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Leahdette Padua, MD, FPCP

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Editorial

Translating Research Into Practice (TRIP): from bench to where?

Leadette Padua, MD, FPCP

Our institution produced numerous researches since its establishment. Majority of these were made by the trainees. Although research is often times considered as a coursework requirement, it should be viewed as a way to bridge the knowledge gap as well as to test hypotheses generated during patient encounters and conferences.

The repertoire of researches made in our institution includes risk-scorings, diagnostic exams and some clinical investigations. These were made to address clinical needs. Although we have made lots of researches in certain topics, there remains scarcity of researches in some aspects of cardiovascular care in our institution. This needs to be addressed as well.

Risk scorings, either original or adapted, are available for various clinical applications, from prognostication of ACS patients to the post-operative outcome of critically ill pediatric patients to the pulmonary function post-operatively. Some of these were devised based on the data gained from institutional registries or some of our retrospective studies. Some of these scoring systems, adapted from international studies, had been modified to suit our needs. Majority of them had been validated already in our institution. However, majority of the risk scoring systems had never been implemented.

Several researches on diagnostic tests had been made. Some of these, like BNP and D-dimer, had been made available in our laboratory initially for research purpose. However, the frequency of clinicians ordering these exams, despite these having known indication, is low.

Some of our original researches had therapeutic implications, like the use of colchicine to prevent post-pericardiotomy syndrome. But, how many clinicians utilize information gained from these clinical investigations in patient care?

The ideal flow of researches is from bench to bedside (and sometimes, back again to the bench). What usually happens is that some of our researches never made it beyond the work table. Our experience is not far from the real world scenario wherein countless biomedical research, especially basic science research, sometimes never made it to publication, and in those published, only a few made an impact in the clinics. [1]

It does not mean that all of our researches should make it to the clinics. We should of course practice discernment in selecting which researches should make an impact in our practice. After all, in this era of evidence-based medicine, it is not just the evidence that should matter. More importantly, the quality of evidence should be one of the main concerns.

[1] Ioannidis JPA (2006) Evolution and translation of research findings: From bench to where? PLoS Clin Trials 1(7): e36. doi:10.1371/journal.pctr.0010036. Accessed April 6, 2009.

Assessment of Left Ventricular Function by Doppler Velocity Tissue Imaging of the Mitral Annulus in Patients with Mitral Stenosis before and after Percutaneous Transvenous Mitral Commissurotomy

Neil D. Erguiza,MD; Edwin S. Tucay, MD; Viannely Berwyn Flores,MD; Romeo J. Santos,MD; Raul D. Jara,MD.

Background --- Several methods of assessing the post-PTMC cross-sectional area of the mitral valve by echocardiography in patients with rheumatic mitral stenosis are limited by several factors. Tissue Doppler imaging, a new echocardiographic technique that is being used for to evaluate LV function, eliminates some of the limitations that are encountered with the conventional methods. This study is aimed to determine if there is significant improvement in the mitral annular peak velocity after PTMC and if the change(s) is/are correlated with the planimeterized mitral valve area (MVA).

Methods --- Patients with mitral stenosis (MS) in Sinus Rhythm who underwent PTMC from June 01, 2006 to January 15, 2007 were included in the study. Transthoracic Echocardiogram (TTE) and Transesophageal Echocardiogram (TEE) were performed within 24 hours before PTMC. Repeat TTE were performed within 48 hours after the procedure. Tissue Doppler velocities were taken from the lateral and septal annuli during ejection, early diastole and late diastole. Changes between the pre-PTMC values and post- PTMC values were then correlated.

Results --- A total of 14 patients who underwent PTMC were included in the study. There is attenuation of all the echocardiographic parameters after PTMC. Among the annular velocities measured, significant improvement is observed only in lateral Sm and Em post PTMC, (p-value 0.011, 0.025). Also, no significant correlation was noted between pre- and post PTMC annular velocities with MVA by planimetry, (ejection: r=.30; p=0.285; early diastole: r= 0.28; p=0.329).

Conclusion --- There is a significant improvement in lateral Sm and Em post PTMC. There is a trend towards good correlation between the noted improvement in the peak velocities and the change in mitral valve area (MVA) by planimetry. ***Phil Heart Center J 2007; 13(2):89-91.***

Key Words: Mitral Valve Area ■ Percutaneous Transvenous Mitral Commissurotomy ■ Doppler Tissue Imaging

Mitral stenosis, a known sequela of Rheumatic Heart Disease, is brought about by structural changes in the mitral valve apparatus consisting of the valve itself and its associated structures such as the annuli, chordae, papillary muscles and the subvalvular apparatus.

Previous studies have shown that pure MS impairs left ventricular performance.[5] In approximately 15% of patients with isolated MS, the left ventricular end diastolic volume is reduced while the ejection fraction and other ejection indices of systolic performance is below normal in 25%.9 This deterioration of LV performance may be a result of functional factors. Functional factors result from restriction due to adhesion of the thickened and immobile mitral valve apparatus to the ventricle. In a study done by Lee et al, the majority of patients with deteriorated LV ejection fraction recovered after PTMC. The improvement of LVEF indicates that the deterioration of performance is primarily a result of functional restriction which was attenuated after the PTMC. Tissue Doppler imaging (DTI), a new echocardiographic technique that is now being used to evaluate the LV function,[3] measures myocardial velocities. Because of this, limitations such as unsatisfactory imaging quality are eliminated. One of its applications is the evaluation of LV function by measuring the mitral annular velocity along its long axis. The major advantage of pulsed wave annular velocity measurements is the ultrasound beam being parallel to the ventricular contraction. It is also non-invasive and repeatable.[6]

The first study using DTI in the evaluation of LV functions in patients with severe MS were done by Ozdemir et al. Their study had shown that myocardial velocities obtained from LV wall annuli were found to be significantly lower in patients with MS.

PTMC is an established technique for managing

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MS.[7] Several methods of assessing the procedural outcome are being used. These include the measurement of cross-sectional area by two dimensional planimetry and/or using the flow dependent parameters such as pressure half time, continuity equation and PISA. Since the flow dependent parameters are relatively inaccurate after PTMC, 2D planimetry is used as the non-invasive standard. However, this method also has technical limitations because it requires optimal image quality and that the operator must have a certain level of expertise tracking the mitral orifice, especially after PTMC when the orifice has assumed an unpredictable geometry. Aside from this, the change in the area of the orifice does not reflect the changes in the entire mitral valve apparatus' geometry and function. In the only study of patients with MS pre- and post-PTMC done by Sengupta et al, evaluation of changes in mitral annular velocities by Doppler tissues imaging aids clinical assessment of immediate improvement in left ventricular function after PTMC.[1] In the Philippine Heart Center where 50 to 60 PTMC procedures are done yearly,[4] DTI could help in the assessment of LV function in patients with MS after PTMC. Improvement in the myocardial velocities immediately after PTMC could explain the role of functional factors. This study was done to determine if there is significant improvement in the mitral peak annular velocity after PTMC and whether this improvement correlates well with the changes in planimeterized mitral valve orifice area. This is the first descriptive study that was done in this institution.

Methods

This is an observational study involving patients 18 years of age or older with pure MS in sinus rhythm who underwent PTMC at the Philippine Heart Center from June 01, 2006 to January 15, 2007. Excluded were patients with past interventions of the mitral valve such as close or open valvotomy and past PTMC, presence of co-morbidities such as hypertension, diabetes mellitus, coronary artery disease, pericardial disease and reactivation.

Echocardiographic evaluations were performed 1 to 24 hours before PTMC and 48 to 72 hours after the PTMC. The studies were performed by two operators. The following echocardiographic Tissue Doppler Imaging (DTI) protocol was used. The mitral annular velocities in the lateral and septal corners of mitral annulus were measured during ejection time, early diastole and late diastole. The procedure was performed using standard apical views with a sector angle of <60 degrees. The spectral Doppler signal filters were adjusted to obtain Nyquist limits of -60 and +60 cm/sec, with the lowest wall filter settings and the minimal optimal gain, to eliminate the signals produced by transmitral flow. The peak annular velocities were averaged over 2- 3 heartbeats.

Statistical Analysis

Data was reported as mean and standard deviation. Student t-test was used to compare echocardiographic variables before and after PTMC. $P < 0.5$ was considered significant. Correlation study between the changes in peak mitral velocities and MVA by planimetry was done.

Results

The table below shows that there is attenuation of all the echocardiographic parameters after PTMC. However, on statistical analysis, the ejection fraction (EF), Pulmonary Artery Pressure (PAP), all of the peak annular velocities taken from the septal annulus and the peak annular velocity from the lateral annulus during late diastole did not show significant improvement. Among the annular velocities measured, only the change in the peak annular velocities from the lateral annulus during ejection and early diastole are statistically significant. When the difference in mitral peak velocities from the lateral wall in ejection and early diastole pre- and post- PTMC was compared with the difference between the pre and post- PTMC MVA by planimetry, no significant correlation was noted.(ejection: r=.30; p=0.285; early diastole: r= 0.28;p=0.329).

Table 1. M-mode, 2-Dimensional and Doppler tissue Echocardiography findings in patients with mitral stenosis before and after PTMC

Features	Pre PTMC (n=14)	Post PTMC (n=14)	P value
MVA-2D PLN (cm2)	0.801 ± .18	1.63 ± .22	0.000 *S
MVA by PHT	0.839 ± .14	1.78 ± .63	0.000 *S
Mean MVG	12.977± 5.49	4.84 ± 1.69	0.000 *S
PAP	50.778 ± 36.53	35.44 ± 18.80	**0.067**
Ejection Fraction	62.727± 5.76	66.00± 4.96	**0.139**
Lateral Wall			
Sm *(m/sec)	0.114 ± .026	0.13 ± 0.33	0.011 * **S**
Em+	0.133 ± .037	0.15 ± 0.04	0.025 * **S**
Am±	0.111 ± .034	0.13 ± .041	>.05
Septal Wall			
Sm* (m/sec)	0. 119 ± .029	0.13 ± .030	0.221
Em+	0.124 ± .026	0.14 ± .052	0.256
Am±	0.094 ± .019	0.11 ± .030	0.058

*Sm= peak annular velocity of systolic excursion in ejection
+ Em = peak annular velocity in early diastole
±Am = peak annular velocity in late diastole

Discussion

Previous studies have shown that in about ¼ of patients with pure MS, the systolic performance is under a normal level. This deterioration in LV performance may be a result of functional and myocardial changes.[1] Functional factors result from extension of the scarring process from the mitral valve into adjacent mitral valve apparatus. Myocardial factors may result from rheumatic changes in the myocardium itself and from structural adaptations like cellular atrophy in response to hemodynamic derangements such as decrease in preload. Tissue Doppler imaging is a relatively new

method used for quantification of systolic and diastolic myocardial function. The first study where pure MS was evaluated by DTI had shown that the myocardial velocities of the left ventricle were found to be significantly lower in patients with pure MS as compared to the healthy individuals.[2] Later, a study was done by Sengupta et al in patients who underwent PTMC had shown that evaluation of changes in mitral annular velocities by Doppler Tissue Imaging aids in clinical assessment of immediate improve-ment in left ventricular after PTMC.[1] In our study, we found improvement in most of the peak annular velocities. On statistical analysis, we noted significant improvement of the peak annular velocities of the lateral annulus in ejection and early diastole. This increase in mitral annular velocities could be explained by the rapid reversal of the increased myocardial stiffness and improved motion and function of the subvalvular structures and myocardial segments brought about by mobilization of the mitral valve apparatus after PTMC.[8] The more prominent changes in the lateral annulus as compared to that in septal annulus can be explained by abnormal right and left sided heart interaction, which are likely to be more pronounced in the septum.

