5]

We would like to present our case of ectopia cordis who underwent surgical intervention at the Philippine Heart Center. Consent was secured for the case to be presented. Our main objective for submitting this case report is to describe the multidimensional challenges we hurdled in the process of anesthesia management and perioperative care.

Preoperative Course: This patient is the second of twins, born to a G1P2 (2-0-0-2) mother, delivered via Low Segment Cesarean Section at 37-38 weeks age of gestation by Ballard's Score, with an Apgar Score of 7, 9, and a birth weight of 2.55kg. Upon delivery, she was noted to have ectopia cordis, cleft lip, and cleft palate. Routine newborn care was given. Expecting early demise, no additional test and diagnostic workups were done. Despite the conservative care rendered, she reached her fourth day of life. This prompted the parents to bring her to this Institution and give her the best possible care to support her survival.

On admission, she was awake, with regular spontaneous respiration and clear breath sounds. Oxygen support was given via face mask at 6 liters per minute (lpm). Her beating heart was covered by soft cloth, seen on top of her chest (*Figure 1*). Chest x-ray confirmed that the cardiac silhouette was extrathoracic, and the aortic silhouette cannot be assessed. The epicardial echo done revealed an intracardiac lesion described as Atrioventricular Septal Defect (AVSD), Pulmonary Stenosis (PS), with Patent Ductus Arteriosus (PDA).

Finalist, Poster Presentation - Case Report. 27th PHC Annual Research Paper Competition and Poster Presentation held on February 26, 2019 at Philippine Heart Center. Correspondence *to* ***Dr. Anne Reichel M. Lasquite.*** Division of Cardiovascular Anesthesia. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

Pediatric Cardiology started Ampicillin 120mg via intravenous (IV) route every twelve hours, to be shifted to every 8 hours at the seventh day of life, Amikacin 30mg IV once daily (OD), and Vitamin K 12.5mg IV every eight hours to complete three doses. On the ninth day of life, she was referred to Pediatric Cardiac Surgery and Cardiovascular Anesthesia for surgical repair and management. Weight was noted to be lower at 2.4 kilograms with length of 42 centimeters. Laboratory workups showed normal results, except for the blood culture which was found to be positive for Penicillin-resistant *Staphylococcus aureus*. Hence, the antibiotic was shifted to Oxacillin. Patient was scheduled for surgical management on the tenth day of life.

Intraoperative Course: The Operating Room (OR) Suite was prepared to cater to the environment that is appropriate for a critically ill neonate. This included having the proper OR room temperature, proper breathing circuits, computed doses of emergency drugs and cardiovascular support medications to be used.

Slow intravenous induction was done with midazolam – ketamine – atropine given through the existing umbilical vein catheter. There is some difficulty with the process of laryngoscopy and placement of the laryngoscope blade because of the complete cleft lip and complete cleft palate anomalies. (*Figure 2*) This is further aggravated by the obstruction posed by the beating extra thoracic heart (*Figure 3*). With the aid of a pediatric video laryngoscope miller blade 1, a size 2.5 uncuffed endotracheal tube (ET) was inserted and secured. The presence of the NGT help in the identification of the anteriorly placed glottic opening.

Because of the extrathoracic location of the heart, we cannot obtain a good electrocardiogram (ECG) tracing since the vector of electrical potentials are not properly aligned with the heart. (*Figure 4*) We relied on the information derived from pulse oximetry, capnography and direct blood pressure (BP) monitoring from the femoral arterial line. A central venous line was inserted through the femoral vein for purposes of blood transfusion and administration of support drugs.

Arterial blood gas determination was immediately requested after an A-line access was obtained. Prompt correction of the metabolic acidosis state of the patient was done. This fragile neonate was maintained on total intravenous anesthesia (rocuronium, midazolam, and ketamine), supported by controlled ventilation using the modified Jackson Reese breathing system.