When the difference in mitral peak velocities from the lateral wall in ejection and early diastole pre- and post-PTMC was compared with the difference between the pre and post- PTMC MVA by planimetry, no significant correlation was noted.(ejection: r=.30; p=0.285; early diastole: r= 0.28;p=0.329). The study done by Sengupta MD et al showed significant correlation between the improvement in peak annular velocity in early diastole and the MVA by planimetry.[1] That study however included more number of patients. The paucity of sample population in our study possibly could have affected the correlative study.

Conclusion

There is a significant improvement in lateral Sm and Em post PTMC. This has confirmed that the functional change in LV myocardium is partly reversible.. Its use in the assessment of outcome of PTMC could be helpful especially in cases where limitations of the conventional echocardiographic methods are apparent. There is a trend towards good correlation between the noted improvement in the peak velocities and the change in mitral valve area (MVA) by planimetry. Additional sample population should be included for further evaluation of the correlation between the changes.

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A Comparative Study of Bioimpedance and the Thermodilution Method in Cardiac Output Monitoring After Coronary Artery Bypass Grafting

Joseph George G. Tamayo, MD; Santos-Jose Abad, MD.

Background --- Cardiac Output can be reliably monitored noninvasively after Coronary Artery Bypass Grafting Surgery. It is the aim of this study to determine the reliability of cardiobioimpedance in monitoring the cardiac output after coronary artery bypass grafting in comparison with thermodilution method.

Methods --- This is a validation study involving patients who underwent coronary artery bypass grafting who had a pulmonary artery catheter inserted and admitted to the PHC Recovery Room from May to December 2006. Cardiac output, cardiac index and systemic vascular resistance were measured using bioimpedance cardiography and thermodilution method simultaneously in the first, second, fourth and eight hour after Coronary Artery bypass grafting

Results --- A total of 38 patients who underwent Coronary artery bypass grafting were investigated. Mean cardiac output on the 1st, 2nd , 4th and 8th hour by cardioimpedance were 3.22 L/min (r=0.937, p-value 0.0), 3.61 L/min (r=0.963, p-value 0.086), 3.81 L/min (r=0.934, p-value 0.01) and 4.33 L/min (r=0.958, p-value 0.010) compared to thermodiltion results of 3.4 l/min, 3.6 L/min, 3.99 L/min and 4.23 L/min. Mean Cardiac Index on the same monitoring by cardioimpedance were 2.24 (r=0.934, p-value 0.396), 2.35 (r=.969, p value 0.481) 2.82 (r=0.999, p-value 0.231) and 2.91 (r=0.994, p-value 0.458) compared to thermodilution which showed 1.94, 2.17, 3.06 and 3.13 respectively.

Conclusion --- Cardioimpedance reliably measures cardiac output in patients after Coronary artery bypass grafting operation. It enhances the value of the method in continuous monitoring of patients after the said operation. ***Phil Heart Center J 2007; 13(2):92-95.***

Key Words: Bioimpedance ■ Thermodilution ■ Cardiac Output ■ Validation ■ Coronary artery bypass graft surgery

The early period after Coronary Artery Bypass Grafting operation provides a crucial opportunity for early assessment and rapid therapeutic interventions that may affect the outcome of the said procedure. After CABG, patients require careful hemodynamic monitoring for at least the first postoperative day, because the patient shows significant hemodynamic instability during this initial intensive care unit period.[1] The primary purpose of circulatory monitoring is to obtain frequent, repetitive or continuous measurement of circulatory functions to allow prompt recognition and early initiation of therapy.

Invasive and noninvasive monitoring systems can provide similar information that identifies episodes of hypotension, low cardiac output and deranged vascular resistance. In practice, a 10 to 15% difference between invasive and noninvasive cardiac estimations would be acceptable when 30% to 50% changes from the normal range are present.[2]

Thermodilution used in conjunction with PA balloon flotation catheter to obtain simultaneous PA opening pressure has become the standard for hemodynamic evaluation particularly in the early stages of acute critical illness and high risk surgical procedures. The use of the invasive method for measuring cardiac output has its controversies from infections to its associated increased morbidity and mortality.[3] Although in a recent study by Chittock et al, the use of pulmonary artery catheter was associated with decreased mortality in the most critically ill patients and with increased mortality in patients with less severe illness. Thermodilution also has an appreciable inaccuracies in both high and low cardiac output ranges and especially when the patient has hypothermia and arrhythmias, which is usually seen in post CABG patients.

Cardiac output can be determined non invasively by impedance measurement. In this method the injecting electrode produce an electrical field across the thorax from the base of the neck to the level of the xiphisternal junction, the electrical signals travel predominantly down the aorta rather than through the alveoli. Clinical evaluation under the worst case scenario of emergency trauma in an inner-city county hospital have shown improved stability of signal and satisfactory agreement with simultaneous thermodilution cardiac output measurements. The correlation of bioimpedance versus thermodilution cardiac output measurement were equivalent to those of pulse oximetry

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compared with the standard blood gas analysis. No instance of spurious impedance values that would have led to incorrect or harmful therapy was observed.[4]

Because of this, it is being considered that non invasive cardiac output monitoring by bioimpedance can be an acceptable cheaper and safer alternative to invasive monitoring in post CABG patients. This study is aimed to compare the cardiac output monitoring measured by thermodilution and bioimpedance in the first eight hours after coronary artery bypass grafting operation as well as to determine if there is a significant difference between thermodilution and bioimpedance cardiac output estimations after coronary artery bypass grafting surgery.

Methods

This is a validation study involving patients who underwent coronary artery bypass grafting who had a pulmonary artery catheter inserted and was admitted to the PHC Recovery Room from May to December 2006. After establishing the patient's eligibility, written informed consent was obtained. Baseline demographic data, comorbidities, ejection fraction by echocardiography, coronary angiographic findings and drugs used after the operation were also obtained.

Data were collected during the first eight hours postoperatively at the recovery room from each patient using thermodilution bolus method and by using bioimpedance monitoring (BioZ System 1.52) simultaneously. The data were collected within the first hour and then every two to four hours (1st hr, 2nd hr, 4th hr and 8th hr) for three determinations. Thermodilution data was obtained using the pulmonary catheter. The position of the pulmonary catheter was verified by waveform analysis, the computation constant was confirmed and the transducer leveled and zeroed. For each patient , cardiac output was measured using a room temperature fluid bolus technique. Exactly 10 ml of normal saline was injected through a cardiac output injection kit connected to the right atrial port of the pulmonary artery catheter. Injection time was less 4 seconds. The cardiac output curve was examined with each injection to ensure that the curve and the injection time were normal. A total of 3 thermodilution measurements were obtained for each patient. Cardiac output, cardiac index, systemic vascular resistance was recorded as indicated by the bioimpedance monitor each time a bolus was injected for the thermodilution measurements.

Statistical Analysis

Data were described as mean, standard deviation, frequency and percent distribution. Paired t-test and Pearson Correlation Analysis were used for comparing results of cardiac output, cardiac index and systemic vascular resistance of bioimpedance and thermodilution method. A p value ≤ 0.05 was considered significant.

Results

A total of 38 patients who underwent Coronary artery bypass grafting were included in the study. Majority (71%) were males and the mean age was 58.3 ± 10.5 years, although about a quarter were less than 50 years-old. Co-morbidities present were hypertension which was seen in 58% of the cases, followed by diabetes (42%). Echocardiographic data showed a mean left ventricular ejection fraction of 58.9 ± 13.9, with 21% of these patients having an ejection fraction lower than 50 percent. A total of 76 % have 3 vessel disease, while 26 % had Left Main involvement. Only 18% had 2 vessel disease. All patients were on inotropics after CABG and 36% were on vasodilator. All of them were on mechanical ventilator (Table 1). Data on hemodynamics on the patients analyzed were shown in Table 2. The said data were collected on the 1st hr, 2nd hr, 4th and 8th hr post CABG. Mean cardiac output on the 1st, 2nd , 4th and 8th hour by cardioimpedance were 3.22 L/min (r=0.937, p-value 0.0), 3.61 L/min (r=0.963, p-value 0.086), 3.81 L/min (r=0.934, p-value0.01) and 4.33 L/min (r=0.958, p-value 0.010) compared to thermodiltion results of 3.4 l/min, 3.6 L/min, 3.99 L/min and 4.23 L/min. Mean Cardiac Index on the same monitoring by cardioimpedance were 2.24 (r=0.934, p-value 0.396) 2.35 (r=.969, p value 0.481) 2.82 (r=0.999, p-value 0.231) and 2.91 (r=0.994, p-value 0.458) compared to thermodilution which showed 1.94, 2.17, 3.06 and 3.13 respectively. Mean SVR on the same monitoring by cardioimpedance were 1973.89 (r=0.920, p-value 0.169) 1834.24 (r=0.969, p value 0.173) 1764.26 (r=0.914, p-value 0.637) and 1708.34 (r=0.967, p-value 0.652) compared to thermodilution which showed 2037.74, 1860, 1749.97 and 1715.60 respectively. The p value on cardiac index and SVR showed a non significant difference between thermodilution and bioimpedance. A non significant difference was noted only on the 2nd hour of cardiac output monitoring. A high Pearson Correlation coefficient was noted on the three hemodynamic parameters.

Discussion

Traditionally, pulmonary artery catheters have been used to monitor and adjust medications to optimize hemodynamic status after coronary artery bypass grafting. Hemodynamic status can be measured intermittently or sequentially using such method. A continuous measurement of cardiac output increased the number of treatment decisions and this will provide a hemodynamically guided care to monitor the course of treatment in post CABG patient since most of them have altered hemodynamics status, on inotropics and on vasodilator therapy.

Impedance cardiography can be an accurate method of measuring cardiac output, cardiac index and other hemodynamic parameters. It is a viable alternative to

pulmonary artery catheters in patients who will undergo CABG or hemodynamic study. The measurements of hemodynamic data should be compared with the current method or technique to examine the reliability of a new method. Patients who underwent CABG should have a continuous monitoring for the primary purpose of hemodynamically guided therapy for stabilization of their altered hemodynamics. In our study, cardioimpedance showed no significant difference to thermodilution in measuring cardiac output, cardiac index and SVR. Both methods for the said hemodynamic study were acceptable even though there were conflicting data on cardiac output monitoring which could be affected by stroke volume, heart rate or body surface area. Woltzer et al showed that weight can influence stroke volume in impedance cardiography.[5] Evidence indicates that factors related to clinicians and equipment and intrinsic to patient, may affect the accuracy and reproducibility of thermodilution measurements likewise the accuracy of impedance cardiography may be influenced by factors related to clinician such as sensor placement, the digital; signal processing systems, and the algorithm and equations used to calculate cardiac output. Therefore many human and technological factors would affect the correlation of cardiac output measurements made with clinical standard (thermodilution) and measurements made with impedance cardiography.[6]

The agreement between thermodilution method and impedance cardiography is similar to reported comparisons between invasive methods in analogous setting.[7] Drazner et al found that Pearson Correlations between impedance cardiography and thermodilution were 0.76 for cardiac output and 0.64 for cardiac index, much less than we found in our study (0.96 and 0.93) respectively. A high Pearson correlation coefficient may mean high agreement between methods of measuring cardiac output. Despite differences in methods, these studies both indicate that impedance cardiography provides results that are comparable to results of accepted invasive techniques. Cardioimpedance reliably measures cardiac output in patients after CABG. The excellent repeatability of bioimpedance enhances the value of this method in continuous monitoring of patients after CABG.