For cardiovascular support, we started milrinone and epinephrine infusion, titrated to desired hemodynamic effects. With this set up, she tolerated the rest of the preparations until cardiopulmonary bypass (CPB) was initiated to safely allow the surgical plan of liberating the heart and dissection of the pericardial and inner thoracic cavity, with the objective of accommodating the heart inside the thoracic cavity without undue compression. (*Figure 5*) However, there was deficient muscle and skeletal support --- the heart can only be partially deposited into the thoracic cavity. The heart was covered using a polytetrafluoroethylene (PTFE) graft and this sealed the anterior thoracic wall. (*Figure 6*)

In the process of weaning from CPB, we noted that the lungs cannot be properly inflated and there was some bleeding coming out of the endotracheal tube. Thus, weaning was stopped, and the problem at hand was addressed. With the aid of the video laryngoscope and neonatal endotracheal tube changer, we smoothly replaced the ET 2.5 to an uncuffed ET 3.0. Such action facilitated better lung ventilation and improved the cardio-respiratory dynamics.

Intraoperative fluid and blood replacement included packed red blood cell (PRBC), fresh frozen plasma (FFP) and platelet concentrate. CBG monitoring was done and maintained at 150 mg/dL. Weaning from the CPB was done cautiously and slowly, with support from milrinone and epinephrine infusions. Arterial blood gas (ABGs) and electrolytes were corrected and volume loading to the heart was carefully done, guided by central venous pressure (CVP) and arterial BP monitoring. Intraoperative urine output during CPB was 0.7 cc/kg/hr. The chest was successfully covered with PTFE and vital signs were maintained as follows: Systolic blood pressure (SBP) 50 – 60's / Diastolic blood pressure (DBP) 20 – 30 / Mean arterial pressure (MAP) 40s / cardiac rate (CR) 140s to 160/ Sp02 80 – 83% / ETC02 20s to 30s.

Induction to cutting time was one hour and forty-two minutes; Total bypass time was three hours and forty-six minutes. Total OR duration was eight hours and twenty-seven minutes. The patient was then endorsed to the pediatric cardiology intensive care for continuing management by the pediatric intensivist.

Figure 2. Complete cleft lip and complete cleft palate anomalies.

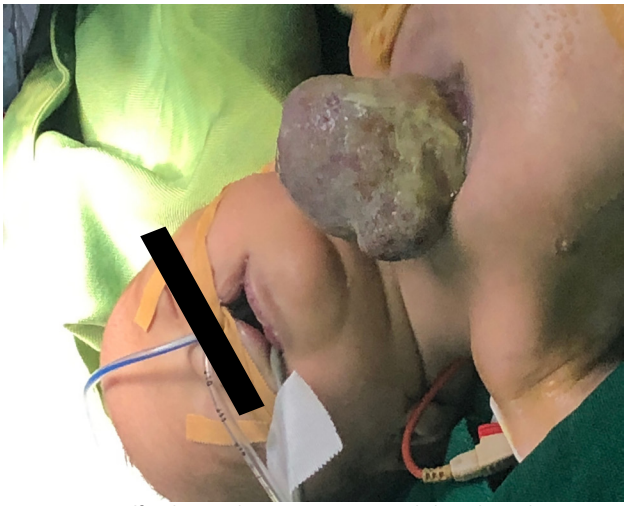

Figure 3. Difficult intubation aggravated by the obstruction posed by the beating extrathoracic heart.

Figure 1. Beating heart was covered by soft cloth, seen on top of the neonate's chest.

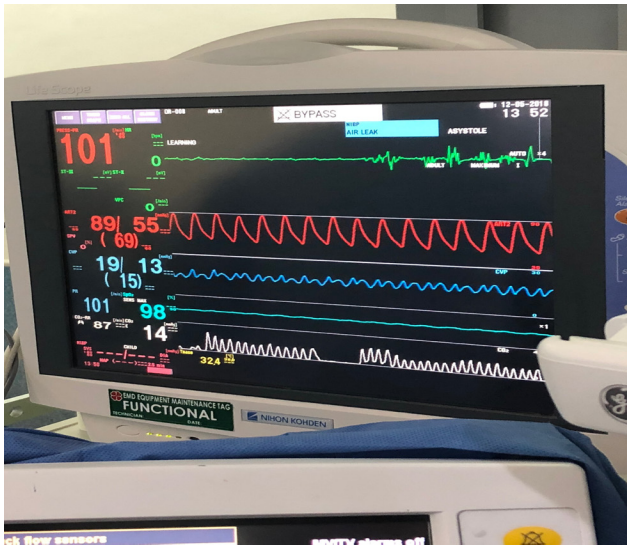

Figure 4. ECG tracing cannot be obtained since the vector of electrical potentials are not properly aligned with the heart.

Figure 5. Objective of the surgery was to accommodate the heart inside the thoracic cavity without undue compression.