Since all our patients were on mechanical ventilation and can have a possible influence on accuracy of cardioimpedance. Our study showed that comparable results were obtained using thermodilution and cardioimpedance in our patients. The present study indicates that cardioimpedance can be reliable in mechanically ventilated patients similar to other researches who have reported positive clinical results with impedance cardiography in patients receiving mechanical ventilation.[8]

Impedance cardiography is a useful monitoring technique in a critical care unit[9] and could decrease hospital costs associated with invasive and hemodynamic monitoring.[10] In a small study[11] in which the investigators evaluated whether the availability of impedance cardiography could reduce the need for pulmonary artery catheterization, patients who were first determined to need invasive monitoring were subsequently monitored with impedance cardiography. In 71% of patients, use of impedance cardiography eliminated the need for a pulmonary artery catheter.

Conclusions

Bioimpedance is a noninvasive technology use to measure cardiac output and can provide other hemodynamic measurements. Our study provided evidence that hemodynamic measurement done using this method is almost in agreement when compared with bolus thermodilution method. Cardiac output is easier to measure by impedance cardiography than by thermodilution. It can be applied quickly and does not pose a risk of infection and other complications associated with arterial catheters. Our findings provided further validation of the use of cardioimpedance for continuous monitoring post CABG patients. In addition the increased frequency of cardiac output data available with impedance cardiography might lead to more timely interventions.

Table 1. Clinico-demographic Characteristics of post-CABG patients

Variable	N (%) N=38
Age (yrs) Mean ± SD	58.3 ± 10.6
Sex Male	27 (71%)
Female	11 (29%)
Co-morbidity	
Hypertension	22 (58%)
Diabetes Mellitus	16 (42%)
Smoking history	11 (29%)
Dyslipidemia	3 (8%)
Renal insufficiency	1 (2%)
PAOD	1 (2%)
Echocardiography (EF) (mean,SD)	58.9 ± 13.9
Coronary Angiogram	
1 vessel disease	2 (5%)
2 vessel disease	7 (18%)
3 vessel disease	29 (76%)
Left main involvement	10 (26%)
Drugs used after bypass	
IV inotropic	38 (100%)
IV vasodilator	10 (26%)
IV inodilator	1 (5%)

Table 2. Comparison of hemodynamic parameters obtained using Bioimpedance with Thermodilution Method

	BIOIMPEDANCE Mean	SD	THERMODILUTION Mean	SD	CORRELATION (r)	P Value
CARDIAC OUTPUT						
1st hr	3.22	0.70	3.40	0.71	0.937	0.000
2nd hr	3.61	0.73	3.66	0.70	0.963	0.086
difference	0.38		0.27			
p-value	0.000		0.000			
4th hr	3.81	0.80	3.99	0.65	0.934	0.001
difference	0.59		0.59			
p-value	0.000		0.000			
8th hr	4.33	0.75	4.23	0.68	0.958	0.010
difference	1.11		0.84			
p-value	0.000		0.000			
CARDIAC INDEX						
1st hr	2.24	2.23	1.94	0.44	0.934	0.396
2nd hr	2.35	1.67	2.17	0.50	0.969	0.481
difference	0.11		0.23			
p-value	0.277		0.000			
4th hr	2.82	3.86	3.06	5.06	0.999	0.231
difference	0.58		1.12			
p-value	0.039		0.177			
8th hr	2.91	2.30	3.13	4.07	0.994	0.458
difference	0.67		1.19			
p-value	0.000		0.078			
SVR						
1st hr	1973.9	706.91	2037.74	697.87	0.920	0.169
2nd hr	1834.2	586.34	1860.00	614.54	0.983	0.173
difference	139.66		177.74			
p-value	0.108		0.044			
4th hr	1764.3	438.29	1749.97	452.80	0.914	0.637
difference	209.63		287.76			
p-value	0.033		0.001			
8th hr	1708.3	386.52	1715.60	380.63	0.967	0.652
difference	265.55		322.13			
p-value	0.006		0.001			

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Diagnosis of Arterial Disease of the Lower Extremities With Duplex Scanning: A Validation Study

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Background --- While standard x-ray arteriography remains the traditional gold standard for peripheral arterial imaging, it has obvious limitations and is associated with significant local and systemic complications. Technological advances in duplex ultrasonography have allowed lower-extremity arterial mapping, primarily of the femoropopliteal segment, based on morphological and hemodynamic parameters. However, inadequate sonographic visualization of the infrapopliteal arteries is seen as a major limiting factor for the liberal use of duplex ultrasonography as a sole preoperative imaging modality. Others have documented the feasibility and reliability of infrapopliteal duplex ultrasound arterial mapping. These divergent results may be partially explained by the operator-dependent nature of this exam and different types of scanners utilized by various investigators. To date, there has been no validation study done in the Philippine Heart Center on the duplex sonographic evaluation of the peripheral arteries in patients suspected of having peripheral arterial occlusive disease. This study was conducted to determine the diagnostic accuracy of duplex scanning in patients suspected of having peripheral arterial disease.

Methods --- This was a cross-sectional validation study involving duplex ultrasonography studies of femoral arterial segments of patients suspected of peripheral arterial disease. The results of these were compared to the results obtained using subtraction angiography. Each segment was graded as normal, <50% stenosis, > 50% stenosis, near total-occlusion , and total occlusion. The duplex scan results were evaluated independently by two vascular specialists while the arteriogram result was evaluated by an experienced interventional cardiologist. The Kappa statistic was used to examine the level of agreement between angiography and ultrasound.

Results --- The Kappa level (95% confidence interval) of agreement between ultrasound and angiographic assessments for distinguishing hemodynamically significant (>50%) stenosis was 0.55. Poorest agreement was observed from ultrasound assessments of the popliteal artery as compared to the other arterial segments studied.

Conclusion --- It has been demonstrated that Duplex ultrasonography produces satisfactory agreement with arteriography for the diagnosis of peripheral arterial occlusive disease, and this technique can even limit the need for arteriography in assessing this subset of patients. ***Phil Heart Center J 2007; 13(2):96-100.***

Key Words: Peripheral arterial disease ■ duplex ultrasonography, digital subtraction angiography ■ validation study

Peripheral arterial disease is part of a more generalized involvement of the arteries by atherosclerosis. Risk factors for peripheral arterial disease are the same as those for coronary and carotid artery disease, namely, smoking, hypercholesterolemia, hypertension and diabetes. Its prevalence is difficult to establish because majority of patients are asymptomatic.[1] While standard x-ray arteriography remains the traditional gold standard for peripheral arterial imaging, it has obvious limitations and is associated with significant local and systemic complications. For these reasons, the interest in less invasive arterial imaging techniques has grown recently. Technological advances in duplex ultrasonography have allowed lower-extremity arterial mapping, primarily of the femoropopliteal segment, based on morphological and hemodynamic parameters. In fact, several investigators reported an acceptable correlation between duplex ultrasonography and catheter arteriography. The sensitivity and specificity of duplex ultrasonography for the detection and grading of peripheral arterial disease involving the aorta-iliac and femoropopliteal segments are generally moderate to high, ranging from 70-92%.[2,3,4,5] However, inadequate sonographic visualization of the infrapopliteal arteries, as reported in some series, is a major limiting factor for the liberal use of duplex ultrasonography as a sole preoperative imaging modality.[6] Others have documented the feasibility and reliability of infrapopliteal duplex ultrasound arterial mapping.[7,8] These divergent results may be partially explained by the operator-dependent nature of this exam and different types of scanners utilized by various investigators. To date, there has been no validation study done in the Philippine Heart Center on the duplex sonographic evaluation of the peripheral arteries in patients suspected of having peripheral arterial occlusive disease. This study was therefore conducted to determine the diagnostic.

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accuracy of duplex ultrasonography in patients suspected of having peripheral arterial disease. Specifically, the study was aimed to determine the concordance between the duplex ultrasonography and arteriography in patients with peripheral arterial occlusive disease, as well as to compare the accuracy of our local duplex ultrasonography with international validity studies in the detection of peripheral arterial occlusive disease.

Methods

This was a cross-sectional validation study involving patients who underwent catheter arteriography of the lower extremities at the Philippine Heart Center from January1, 2005 to December 31, 2006. The roster of subjects was identified from the Department of Radiology database. The identified names were checked against the Vascular Section database to see if they also had undergone arterial duplex ultrasound. Patients with both duplex ultrasound and catheter arteriography were included in the study, provided that the latter was done within two months after the duplex ultrasound was performed. Catheter arteriography was used as the reference standard.

Duplex Scanning

All the peripheral arterial duplex procedures were done by expert vascular technologists who have had more than 5 years experience in performing the procedure. The color duplex equipment used was Logic 700 Pro-series, General Electric (Japan). Patients were placed supine on the examination table. The bilateral lower extremity arterial segments were insonated at an angle of less than 60 degrees, starting at the level of the distal external iliac artery down to the dorsalis pedis artery using a 5-7 MHz linear transducer. For the purpose of this study, only the data from the distal external iliac artery and femoropopliteal segments were obtained for analysis. In arteries with different categories of lesions, the most severe lesion was taken for comparison with arteriography.

In every arterial segment that was accessible and could be evaluated, gray-scale B-mode imaging, color-flow imaging and pulsed-Doppler spectral waveform analysis were done to get information regarding presence or absence of obstruction, type of obstruction and evaluation of blood flow velocity. Peak systolic velocity (PSV) was measured. The total examination time would take 30-45 minutes.

Catheter Arteriography

Catheter arteriography was performed by experienced interventional radiologists who may or may not be aware of the duplex scan findings. The procedure was performed using 5-F universal flush catheters placed in the infrarenal abdominal aorta at the level of the third lumber vertebra. Non-ionic dye (Ultravist), 370mg iodine/ml, was injected via a power injector at 5 ml/second. After the film was reviewed, a second injection was done in the common femoral artery and a third injection may be done in the mid-distal superficial femoral artery to clearly visualize the distal arterial segments. Each of the lower extremity was assessed. Digital subtraction arteriography (DSA) was employed usually at the popliteal artery level but may be employed in the upper segments if there is technical difficulty in visualizing the upper arterial segments. Approximately, 100 cc of contrast agent was used per procedure.

Image Evaluation

The arterial duplex scan results were analyzed and interpreted independently by two experienced vascular specialists. The B-mode and color flow images as well as the spectral Doppler velocities and waveform patterns in a particular arterial segment were analyzed independently by the two readers. The severity of stenosis was determined by the PSV ratio at the site of the stenosis and the normal adjacent artery and was translated to percent diameter reduction. Stenosis category scale9 used were as follows: 0% diameter reduction (normal), if PSV was within normal limits without presence of plaque/obstruction, and with triphasic waveform pattern (Table 1); 1-19% (mild) if PSV was within normal limits but with presence of plaque/obstruction, with triphasic waveform pattern; 20-49% (moderate) if PSV was increased by 30-99% from the normal adjacent segment and with signs of obstruction, with triphasic waveform pattern; 50-99% (hemodynamically significant) if PSV was increased by >100% from the adjacent normal segment or with biphasic waveform pattern; >75% stenosis was reported if the PSV was >400cm/sec; near-total occlusion if with monophasic or thump waveform pattern and very low PSV; and lastly, total occlusion if there was no Doppler signal seen. The arteriogram result was interpreted by an experienced interventional radiologist. The severity of stenosis was determined by the luminal diameter ratio at the site of the stenosis and the normal adjacent segment, reported as percent diameter reduction. For research purposes, a particular arterial segment stenosis was graded as follows: 0% diameter reduction (normal); 1-49% diameter reduction (hemodynamically insignificant stenosis); 50-99% diameter reduction (hemodynamically significant stenosis); near-total occlusion if there was a hairline flow of the contrast within the stenosed segment; and, total occlusion if there was no flow of contrast within the segment. Other clinically relevant clinical findings were: diffuse long-segment atherosclerotic plaque, thrombotic occlusion, and ulcerated plaques. Plaques may be described as focal or long, calcified or non-calcified, concentric or eccentric, smooth or ulcerated. Multiple projections may be needed to uncover significant stenosis, but the anteroposterior view was the one was uniformly used.

Table 1. Classification of the spectral waveform pattern[9]

Waveform	Characteristics
Triphasic	three waveform "phases" consisting of a sharp systolic forward up rise and fall, an element of reverse flow during diastole, and an element of forward flow during diastole
Biphasic	two waveform "phases" consisting of a systolic forward up rise and fall with loss of reverse flow during early diastole
Monophasic	one waveform "phase" consisting of slow and blunted systolic rise and fall with loss of diastolic flow
Thump	no waveform is seen on the Doppler spectral display

Results

Twenty one non-consecutive patients were included in the study (Table 2). Their average age was 61 years. The youngest was 32 while the oldest was 86 years old. Eighteen were males. Majority of patients were hypertensives (71%), smokers (67%) and with concomitant coronary artery disease. Less than half of the patients were diabetic (38%). One patient had a previous aortofemoral bypass surgery on the left with concomitant above the knee amputation on the right 8 years ago. Another patient had below the knee amputation more than 50 years ago. Table 3 shows the patients indications for the non-invasive and invasive work-ups for their peripheral arterial occlusive disease.

Table 2. Baseline Characteristics of Included Patients

Characteristic	N	(%)	SD
Age (mean)	61		± 15.45
Sex			
Male	18	(86)	
Female	3	(14)	
Diabetes	8	(38)	
Hypertension	15	(71)	
Smoking	14	(67)	
Coronary artery disease	12	(57)	
Previous lower extremity surgery	2	(10)	
Abdominal aortic aneurysm	1	(5)	

Of the 21 patients, 20 patients had their catheter arteriography done within 20 days after their lower extremity arterial ultrasound was done and one patient had his arteriogram done on the 60th day after his ultrasound.

A total of 278 arterial segments were evaluated both by duplex ultrasound and arteriography. The two-way contingency table for classification of disease by duplex ultrasound and arteriography is given in Table 4. Accuracy, sensitivity, specificity, positive predictive value, negative predictive value and kappa values were calculated. Kappa statistic is a method to relate the found agreement between Duplex ultrasound and arteriography to the proportion of agreement expected by chance. A kappa value of 1.0 means a perfect correlation whereas 0 means a total lack of correlation.

Table 3. Frequency of indications for work-up

Indications	No.
Disabling claudication	2
Rest pain	7
Gangrene	5
Non-healing ulcer	2
Acute limb ischemia	2
Popliteal aneurysm	1
Femoral artery aneurysm	2
Total	21

Table 4. Two-way contingency table for results of duplex ultrasound as compared to arteriography (N= 278 segments)

	Arteriogram Classification (% stenosis)				
	0	<50%	≥50%	Near-Total Occlusion	Total Occlusion
Duplex Classification (% stenosis)					
0	70	2	0	0	0
< 50%	8	75	7	0	3
≥50%	0	20	30	5	4
Near-Total Occlusion	1	0	5	5	11
Total Occlusion	0	0	0	0	32

There were a total of 32 segments which were seen to be totally occluded on duplex ultrasound and were all confirmed by arteriography. Of the 32 occluded segments, 7 were thrombotic in nature, 2 of which occurred in femoropopliteal aneurysms and 1 occurred inside a bypass graft. The two aneurysms mentioned were clearly demonstrated in the duplex ultrasound but not in the arteriogram. The rest of the total occlusions were brought about by heavy calcified intraluminal plaques. There were three segments which were interpreted as having insignificant arterial occlusive disease on ultrasound but were interpreted as totally occluding lesions by arteriography. Table 5 lists sensitivities, specificities and kappa values for the various arterial segments.

Table 5. Validity Measures of Duplex scanning as compared to arteriography

Segment		n	Kappa	Accuracy %	Sensitivity %	Specificity %	PPV %	NPV %
DEIA		39	0.92	82	92	89	90	97
CFA		39	NA	94	86	92	84	96
DFA		37	NA	73	85	89	89	92
SFA	proximal	41	0.74	76	72	96	96	90
	Mid	40	0.68	70	78	94	83	90
	Distal	41	0.75	73	81	98	98	98
Popliteal A		41	0.56	68	88	84	87	95

Discussion

Arteriography has long been the definitive test for symptomatic aortoiliac and lower extremity arterial disease. However, this approach provides anatomic rather than functional data and has many limitations. Interpretation is also subject to wide inter-observer variability. Because atherosclerotic lesions are often eccentric, the angiographic appearance may be misleading, especially if only unipolar views are obtained. The best way to determine the hemodynamic significance of arterial lesions is to measure the pressure gradient at angiography, but this is not always practical or anatomically possible. Moreover, the invasive nature and relatively high cost of angiography make it unsuitable for screening purposes or routine follow-up. Although MRA and CTA are increasingly used for non-invasive vascular imaging, DUS has proved to be cost-effective and accurate for the detection of significant vascular stenoses and is therefore often used as the first diagnostic modality.

From a clinical standpoint, duplex scanning can localize and classify peripheral arterial stenoses nearly as well as angiography. A normal duplex study excludes significant occlusive disease. In this study, the negative predictive value is 92% which is in agreement with previous reports, and abnormal studies can direct further examination. However, the sensitivity of duplex scanning for detecting hemodynamically[6] significant stenoses was decreased in low-flow segments distal to total occlusions. Recognition of this difficulty should allow us to improve accuracy.

In the validation study by Jager et al[4] using 338 arterial segments of 30 patients, the kappa value for duplex scanning vs. angiography was 0.69, and that for one radiologist's interpretation of the angiograms vs. the other's was 0.63. Kohler et al[14], in their study on symptomatic aortoiliac and femoropopliteal artery disease, found an overall agreement between duplex scanning and arteriography to be slightly less than that of Jager (kappa value 0.55 vs. 0.69), specificity was comparable (92% vs. 98%) and sensitivity was slightly higher (82% vs. 77%). In another study by Polak et al[11], duplex scan had a sensitivity of 0.88 for detecting significant stenoses or occluded segments. Specificity was 0.95 and accuracy was 0.93.

No occlusions were missed in this study. There was an ultrasound finding of total occlusion in an arterial segment that was seen to be patent or normal in the arteriogram. This false- positive segment was noted to be in the popliteal artery and was distal to a high-grade stenosis. Large collaterals were present and most likely decreased the amount of blood carried by these segments. There also seems to be a tendency for duplex ultrasound to classify angiographically normal arteries as minimally diseased and they were seen in seven arterial segments deemed to be normal by arteriography.

Two femoropopliteal thrombosed aneurysms were not by the duplex ultrasound. Negative arteriographic findings such as these are thought to occur in up to 36% of diagnosed popliteal aneurysms.[11] Exact agreement occurred in 207 arterial segments (74%). The finding of total occlusion in the duplex ultrasound has a 100% sensitivity and specificity. For identifying lesions with >50% diameter reducing lesion has a sensitivity of 83%, a specificity of 92%, a positive predictive value(PPV) of 88% and a negative predictive value(NPV) of 92%. The Kappa is 0.55. For identifying lesions that are <50% diameter reducing, the sensitivity and specificity are 89% and 83% respectively. The PPV and NPV are 89% and 91% respectively. The Kappa is 0.62. Kappa values were relatively high in the distal external iliac artery (DEIA) which means that there is very good agreement between the duplex ultrasound and the arteriogram. This finding can be attributed to the size of the DEIA and ease in insonating this particular arterial segment. On the other hand, Kappa values were relatively low for the popliteal artery because of the fact that most of the popliteal arterial segments studied were diseased or there were presence of more proximal stenoses which rendered duplex ultrasound difficult to interpret. Moreover, the accuracy and sensitivity of duplex ultrasound for detecting hemodynamically significant stenosis was decreased in low-flow segments distal to total occlusions. The over-all statistical findings obtained from this study are equivalent to the rates previously reported in studies abroad. It is the limitation of this study that the infrapopliteal segments were not evaluated. The experience with duplex scanning for diagnosis of infrapopliteal stenoses is limited.[8] In fact, the use of arteriography as the gold standard in the diagnosis of peripheral arterial occlusive disease has certain limitations in its application for infrapopliteal segments. It is difficult to judge the infrapopliteal segments optimally in patients with proximal obstruction, considering the technical aspects of the procedure. Therefore, it can be said that at least partially the lack of accuracy of duplex ultrasound , and specially the low specificity concerning hemodynamically relevant lesions, may be a reflection of the limitations of arteriography as the reference method.

Conclusions

It has been demonstrated that Duplex ultrasound produces satisfactory agreement with angiography for the diagnosis of iliac and femoropopliteal arterial occlusive disease. It has grown from an ancillary diagnostic test to a critical component in the diagnostic work-up and even in monitoring of patients after various interventions with its high level of diagnostic accuracy in the femoral and popliteal arteries. Non-invasive testing with duplex ultrasound allows the clinician to choose intervention more wisely be it a selective diagnostic arteriogram, percutaneous angioplasty or surgery. As duplex scanning

becomes more sophisticated, it may eliminate the need for routine preoperative contrast studies in the assessment of patients with lower extremity arterial occlusive disease.

It is the recommendation of this paper that a prospective comparative study be done on the infrapopliteal arterial segments using catheter arteriography, magnetic resonance angiography and duplex ultrasonography.

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Validation of a Clinical Prediction Rule For A Preserved Left Ventricular Systolic Function In Patients After Myocardial Infarction

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Background --- LV systolic function is the single most important predictor of mortality following myocardial infarction. Several indicators of LV dysfunction such as non-invasive estimations of Ejection Fraction (EF) like echocardiography have been examined for prognostic implication. Several studies have yielded clinical predictors of LVEF which were either difficult to use at bedside, have substantial misclassification rates or have never been validated for easy use. This study was conducted to validate the Silver Criteria for a preserved Left Ventricular systolic function in patients after myocardial infarction and adopt a clinical prediction rule that is reliable & applicable to our local setting.

Methods --- This is a validation study involving 108 patients admitted at the Philippine Heart Center from April 2005 to April 2006 due to Acute Myocardial Infarction. Clinical and radiologic evidences of congestive heart failure were noted. Electrocardiographic recordings were reviewed and classified as interpretable or uninterpretable based on the Silver Criteria. Echocardiographic determination of LV EF was done and was compared to the Silver clinical criteria, which consists of 4 clinical parameters. Validity measures, such as sensitivity, specificity, PPV and NPV were then determined

Results --- In the group with predicted EF to be at least 40% (n=34), the most common location of infarction was inferior wall and all patients (100%) had an actual EF of at least 40%. Whereas in the group with unpredictable EF (n=74), 41% had an EF between 40-54%, 34% had EF <40% and 25% above 55%. The Positive Predictive Value (PPV) of this prediction rule was 100% while its Negative Predictive Value (NPV) was 34 %. The sensitivity was 41% while the specificity was 42% .