Figure 6. The heart was covered by a PTFE graft, sealing the anterior thoracic wall.

DISCUSSION

The management of ectopia cordis on a neonate with co-existing congenital anomalies of cleft lip and cleft palate truly presents several challenges in perioperative care. The critical areas we experienced in this particular patient were (1) airway management (2) optimum patient monitoring and (3) pulmonary and hemodynamic stability during anesthesia.

Airway Management: The anesthesiologist must approach the anticipated difficult airway with both the science and art of anesthesia practice. As the protruding heart was lying on the anterior chest wall, there was a very limited space available for maneuvering the handle of the laryngoscope during the process of laryngoscopy and endotracheal intubation. Utmost care must be observed not to injure the exposed beating heart that lies very close to the patient's chin. Neonates usually have short neck, and the chin almost touches the anterior chest wall, where the beating heart sits. Thus, to facilitate the laryngoscopy, we elevated the torso of the neonate on folded linens, to a height good enough to allow the patient's head to drop back, naturally assuming a sniffing position. With the help of a pediatric video laryngoscope, successful visualization and intubation of the glottis opening was achieved.

Patient Monitoring: Cardiovascular monitoring in neonates with ectopia cordis definitely presents another major concern. Since the heart lies outside the thoracic cavity, the vector did not cross the ECG electrodes. The ECG complexes on the monitor were very small and inconclusive even with adjustments on gains and filtering modes.

Direct observation of the beating heart becomes very essential. Information derived from the invasive arterial pressure monitoring, pulse oximetry and capnography serve as the best surrogates to assess cardiac contractility, cardiac output and perfusion.

Hemodynamic Stability: A proper understanding of the existing cardiac congenital anomaly and pulmonary dynamics in neonates shall guide the anesthesiologist on which drugs should be used to support cardiac contractility and overall patient circulation and perfusion and the manner of ventilatory support to adopt intraoperatively. Because of the low birth weight, we opted to support respiration by simply using the modified Jackson Reese system. Milrinone and epinephrine infusions were initiated to support the function in AVSD, PS, with PDA since we anticipated the pulmonary hypertension that may occur in this neonate. The pulmonary hypertension can be primary or may be secondary to the AVSD, PS, and PDA. However, what is important is to support both ventricular functions.

CONCLUSION

Anesthesia management for the repair of ectopia cordis remains to be very difficult for the anesthesiologist, and would require the use of both invasive and non-invasive hemodynamic monitoring.[6] Use of cardiovascular drugs and fluid or blood replacement must be judicious and goal-directed. Concomitant airway abnormalities must be properly evaluated preoperatively to allow preparation of airway tools for proper intubation.

In summary, this patient was a great challenge in view of the difficult airway, limitations in perioperative monitoring. Cardiac and hemodynamic embarrassment encountered during surgery.

REFERENCES

1. Amato JJ, Zelen J, Talwalkar. Single-stage repair of thoracic ectopia cordis. Ann Thorac Surg. 1995 Feb; 59(2):518-20.
2. Apte V. Thoraco-abdominal ectopia cordis: a rare entity-case report and review of literature. People's J Scientific Research. 2008;1:31-3.
3. Taussig HB. World survey of the common cardiac malformations: developmental error or genetic variant? Am J Cardiol. 1982 Sep;50(3):544-59.
4. Morales JM, Patel SG, Dugg JA, Villareal RL, Simpson JW. Ectopia cordis and other midline defects. Ann Thorac Surg. 2000 Jul;70(1):111-4.
5. Shamberger RC, Welch KJ. Sternal defects. Pediatric Surgery Intl. 1990 May 1;5(3):156-64.
6. Whiteman AR, Dhesis JK, Walker D. The high-risk surgical patient: a role for a multi-disciplinary team approach? Br J Anaesth. 2016 Mar;116(3):311-4.

Dipyridamole Induced Stress Myocardial Perfusion Scintigraphy with Technetium-99m Sestamibi on an Infant

Irene S. Bandong, MD

The patient is a cyanotic 2-month-old male born with an electrocardiographic finding of an ST segment elevation and positive serum Troponin T. The patient was referred to undergo a dipyridamole stress myocardial perfusion scintigraphy with Tc-99m Sestamibi.