Conclusion --- This simple yet reliable clinical prediction rule (Silver Criteria) for a preserved LV systolic function for post MI patients is of great value in the management of such patients especially when limited medical resources is a major concern. ***Phil Heart Center J 2007; 13(2):101-104.***

Key Words: Acute Myocardial Infarction ■ ejection fraction ■ systolic function ■ Silver criteria ■ clinical prediction rule ■ validation study

Left ventricular (LV) systolic dysfunction has a major prognostic significance in determining the hospital course of patients after a myocardial infarction.1 It is the single most important predictor of mortality following myocardial infarction. Among patients with an LVEF of <40%, the rate of mortality is markedly increased at 6 months.[2] Several indicators of LV dysfunction have been examined for prognostic implication such as clinical parameters, hemodynamic findings and non-invasive estimations of Ejection Fraction (EF) like echocardiography. In a study by Nijland et al, myocardial viability was compared with clinical indicators of LV systolic dysfunction in terms of prognostic significance. Myocardial viability is the single best predictor of recurrent in-hospital ischemic events and unstable angina after discharge while clinical parameters (age, hypertension & EF) have a higher prognostic value for hard cardiac events (Death & VT) and occurrence of heart failure.[3]

In a study by Thomas et al, clinical parameters (age, obesity, tachycardia, HPN, LVH, LA abnormality and congestion on CXR) had a low sensitivity, specificity and predictive values for differentiating normal versus decreased systolic LV function.[4]

Several studies have yielded clinical predictors of LVEF, which were either difficult to use at bedside, have substantial misclassification rates, or have never been validated for easy use.

The Silver Criteria, consisting of 4 clinical parameters, allows one to predict who among post MI patients would have a LVEF of >40% with a 98% predictive value.[5] (Figure 1). Such correlation is expected if all of the following are met:

1. Absence of a history of Congestive Heart Failure
2. No previous Q-wave M.I.
3. An index M.I. that is not a Q-wave anterior infarction
4. An interpretable ECG (No LBBB, no LVH or ventricular pacing)

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Determination of post M.I. patient's LV function whether preserved or impaired, rather than knowing the exact LVEF is more essential in deciding which group of patients require further evaluation like revascularization or subsequent medical management.

Accordingly, as much as 40% of patients may be subjected to unnecessary invasive or non-invasive testing after myocardial infarction if LVEF is the major indication for such study.

Hence, predicting the presence of a preserved LV systolic function (EF>40%) with a high probability would be a challenging and cost-effective task. It distinguishes those patients who need further reasonable testing (invasive or non-invasive) that may influence decision-making. The cost of such procedures for a financially drained patient cannot be overlooked. Therefore, if this prediction rule is validated in our institution, results of which will determine its applicability in the local setting and would benefit most patients with limited resources. Thus, this paper was conducted to validate the clinical prediction rule (i.e. the Silver Criteria) for a preserved

Methods

This is a validation study involving patients diagnosed with acute myocardial infarction and admitted at the Emergency Room Chest pain Unit & Coronary Care Unit. The Emergency Room Chest pain Unit & Coronary Care Unit of the Philippine Heart Center from April 2005 to April 2006. Prospective patients presenting with chest pain that had either elevated Troponin/CK-MB or had electrocardiographic evidence of MI were included in the study. Excluded were those with other causes of systolic heart failure such as Cardiomyopathy, Valvular Heart Diseases, Congenital Heart Diseases, Pericardial Diseases and Drugs & Toxins (Alcohol, Anthracyclines). All patients were listed in Acute Coronary Syndrome Registry.

Initially, patients were noted whether clinical features of congestive heart failure were present prior to or during admission. Then, chest radiographic evidences of pulmonary congestion/edema were verified. Congestive Heart Failure (CHF) was defined as presence of 2 major criteria or 1 major plus 2 minor criteria based on Framingham's study, a previous record of CHF in the past, or the presence of radiologic evidence of pulmonary congestion and / edema.

After which, the patient's ECG were taken. Patients' ECG were also classified as interpretable or uninterruptable based on the inclusion criteria as proposed by Dr. Silver et al. Patients were subsequently classified as having STEMI or NSTEMI. Electrocardiographic criteria used in the study were as follows: 1) ST segment elevation/depression was defined as a deflection of at least 1 mm from the baseline PR segment. STEMI (ST Elevation MI) was designated to patients with ST elevation in at least 2 limb leads or 2 contiguous precordial leads.

NSTEMI (Non ST Elevation MI) was labeled in its absence or presence of ST depression / T-wave inversion and elevated cardiac enzymes. 2) Q-waves were defined as a negative initial deflection in the QRS complex of at least 1 mv in amplitude or 40 ms in duration. 3) Old MI was defined as presence of Q waves outside the area of the index MI. 4) LBBB was defined as a widened QRS with a duration of at least 110 ms with a typical QRS morphologic pattern in leads V1 & V6. 5) LVH with strain pattern is a widened QRS of at least 110 ms and standard voltage criteria for LVH (by Sokolow) in the presence of repolarization changes (T-wave inversion). ECG changes were classified as anterior in location if changes appeared in V1-V4; inferior if located in II, III & aVF; lateral for leads V5-V6; inferolateral if on II, III, aVF, V5 and V6; inferior with RV extension if changes occurred in leads V3R and V4R. Finally, using the Silver Criteria (see Fig. 1), the 4 clinical parameters for a preserved LVEF (EF =>40%) were noted. Each patient's EF was then classified as predictable (EF=>40%) if all of the 4 parameters were met and unpredictable if at least 1 of the 4 was not met.

Lastly, the LVEF of all patients were determined from transthoracic echocardiographic study. Transthoracic echocardiographic determination of LVEF by Simpson was obtained in all patients within 48 hours of admission. The LVEF's were dichotomized as either 40% or more or <40%. This cut-off point was preselected because of its well-recognized clinical significance.[6]

Results

The baseline demographic data of the validation set consisting of 108 patients were noted. Majority of the patients were between 40-60 years of age (Table 1). In the group with predictable EF (n=34), the most common location of infarction was inferior (55%), followed by inferolateral wall (18%) & NSTEMI (18%). Only 9% constitute inferior wall with RV extension. In the group with unpredictable EF (n=74), the most common location of infarction was anterior wall which was actually one of the criteria for an unpredictable EF. NSTEMI and inferior wall involvement were 17% and 14% respectively (Table 2).

The Clinical Prediction Rule (Silver Criteria) was then applied to all patients (Figure 1). All patients belonging to the predictable group actually had an LVEF of 40% or more. Majority (74%) had an EF > 55%, and the rest (26%) had an EF between 40-54%. In the group with unpredictable EF (n=74), majority (41%) had an EF between 40-54% and 34% had an EF <40%. 25% of the group even had an EF >55% (Table 3). Most of the patients (44 out of 74) under this group did not satisfy 1 criterion. Only 9% of them had not satisfied 3 criteria. (Figure 2). Thus, the Positive Predictive Value (PPV)

of this prediction rule was 100% while its Negative Predictive Value (NPV) was 34%. Sensitivity (41%) and Specificity (42%) of this rule were however low, but were not of major concern in this study (Table 4).

Discussion

Results of this study has validated with high predictive value the earlier assumption that the likelihood of having a LVEF >40% after MI can be best predicted based on simple clinico-electrocardiographic data. It yielded even a higher PPV (100%) than those of Dr. Silver et al (PPV: 98%). As was previously observed in its derivation, this clinical prediction rule has a low Negative Predictive Value (34% vs. 43%). However, since the aim of this study was to predict the EF of patients with a high likelihood of a preserved EF (>40%) but not to predict the EF of patients under the unpredictable group, the value of a low NPV is therefore less meaningful.

The validation set (n=108) with a desired Confidence interval of +/-10% is more than the required sample size of 95. Hence, insufficient number of patients is therefore not a limitation of this study.

The format of classifying patients' EF as to predictable or not has shown that probably because of smaller area of jeopardized myocardium in the absence of other confounding factors, patients with inferoposterior infarctions have a more preserved LV systolic function than those with anterior infarctions.

Due to its promising value in cost-cutting of medical expenses, clinicians especially in areas with limited diagnostic technology might find great application of this simple and reliable clinical prediction rule in the management of patients with acute myocardial infarction. Likewise, for patients with a predictable EF in whom the only indication for a diagnostic procedure is LVEF determination, a second thought against ordering such tests might be considered.

Table 1. Baseline Characteristics of Included Patients with Acute Myocardial Infarction

		Frequency N=108	Percentage %
Sex	Males	75	69
	Females	33	31
Age Group			
	<40 years	9	8
	40-60	62	58
	>60	37	34
Risk Factors			
	HPN	62	57
	DM	48	44

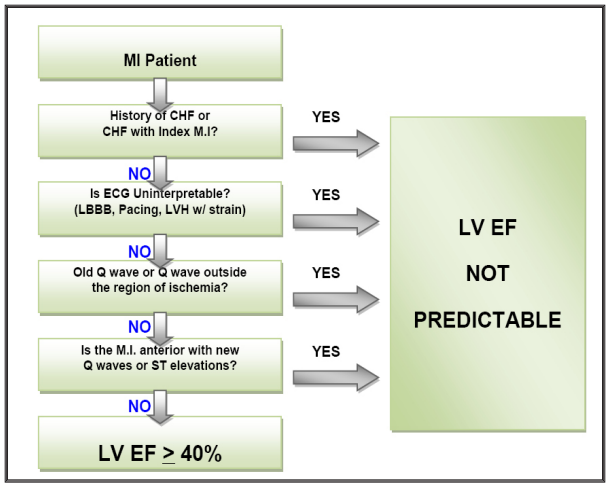

Figure 1. Clinical Prediction Rule

Table 2. Distribution of Location of Myocardial Infarction According to the Ejection Fraction (EF) by Clinical Prediction Rule

LOCATION OF MI	EJECTION FRACTION (EF) BY CLINICAL PREDICTION RULE			
	PREDICTABLE EF N=34		*UNPREDICTABLE EF* N=74	
	N	%	N	%
Inferior	19	55	10	14
Inferior with RV extension	3	9	4	5
Inferolateral	6	18	0	0
Anterior	0	0	47	64
NSTEMI	0	0	13	17

Table 3. Distribution of Patients according to their Ejection Fractions (2 D Echo and Clinical Prediction Rule)

EJECTION FRACTION By 2 D Echo	EJECTION FRACTION (EF) BY CLINICAL PREDICTION RULE			
	PREDICTABLE EF N=34		*UNPREDICTABLE EF* N=74	
	N	%	N	%
<40%	0	0	25	34
40-54%	9	26	30	41
≥55 %	25	74	19	25

Table 4. Measures of Validity of the Clinical Prediction Rule as Compared to EF Obtained by 2D Echo

Ejection Fraction by Clinical Prediction Rule	Ejection Fraction (EF) by 2 D Echo		
	EF ≥ 40%	EF <40%	TOTAL
Predictable	34	0	34
Unpredictable	49	25	74
TOTAL	83	25	108

Positive Predictive Value (PPV): 100% **Sensitivity: 41%**
Negative Predictive Value (NPV): 34% **Specificity: 42%**

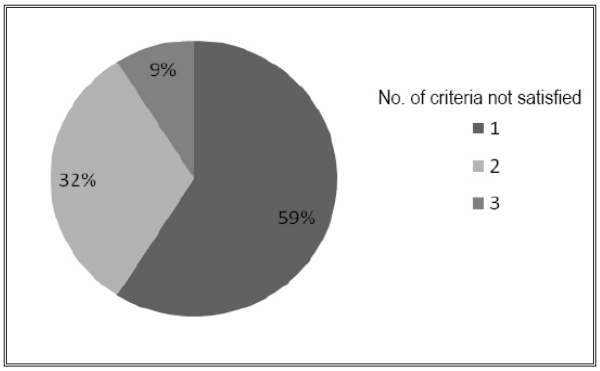

Figure 2. Distribution of Unpredictable EF subgroup according to number of criteria not satisfied (n=74)

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Evaluation of Cardiac Markers for Ruling Out Myocardial Infarction After Coronary Artery Bypass Grafting in Patients

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Background --- This study was conducted to evaluate the value of serum troponin T and creatine kinase (CK)-MB concentrations for ruling out perioperative myocardial infarction (PMI) early after cardiac surgery.

Design: Prospective study.

Setting: Recovery room of a tertiary hospital.

Patients: Twenty three patients undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass were included.

Methods --- Serum concentrations of troponin T and CK-MB concentrations were measured preoperatively (baseline), on arrival at the recovery room (RR), and at 0, 8, 16, and 24 h after arrival at the RR. The strength of markers studied for ruling out PMI was studied using receiver operating characteristics (ROC) curves. Based on these curves, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for each marker at every time point were calculated.

Results --- PMI developed in 2 patients. On arrival at the RR, all markers were significantly increased from baseline concentrations in both patient groups. In patients with PMI, serum concentrations of troponin T and CK-MB were significantly higher than in control patients from 8, 16, and 24 hours after arrival at the RR. CK-MB concentration was the earliest marker, and its NPV reached 98.6% 8 hours after arrival at the RR. On arrival at the RR, the NPV for CK-MB concentration already reached 96.7%. Troponin T was not an early marker for ruling out PMI, with an NPV reaching 98.6% 8 hours after arrival at the RR. During the first 8 hours after arrival at the RR, sensitivity, specificity, PPV, and NPV of CK-MB exceeded that of troponin T.

Conclusion --- For ruling out PMI at the RR after CABG, CK-MB is a better marker than troponin T during the first 8 hour after arrival at the RR. Using these markers, postoperative treatment of cardiac surgical patients might be further improved. ***Phil Heart Center J 2007; 13(2):105-108.***

Key Words: CK-MB ■ Troponi T ■ Prei-operative myocardial infarction ■ coronary artery bypass grafting

In patients undergoing coronary artery bypass graft ing (CABG), early diagnosis of perioperative myo cardial infarction (PMI) is important because it remains a serious complication.[1,2] Despite many attempts to improve detection of PMI, currently, the diagnosis of PMI is still based on changes in the ECG, increased release of biochemical markers particularly creatine kinase (CK-MB), and a new regional wall motion abnormality on two-dimensional echocardiogram. Only a minority of patients (5-25% of patients undergoing CABG), however, actually experience a perioperative myocardial infarction (PMI), even in tertiary care centers currently operating on higher-risk patients. Potential causes of myocardial ischemia and infarction in the perioperative period include incomplete revascularization, diffuse atherosclerotic disease of coronary arteries, increased myocardial needs as in left ventricular hypertrophy, spasm or thrombosis of the native or bypass graft vessels, hemodynamic derangements and technical problems.[2] Possible risk factors for PMI may include emergency surgery, small coronary vessels, diffuse coronary artery disease, previous CABG, myocardial infarction (MI) in the preceding week, and failed percutaneous procedures. Previously, several biochemical markers for detection of myocardial damage have been proposed. Several studies showed that cardiac marker proteins (fatty acid-binding protein [FABP] and myoglobin) release can be used to determine myocardial tissue loss due to the surgical procedure (3). In addition, other studies showed that these proteins can be used to discriminate surgery-related myocardial injury from tissue loss caused by PMI. FABP was also shown to allow diagnosis of PMI as soon as 4 h after removal of the aortic cross-clamp.

However, next to early diagnosis, markers used for the detection of PMI should also be sensitive and specific. In this respect, FABP and myoglobin do not fulfill these recommendations. Troponin T and CK-MB have been shown to be promising candidates.[1, 4–9] As being part of

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the tropomyosin complex of myocardial tissue, troponin T is highly cardiac specific and is considered a sensitive marker of myocardial necrosis after CABG, which could improve the diagnosis of PMI in cardiac surgical patients.

In many studies, the emphasis of the diagnostic properties of biochemical markers has been on the detection rather than the ruling out of PMI. However, postoperative treatment of cardiac surgical patients could be improved in case PMI could be ruled out as early as possible after surgery. The aim of the present study was to evaluate whether Troponin T and CK-MB measurements enable a sensitive and early rule-out of PMI after surgery

Methods

Patient Selection The study group consisted of prospectively selected private patients who are to undergo "packaged" CABG with possible risk factors for PMI, between April 2006 and December 2006 at the Philippine Heart Center. An informed consent was requested from the patient and attending physician. Exclusion criteria were as follows: (1) treatment with fibrinolytics within 48 hours prior to surgery; (2) patients undergoing a concomitant valvular operation, vascular surgery, or LV aneurysmectomy; and (3) severe coagulation abnormalities. Blood Sampling Blood samples were obtained preoperatively (baseline), on arrival at the RR, and at 8, 16, and 24 h after arrival at the RR. All samples were collected in 10-mL syringe.

Myocardial Infarction Diagnosis

The criteria for definite PMI was based on the following criteria: 1) significant new Q waves (->30 msec and ->0.1 mV) in two or more contiguous leads of II, III, aVF, or two or more leads of V2 through V6, I, and VL 2) total peak CK >700 U/L with CK-MB >30 IU/L, and 3) presence of a new regional wall motion abnormality on two dimensional echocardiogram which was done exclusively for patients positive for the 1st and 2nd criteria. Diagnosis of a new wall-motion abnormality requires severe hypokinesis or akinesis in a previously normal segment. This would result in two patient groups: patients in whom PMI developed (PMI group), and patients without PMI (no-PMI group). Data Analysis All data were presented as mean + SEM. Comparisons between two variables at the same time point as well as the values from one variable between two time points were done. Receiver operating characteristics (ROC) curves were used to compare the performance of the biochemical diagnostic methods of PMI and to determine the appropriate cutoff values for the different cardiac markers. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to analyze the diagnostic value of each marker.

Results

Clinical Characteristics

There are 23 patients included in the study. The perioperative characteristics of all patients are shown in Table 1. Two patients (9.5%) showed evidence of PMI according to ECG changes, CK and CK-MB, and 2-dimensional echocardiogram. These patients had longer cardio pulmonary bypass times and a longer postoperative hospital stay than the patients without PMI.

Table 1. Clinical characteristics of Included Patients who did and did not developed Perioperative MI

Variables	No PMI N=21	PMI N=2	p-value
Age in years (mean)	62.5	65.2	NS
Male gender (%)	85	100	NS
Number of vessels anastomosed	3.8	4.0	NS
Cardiopulmonary Bypass duration in min (mean)	134	167	<0.05
Aortic cross-clamp duration in min (mean)	93	108	NS
Duration of Hospitalization Post-CABG in days (mean)	12	26	<0.05

Cardiac Marker Concentrations

Preoperative CK-MB concentrations in the no-PMI group and the PMI group were 1.7 IU/L and 1.8 IU/L respectively (Fig. 1). CK-MB concentrations in the no-PMI group slightly increased from baseline on the 8th with no significant change until the 24th hour after arrival at the recovery room (RR). In the PMI group, CK-MB concentrations showed a significant increase on the 8th hour which continued until the 24th hour after arrival at the RR. CK-MB concentration was significantly higher in the PMI group ($p<0.05$). On the 24th hour, CK-MB concentrations were 9.9 times higher in PMI patients compared to no-PMI patients. Maximal CK-MB concentration was 21 IU/L in the no-PMI group at 8 hours after arrival at the RR and 207 IU/L in the PMI group at 24 hours after arrival at the RR.

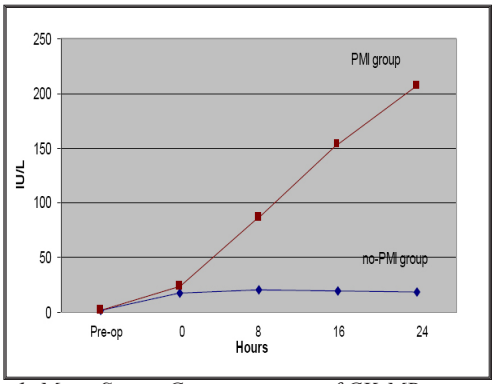

Figure 1. Mean Serum Concentrations of CK-MB

Preoperative troponin T concentrations in the no-PMI group and PMI group were 0.018 and 0.021 ng/ml, respectively (Fig. 2). Postoperative troponin T concentrations in both the no-PMI group and PMI group increased above the baseline upon arrival at the RR. However, on the 8th hour troponin T concentration for the no-PMI group was at its maximal at 0.90 ng/ml and steadily decreased until the 24th hour while the troponin T concentrations for the PMI group persistently increased until the 24th hour after arrival at the RR, at this time being 3.6 times higher than those in the no-PMI group. Thus, troponin T concentrations in the PMI group were significantly higher than in the no-PMI group from 8th hour to the 24th hour after arrival at the RR. Maximal troponin T serum concentrations were 0.9 ng/ml in the no-PMI group at 8 hours after arrival at the RR, and 3.25 ng/ml in the PMI group at 24 hours after arrival at the RR.

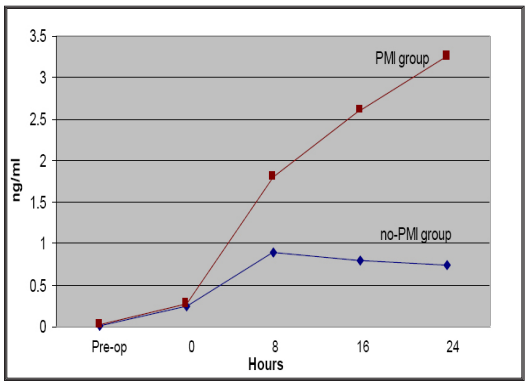

Figure 2. Mean Serum Concentrations of Troponin

Cut-off Values and Test Characteristic

The strength of correlation between standard criteria (ECG, CK with CK MB, and 2-DE) and CK-MB and troponin T concentrations was studied using ROC curves which are a plot of the true positive rate against the false positive rate for the different possible cut points of the mentioned diagnostic tests. The areas under the curve for each marker at every time point served as the measure of the test accuracy as shown in Table 2. Cut-off values were derived form the intersection of the different coordinates of the curve and the ROC curve. Corresponding cut-off values for each marker at every time points are also shown in Table 2. For each marker and at every time point, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of a single sample were calculated as shown in Table 3. Serum levels of troponin T > 1.07 ug/L 8 hours after arrival at the RR confirmed the presence of PMI with a sensitivity of 84.6%, specificity of 84.2%, PPV of 29.7%, and NPV of 98.6%. At the same time point, CK-MB concentration > 28.9 IU/L confirmed the presence of PMI with a sensitivity of 85.7%%, specificity of 86.8%, PPV of 25.6%, and NPV of 97.8%.