Myocardial perfusion scintigraphy of the rest and stress imaging were done on separate days for an easier performance of the procedure. The patient was likewise referred to anesthesiology and was accompanied by the mother during the acquisition for proper positioning. The patient was clothed to prevent any unnecessary movement. Rest imaging was first performed after injection of 112.48 MBq of Tc-99m Sestamibi. Four days after, the stress imaging was done after injection of 113.2 Mbq of Tc-99m Sestamibi on the 8th minute after dipyridamole infusion.

Baseline ECG showed sinus rhythm. Dipyridamole (1.5 mg) was infused for 4 minutes. Baseline blood pressure was 69/34 mmHg to a low of 59/27 mmHg. The cardiac rated was 150 bpm at baseline and reached a peak of 166 bpm. No significant dipyridamole -induced ST-T wave changes were noted. Post-infusion recovery was uneventful.

Stress images showed moderate to severe reduction of tracer activity in the basal to apical inferior/inferolateral segments. The remainder of the LV myocardium exhibited normal tracer distribution.

On interpretation, mainly scarred myocardium in the basal to apical inferior/inferolateral segments were noted. There was no evident inducible myocardial ischemia as well.

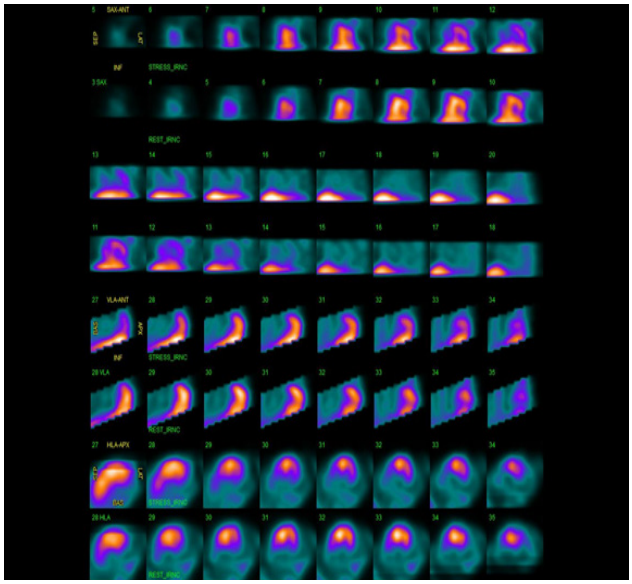

Figure 1. SPECT images showing the stress and rest images in short axis (SA), vertical long axis (VLA), and horizontal long aixs (HLA) views. The first row of images show moderate to severe reduction of tracer activity in the basal to apical inferior/inferolateral segments. This was persistent on rest images.

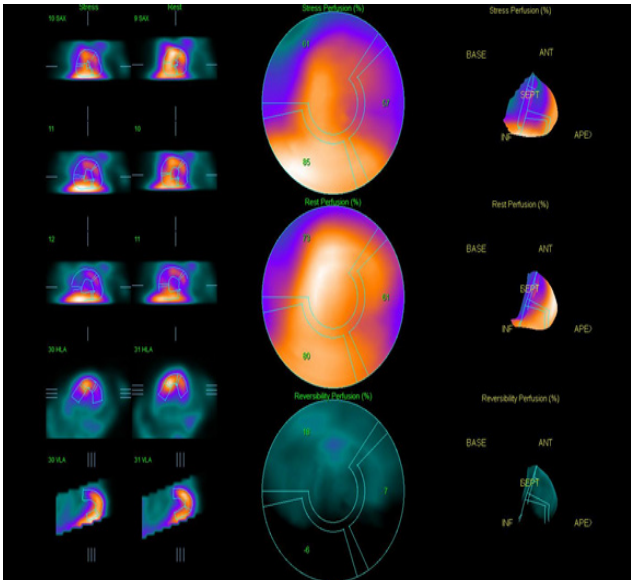

Figure 2. Polar map of the left ventricle perfusion for stress and rest.

COVID Myocarditis

Irene S. Bandong, MD

This is a case of a 24-year-old male who came in due to epigastric pain with a 6-day history of generalized body weakness and body malaise. One day prior to admission, the patient had grade 8/10 epigastric pain which was non-radiating and was accompanied by nausea and vomiting. ECG was done showing Antero-septal ST elevation, was managed as a case of ST elevation. myocardial infarction and was subsequently admitted.