Table 2. Area under the ROC Curves and Optimal Cut-off values for each Marker at Every Post-operative Time Point

Hours after arrival at the RR	CK MB		Troponin T	
	AUC	Cut-off Value	AUC	Cut-off Value
0	0.74	17.9	0.59	0.25
8	0.90	28.9	0.83	1.07
16	0.88	22.2	0.91	0.75
24	0.96	292	0.94	0.81

Table 3. Test Characteristics of CK-MB Mass and Troponin T in diagnosis of Peri-operative MI post-CABG

Variables	Hours after Arrival at the RR			
	0	8	16	24
CK MB				
Sensitivity	71.4	85.7	78.6	64.3
Specificity	71.8	86.8	80.8	89.7
PPV	17.9	35.3	25.6	34.6
NPV	96.7	98.6	97.8	96.7
Troponin T				
Sensitivity	53.8	84.6	80.1	76.9
Specificity	53.3	84.2	73.7	69.5
PPV	8.2	29.7	20.0	16.4
NPV	93.7	98.6	98.4	97.5

Discussion

Peri-operative MI is a serious complication after cardiac surgery with a reported incidence of up to 25%, dependent on the criteria used to select the patient groups. (11) Several studies showed that in case CPB is used, myocardial tissue damage is unpreventable. The ideal markers for the diagnosis of PMI are those that can be used to diagnose early after cardiac surgery and should also be sensitive and specific at the same time. Troponin T and CK-MB are both promising candidates, these noted characteristics could improve the diagnosis of PMI in cardiac surgery. In this present study, we studied the value of serum troponin T and CK-MB concentrations in patients undergoing CABG.

In our study, plasma concentrations of both cardiac markers studied showed moderate elevations from preoperative values in all patients, which may signify minimal myocardial damage. This supports the study done by Fransen et al (12) that in case a patient has undergone CABG with the use of CPB, some myocardial damage occurs and is inevitable. Although the cutoff values have been reported in many studies (13-15) for patients presenting with acute chest pain, these values are not well established after cardiac surgery. Based on the data of the patients in the present study, cutoff values for each marker at every time point was obtained using the ROC

curves. In the study of Carrie et al (1), acceptable test characteristics for troponin T in CABG patients after 24 hours was shown, which increased towards the 48th hour after surgery. However, our study already showed optimal test characteristics at 8 hours after arrival at the RR for both cardiac markers. This finding can be explained by the study of Swaanenburg et al (16) which showed that the release patterns of cardiac markers after uncomplicated heart surgery depend on the type surgery (no. of vessels, ACC duration, etc.) and the circumstances during surgery (emergency, urgent, etc.) which were both not standardized in this study. Thus, our recommendation is that in future studies, the release patterns of cardiac markers for cardiac surgical procedures be determined and subsequently calculate corresponding cutoff values. In addition, the size of infarction influences the sensitivity and specificity in the early hours after MI, that is the larger the infarct the earlier the increase in cardiac markers. (9) As mentioned earlier, the test characteristics of the markers used were calculated using the ROC curves. This resulted in high values, particularly the NPV. The lowest NPV calculated for each marker was 93.7% (Table3), indicating that in the worst case, PMI can be ruled out with 93.7% certainty using any of the markers studied. Although there are higher values of sensitivity, specificity, and NPV in the CK-MB concentration in the early hours after cardiac surgery (0 and 8 hours), it can be said that both have relatively high values at all postoperative time points. This maybe explained by the fact that in our patients the "onset of symptoms", as it is usually called in acute myocardial infarction (AMI), is the same for all patients, supposing that the PMIs in the present study have a preoperative in etiology.

Conclusion

In conclusion, CK-MB concentration is a better marker than troponin T for ruling out PMI during the first 8 hours after arrival at the RR. The data of the present study showed that in patients undergoing CABG, troponin T and CK-MB concentrations should be measured during the first 8 hours after arrival at the RR, not to detect but rather to rule out or exclude PMI. Using these markers, postoperative treatment of cardiac surgical patients might be further improved.

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The Role of Mycobacterium Tuberculosis PCR in the Early Diagnosis of Tuberculosis among Patients with Massive Pericardial Effusion

Onasis Y. Go, MD; Santos Jose Abad, MD; Myrna T. Mendoza, MD.

Background --- Tuberculosis is one of the most common causes of pericardial effusion in the Philippines. The early diagnosis of tuberculosis among patients with pericardial effusion remains elusive to this date. Polymerase Chain reaction, a technique for amplifying small amounts of DNA when only small amount of cells are available, can amplify "fingerprint" strains of M. tuberculosis DNA in pericardial fluid with excellent specificity. This study was conducted to describe the role of Mycobacterium tuberculosis polymerase chain reaction (PCR) in the early diagnosis of TB in patients with moderate to massive pericardial effusion by comparing it to existing diagnostic standards

Methods and Results --- Twenty-three subjects with moderate to massive pericardial effusion were included in this study. Majority were males with an average age of 40.2 ± 15.2 yrs. The average widest diameter of pericardial fluid by 2DED was 3.7 ± 1.3 cm before pericardiocentesis/ pericardiostomy, with 77% of the subjects had RA collapse and 64% had RV collapse on presentation. All pericardial fluid specimen tested were exudative based on Light's criteria. Cytological analyses were done on 19 subjects with 42% had findings characteristic of both acute and chronic inflammation. Five subjects had findings suggesting malignancy. Nine subjects had documented PPD results and two tested positive. All AFB smears done at the Philippine Heart center and Lung center of the Philippines showed negative results. Four out of 22 subjects had positive MTB cultures. Two of the subjects had a positive pericardial biopsy result for tuberculosis. Ten out of 23 subjects had their PCR done with a positive result in only one of the subjects. All of the specimens that tested negative for PCR also had negative results on MTB culture and pericardial biopsy.

Conclusion --- AFB smear appears to have a limited use in pericardial fluid analysis. The role of PCR-TB in the early diagnosis of PTB cannot be fully assessed in this study. The lack of subjects with positive PCR result prevented us from giving any definite conclusion. PCR-TB seemed to correlate well with MTB culture and pericardial biopsy. All of the subjects who had a negative PCR-TB also had negative TB results on their culture and biopsy. TB culture and pericardial biopsy appear to complement each other, with the latter having the advantage of an earlier result and the potential to show other diagnosis aside from TB. The routine use of AFB smear and routine determination of serum and pericardial LDH and protein should be looked into. ***Phil Heart Center J 2007; 13(2):109-112.***

Key Words: Pericardial effusion ■ Tuberculosis ■ Mycobacterium tuberculosis ■ Pericardiocentesis ■ Pericardiostomy ■ Polymerase Chain Reaction ■ Acid Fast Bacilli (AFB) smear ■ TB culture, diagnosis

Tuberculosis remains as one of most common di agnosis among patients with pericardial effusion in the Philippines. Nadurata et al reviewed 438 cases of pericardial effusion admitted at the Philippine heart center from 1985–1999 and reported that 25.1% (n=110) of the cases were attributed to tuberculosis.[1] The early diagnosis of tuberculosis among patients with pericardial effusion remains elusive to this date. Tuberculous pericarditis can either present in a transudative or exudative state depending on its stage.[2] AFB smears are frequently negative. AFB cultures, the current gold standard against which all other methods are measured, lack sensitivity and may take up to 8 weeks to obtain final results. Pericardial biopsies are frequently non-specific. A positive PPD tests supports the diagnosis but does not confirm it. Not infrequently, a trial of anti-Koch's regimen is started when tests are inconclusive.

Polymerase Chain reaction is a technique for amplifying small amounts of DNA when only small amount of cells are available. The technique utilizes oligodeoxyribonucleotides that are complimentary to the DNA strands of interest. The oligodeoxyribonucleotides are then annealed to the ends of the DNA and serve as primers for the in vitro copying of each DNA strand using a heat-stable DNA polymerase. The chemically synthesized primers are in excess so that when the reaction mixture is heated, the DNA strands separate and reanneal with more primer on cooling. This process of heating, cooling, and synthesis can be repeated many times, and in the process the DNA fragment of interest is greatly amplified.[3] Polymerase chain reaction (PCR) amplifies mycobacterial DNA to "fingerprint" strains of

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M. tuberculosis in pericardial fluid with excellent specificity.[4,5] TB PCR has been shown to have a sensitivity and a specificity of 66.7% and 99.6%, respectively, for the diagnosis of pulmonary TB from respiratory samples.[6] TB AMPLICOR was found to be more sensitive than the combination of Ziehl-Neelsen staining of smears and radiometric culture for M. tuberculosis and was a rapid and highly specific diagnostic test for TB meningitis.[7] An early diagnosis of TB pericarditis facilitates definitive treatment. Strang et al noted a decrease in mortality and a decreased need for repeat pericardiocentesis when anti-TB regimen was given with prednisolone for the first 11 weeks.[8] This study was conducted to describe the role of Mycobacterium tuberculosis polymerase chain reaction (PCR) in the early diagnosis of TB in patients with massive pericardial effusion by comparing it to existing diagnostic standards, such as AFB smear, AFB culture, pericardial biopsy, and biochemical and cytologic analysis.

Methods

Inclusion/ exclusion criteria

Patients aged 18 years old and above admitted at the Philippine Heart Center from January 01, 2005 to August 30, 2006 with echocardiographic evidence of pericardial effusion requiring pericardiocentesis and/ or pericardiostomy tube insertion, for diagnostic or therapeutic purposes, were included in the study. Patients with known metastatic disease were not included. Patients who had open heart surgery for the past 3 months were also not included in the study. Clinical data from each patient was collected on a standardized form by the investigator. It included the patients age, sex, hospital number, echocardiographic findings relevant to pericardial effusion, and surgical procedures done if any.

Subjects

Twenty-three subjects were included in the study with an average age of 40.2 ± 15.2 yrs. Fifteen subjects (65%) were male. Patients had an average of 3.7 ± 1.3 cm as their widest diameter in 2DED before pericardiocentesis/ pericardiostomy. Seventy-seven percent of the subjects had RA collapse while 64% had RV collapse on presentation.

Samples

All Pericardial fluid analyses were done at the Philippine Heart Center unless otherwise specified. Portions were sent for cell count, differential count and cytology, biochemistry (LDH, total protein), and for Ziehl-Neelsen staining, gram-stain and culture. Some specimens were sent to the Lung Center of the Philippines for TB culture and sensitivity. Finally, pericardial fluid specimens were sent to San Lazaro hospital (SACTL) or UP PGH for TB PCR (AMPLICOR MTB Test. Roche diagnostic systems, Inc; Branchburg NJ). Pericardial samples were sent for biopsy, if possible. PCR TB. AMPLICOR MTB amplifies a 585-bp region of the 16S rRNA gene sequence common to all mycobacteria. Carryover contamination is prevented by incorporation of dUTP in place of dTTP in the amplification reaction and utilization of uracil-N-glycosylase (AmpErase) to enzymatically cleave any contaminating amplicon carried over from previous reactions. AmpErase is subsequently inactivated at temperatures used for thermal cycling. For amplification, 50 µl of neutralized specimen is added to 50 µl of master mix. The tray containing specimens and controls is then placed in a TC-9600 thermal cycler and amplified according to the following program: hold at 50ºC for 2 min; 2 cycles of 98ºC for 20 s, 62ºC for 20 s, and 72º for 45 s; hold at 72ºC for 5 min; and hold at 72ºC indefinitely. Detection on M. tuberculosis complex organism is accomplished by hybridization of the amplified product to a DNA probe specific for organisms of the M. tuberculosis complex. Following amplification, 100µl of denaturation solution is added to all tubes; this is followed by a 10-min room temperature incubation to allow complete denaturation of the double-stranded products.100µl of hybridization buffer is added to a microwell plate coated with a DNA probe specific for members of the M. tuberculosis complex. Twenty-five microliters of denatured amplicon is then added, and hybridization is carried out at 37ºC for 90 min. Detection of hybridized duplex is accomplished with an avidin-horseradish peroxidase conjugate- tetramethylbenzidine substrate system. The reaction is stopped by addition of dilute hydrosulfuric acid, and the results are read at 450nm. A result is considered positive if the absorbance is greater than or equal to 0.35.5

Results

Table 1. Diagnostic examination done on the pericardial fluid specimens of the patients included in this study

Diagnostic Test	Number of tests done	Number of specimen w/ positive results
PCR	10	1
AFB smear	23	0
AFB culture	22	4
Biopsy	19	2

Table 1 depicts the diagnostic examinations done on the pericardial fluid specimen of the 23 subjects included in this study. Ten out of 23 subjects had their PCR done with a positive result in only one of the subjects. All AFB smears done at the Philippine Heart Center and Lung center of the Philippines showed negative results. Four out of 22 (18%) had positive MTB cultures.