Laboratories showed elevated Troponin I and a positive result on SARS-CoV-2 Assay. Chest X-ray showed hazy densities in the right lower lung with a consideration of pneumonia (*Figure 1*). The admitting impression was COVID-19 pneumonia; ACS, STEMI, Anterior Wall, Killip I, TIMI 2, in sinus rhythm, FC II.

COVID-19 medications were not started due to elevated liver function tests. Antibiotics, steroids and ACS regimen were started. However, the patient was persistently tachypneic with desaturations which lead to intubation. CT scan of the pulmonary arteries was done which showed moderately extensive areas of consolidation in both lower lobes and patchy ground-glass opacities in both upper lobes which were typical CT findings for COVID-19 pneumonia *(Figure 2*). Bilateral pleural effusion was also seen. There was no evidence of pulmonary embolic process on the CTPA.

2D echocardiography showed normal left ventricular dimensions with multi-segmental wall motion abnormality and depressed systolic function with diastolic dysfunction. On the succeeding hospital days, there was progression of the hazy densities in both lower lungs seen on chest x-ray (*Figure 3*). The patient was then managed as fulminant myocarditis and colchicine was started.

2D Echo was repeated which showed normal left ventricular dimension with normal wall motion, contractility and systolic function. Compared to the first 2D echo, there was an increase in ejection fraction from 35% to 55%. Cardiac MRI was done which showed T2W hyperintensity signals in the left ventricular myocardium compared with the skeletal muscle, indicative of myocardial edema (*Figure 4*). Normal chamber dimensions were noted with preserved systolic function. Patchy areas of late gadolinium enhancement in the apical anterior, apical septal, apical inferior and apical cap segments were seen which may represent necrosis (*Figure 5*). The MRI findings were consistent with COVID-19 myocarditis.

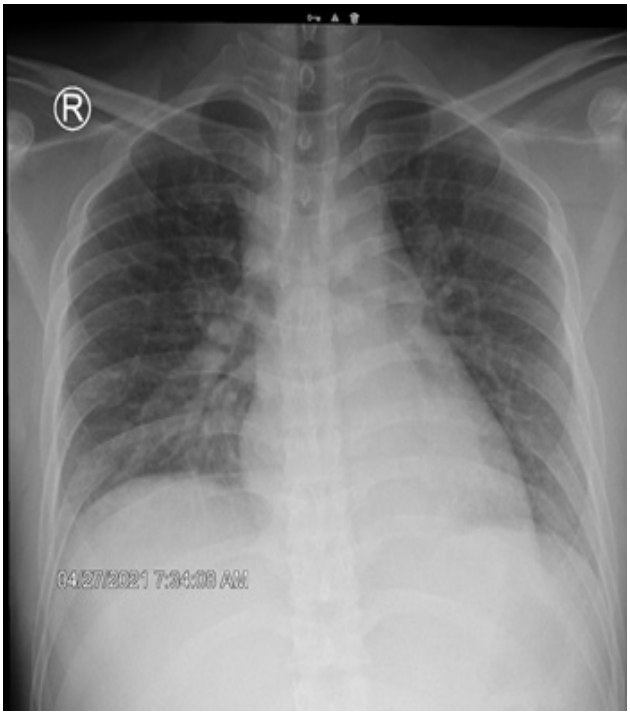

Figure 1. Chest X-ray showed hazy densities in the right lower lung.

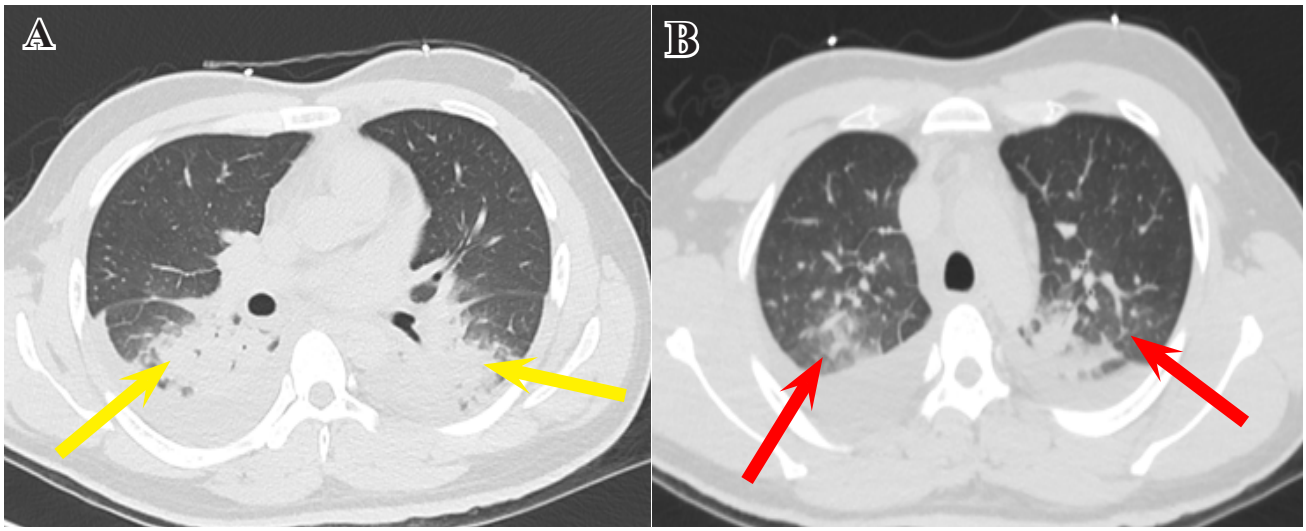

Figure 2. A. Moderately extensive areas of consolidation in both lower lobes (yellow arrows). B. Patchy ground-glass opacities in both upper lobes (red arrows).

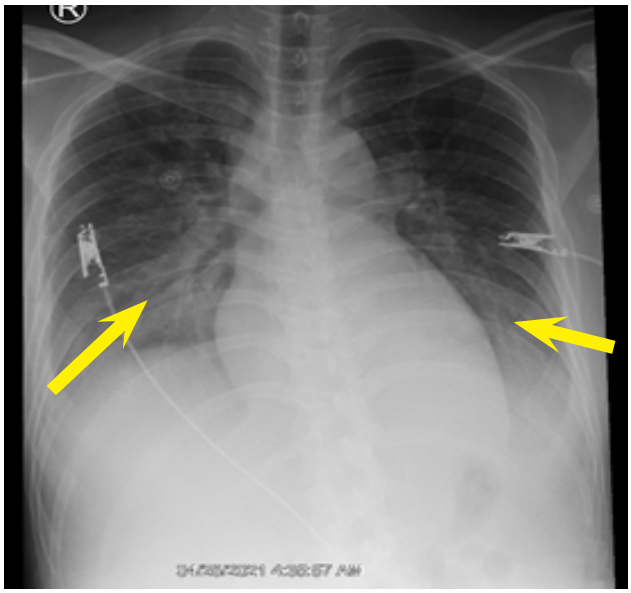

Figure 3. Hazy densities in both lower lungs seen on chest x-ray (yellow arrows).

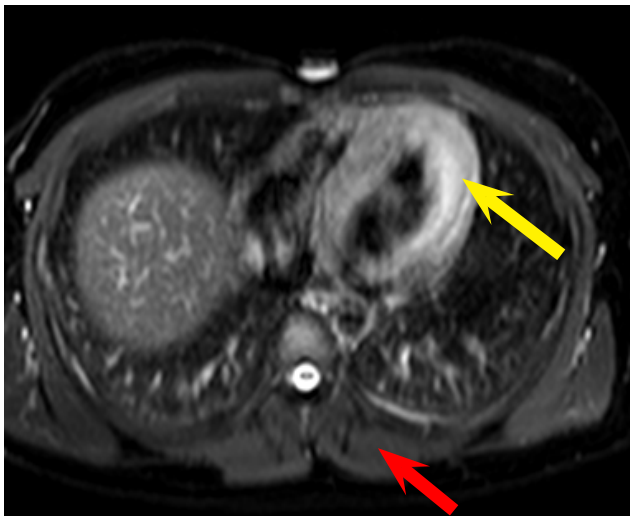

Figure 4. Cardiac MRI was done which showed T2W hyperintensity signals in the left ventricular myocardium (yellow arrow) compared with the skeletal muscle (red arrow), indicative of myocardial edema. Figure 4. Cardiac MRI was done which showed T2W hyperintensity signals in the left ventricular myocardium (yellow arrow) compared with the skeletal muscle (red arrow),

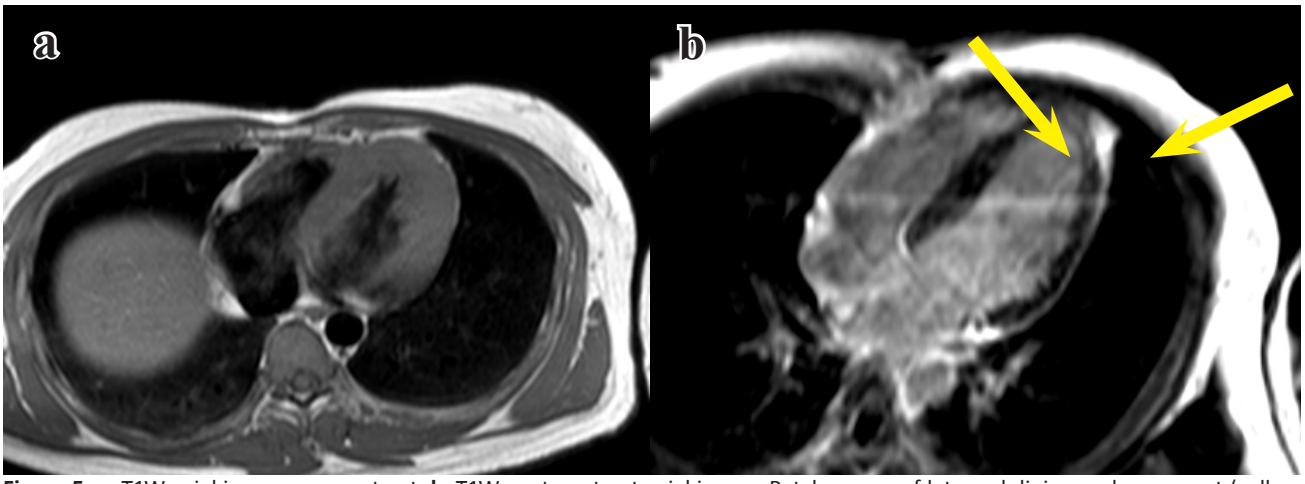

Figure 5. a. T1W axial image non-contrast. **b**. T1W post-contrast axial image. Patchy areas of late gadolinium enhancement (yellow arrows) in the apical anterior, apical septal, apical inferior and apical cap segments. Findings were consistent with non-ischemic pattern of enhancement such as myocarditis.

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.

Copyright Release and Authorship Responsibilities

All manuscripts must be accompanied by the following statements signed by all authors.

1. The undersigned author(s) transfer(s), assign(s) or otherwise convey(s) all copyright ownership of the manuscript [title of article] to the Philippine Heart Center Journal in the event the work is published. The undersigned author(s) attest(s) that the article is original in form and substance and is not under consideration by another journal.

2. The undersigned author(s) certifies (certify) that I (we) have participated to a sufficient degree in the design of this work, analysis of data, and the writing of the manuscript, and that I (we) am (are) taking responsibility for its contents.

Conflict of Interest Disclosure Statement

All authors are requested to disclose any relationship with an individual or organization with direct financial interest in the subject matter or materials discussed in the manuscript, because a perceived or real conflict of interest may otherwise arise. Disclosure of such relationship will be held in confidence during the review process of the work if accepted for publication. Disclosure of financial interest will appear as an annotation to the published manuscript.

MANUSCRIPT PREPARATION AND SUBMISSION

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

Gilbert C. Vilela, MD
Editor-in-Chief
Philippine Heart Center Journal
9th Floor, Medical Arts Building
Philippine Heart Center
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:

General Guidelines

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)
5. References
6. Figures and legends
7. Tables

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.

References

References are to be cited consecutively in the text with numbers enclosed in parentheses. At the end of each article, references should be listed consecutively in the numerical order in which they were cited in the text. The form of references should be as follows

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.

Figures

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.

Legends

Caption for the figures must be typed, double-spaced, and must not appear in the figure. For photomicrographs, the legend should include the original magnification and the stain used.

Tables

Tables should be self-explanatory and should supplement, not duplicate the text. They should be numbered consecutively using Roman numerals.

REPRINTS

Authors will receive ten (10) copies of reprints free of charge. Individual reprints of article must be obtained from the author. The corresponding author will receive a price schedule and order form at the time of publication. Reprints in quantity must be ordered from the publisher with the author's consent.