A pericardial biopsy specimen is considered positive for TB when it shows chronic granulation with caseous necrosis. Two out of 19 subjects who had pericardial

biopsy done, had this finding, while one had chronic granulation with caseous necrosis. Two out of 19 subjects who had pericardial biopsy done, had this finding, while one had chronic granulation without caseous necrosis. It is interesting to note that 4 out of 19 subjects eventually had malignant pericardial biopsy findings.

Table 2. Results of Pericardial Fluid Exam (PCR, AFB smear, TB culture, Pericardial Biopsy) compared to PPD,

Diagnostic Exam		Biochemical (Light's criteria)		Cytology				PPD	
		Transudate	Exudate	Acute	Chronic	both	Malignant	(+)	(-)
PCR	+	0	1	0	0	0	1	0	0
	-	0	7	0	1	2	2	1	4
AFB	+	0	0	0	0	0	0	0	0
smear	-	0	21	1	3	8	5	2	7
TB	+	0	4	0	0	3	0	1	0
culture	-	0	16	1	3	5	4	1	7
Biopsy	+	0	2	0	0	0	0	0	0
	-	0	16	1	2	5	4	2	6

Table 2 shows the biochemical and cytologic analysis of the specimen. All the specimens tested were exudative. The pericardial fluids were categorized into transudate or exudate based on Light's criteria, which includes the determination of pericardial fluid and serum LDH and protein. A pericardial fluid/ serum LDH ratio of more than 0.6, a pericardial fluid/ serum protein ratio of more than 0.5, or an LDH greater than 200 u/L were considered exudative. Cytolological analysis was done on the pericardial fluid of 19 subjects, primarily used to detect malignancy. Eight out of 10 (42%) had findings characteristic of both acute and chronic inflammation. Five subjects had findings suggesting malignancy. All subjects that showed malignant changes in their pericardial biopsy also had findings suggestive of malignancy in their cytological analysis. Nine subjects had documented PPD results and two tested positive. Both of them had negative biopsy results, although one of them had a positive AFB culture.

Table 3. Comparison of Results of Pericardial Fluid

		PCR		AFB smear		TB culture		Biopsy	
		(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)
PCR	(+)	1	0	0	1	0	0	0	0
	(-)	0	9	0	9	0	9	0	8
AFB	(+)	0	0	0	0	0	0	0	0
smear	(-)	1	9	0	23	4	18	2	17
TB	(+)	0	0	0	4	4	0	2	2
culture	(-)	0	9	0	18	0	18	0	15
Biopsy	(+)	0	0	0	2	2	0	2	0
	(-)	0	9	0	17	2	15	0	17

PCR-TB seemed to have a good negative predictive value. All of the specimens that tested negative for PCR (9 subjects) also had negative results on MTB culture and pericardial biopsy. Only one out of ten subjects tested positive for PCR. Whether this is due to lack of sensitivity, still needs to be investigated. Factors that may decrease the yield of PCR-TB include a bloody sample which is quite common in pericardial fluid samples. AFB smear appears to have a limited use in pericardial fluid analysis. All subjects who tested positive for PCR-TB, MTB culture and pericardial biopsy showed negative AFB smear. Four specimens that eventually grew MTB on culture had negative initial AFB smears. Two out of four subjects who had a positive MTB culture had biopsy findings showing chronic granulation with caseous necrosis. One out of four had chronic granulation only without caseous necrosis. Two patients who had a normal pericardial biopsy result were eventually diagnosed to have malignancy.

Conclusion

The role of PCR-TB in the early diagnosis of PTB cannot be fully assessed in this study. The lack of positive results and the scarcity of subjects who underwent this test prevented us from giving any definite conclusion. PCR-TB seemed to correlate well with MTB culture and pericardial biopsy. All of the subjects who had a negative PCR-TB had negative TB results on their culture and biopsy. It was unfortunate that none of our subjects who grew MTB on culture had PCR analysis. This study was primarily limited by the cost of the PCR procedure. With more subjects, PCR-TB may be able to show its real potential. TB culture and pericardial biopsy appeared to complement each other. Though TB culture seems to be more sensitive than pericardial biopsy in this study, the latter has the advantage of an earlier result and the potential to show other diagnosis aside from TB. Pericardial biopsy was able to give a definite diagnosis in 6 out of 19 subjects in this study. The routine use of AFB smear and routine determination of serum and pericardial LDH and protein should be investigated. All specimens tested for AFB smear yielded negative result. AFB smear was so insensitive in this study that all subjects who had definite TB on culture and pericardial biopsy had negative AFB smears. With regards to the routine determination of LDH and protein, all of the subjects were eventually categorized as exudative based on the Light's criteria. The clinical significance of this practice still confuses the author. Massive pericardial effusion is a condition that demands prompt medical attention. In this study, 5 out of 23 patients had already expired while another 5 of them are suffering from metastatic disease. The early diagnosis and management of these cases cannot be overemphasized. Tuberculosis, being the leading cause of massive pericardial effusion in this country must be

diagnosed and excluded early to facilitate definitive management.

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Practices and Attitudes of Physicians on Deep Venous Thrombosis Prophylaxis Among Critically Ill Patients Admitted at The Medical and Neurologic Intensive Care Units

Jasmin Melissa B. Bernardo MD; Imee Caole MD; Giovani Pinili MD; Ma. Teresa B. Abola MD,FPCP, FPCC

Background --- Venous thromboembolism is a complication that is commonly seen among critically ill patients admitted at both surgical and medical ICUs. Prophylaxis for deep venous thrombosis (DVT), early recognition and appropriate treatment can save many lives. Recommendations for use of prophylaxis are available. However, there are different practices among different subspecialties in its use and applications. In general, physicians have different approaches to DVT prophylaxis, and usually this is influenced by the subsets of patients seen and encountered in the practice as well as the availability of the medications used for prophylaxis. The use of standard criteria for stratification of patients for VTE prophylaxis use is sometimes under-utilized. Many patients who might benefit from the routine use of these medications are sometimes not properly identified. Thus, this study was conducted to assess the practices and attitudes of physicians on venous thromboembolism(VTE) among critically ill patients admitted at the medical and neurologic ICU.

Methods --- This was a multi-centered cohort study involving critically ill patients, 18 years old and above, admitted for a minimum of 4 days at the medical and neurology ICU of PHC, MMC and PGH. Patients who were included were evaluated for their demographic characteristics, use of DVT prophylaxis, type, doses and timing of medication used, indications and/or use of mechanical prophylaxis, and techniques for screening and surveillance of DVT and/or pulmonary embolism. Chart review was done and admitting data were collated to answer a standard DVT "risk assessment questionnaire. Interviewer-administered questionnaires for physicians who managed the patients, regarding their attitudes and practices were also used (including a risk-grading sheet to double check their knowledge of the factors that contribute to DVT). Patients enrolled were followed up for an addition of at least 1 more week (or until discharge from ICU) by the investigators to assess clinically for development of DVT/PE and if necessary to recommend either d-dimer, V/Q Scan or venous duplex ultrasound of the lower extremities.

Results --- A total of 106 consecutive patients who were either admitted in the medical or neurologic ICU for at least 4 were studied and followed up for 4 weeks. A total of 27 physician's questionnaire was also distributed to investigate their practices and attitudes. Only 57% of patients received VTE prophylaxis. Out of the 57% who received VTE prophylaxis only 62% (37/60) were deemed appropriate for risk stratification. Around 2.8% developed proven VTE (pulmonary embolism or deep venous thrombosis). Well's score was found to be associated with development of VTE. Seventy four percent believed that the primary indication for using DVT prophylaxis was history of previous DVT/PE. Seventy one percent used prophylaxis only selectively due to fear of bleeding and cost despite seventy percent reporting seeing morbity due to VTE.

Conclusion --- The use of VTE prophylaxis in the said institutions is insufficient and not matched to the level of risk. There is a need to establish a common standardized approach to ensure that patients will receive adequate prophylaxis among medical and neurologic ICU patients. ***Phil Heart Center J 2007; 13(2):113-118.***

Key Words: Venous thromboembolism ■ Deep venous thrombosis prophylaxis ■ critically-ill, intensive care patients ■ attitude and practice

Venous thromboembolism is a complication that is commonly seen among critically ill patients admitted at both surgical and medical ICUs. Thrombosis either develops spontaneously (idiopathic or with underlying abnormality in coagulopathy) or is associated with conditions like surgery, trauma or prolonged bed rest. VTE and its sequelae of pulmonary embolism and post-thrombotic syndrome are not only troublesome and morbid but in cases of massive PE can be fatal.1-2 Therefore, prophylaxis for deep venous thrombosis (DVT), early recognition and appropriate treatment can save many lives. Recommendations for use of

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prophylaxis are available. However, there are different practices among different subspecialties in its use and applications.

In general, physicians have different approaches to DVT prophylaxis, and usually this is influenced by the subsets of patients seen and encountered in the practice as well as the availability of the medications used for prophylaxis. The use of standard criteria for stratification of patients for VTE prophylaxis use is under-utilized. Many patients who might benefit from the routine use of these medications are sometimes not properly identified. In Asia, there is paucity of evidence on the actual incidence of this preventable cause of death. But current studies show that DVT occurs as frequently among Asians as do among Caucasians and that use of DVT prophylaxis should be no different form that in Western patients.[3]

This study was conducted to determine the attitudes and practices of physician on VTE prophylaxis among critically ill medical patients. Other aims of the study included the determination of the rate of venous thromboembolism as well as the association of current practices on DVT prophylaxis with the occurrence of venous thromboembolism.

Methods

A multicenter cohort study involving critically ill patients, 18 years old and above admitted for a minimum of 4 days at the medical and neurology ICU of PHC, MMC and PGH was conducted. Forty-eight hours of immobilty, is generally associated with increased the risk of DVT and we allowed two more days (a total of 4 days) minimum to be able to observe without bias the actual practices in the ICU with regards to DVT prophylaxis. Patient selection and admission to the study were done every first day of the week for 4 consecutive weeks. Patient's data sheet were accomplished. Patients who were included were evaluated for their demographic characteristics. The admitting diagnosis and the working diagnosis on admission were noted. Data pertaining to use of DVT prohylaxis, type of medication used, their doses and timing , indications and /or use of mechanical prophylaxis , and techniques for screening and surveillance of DVT and/or pulmonary embolism were noted. Well's scoring was also performed by the investigators at bedside. Interviewer-administered questionnaires for physicians, who managed the patients, regarding their attitudes and practices were used (including a risk-grading sheet to double check their knowledge of the factors that contribute to DVT). For those identified to be at moderate or high risk for venous thromboembolism (DVT and/or PE), the fellows or residents-in-charge were contacted and advised accordingly.

Patients enrolled were followed up for an addition of at least 1 more week (or until discharge from ICU) by the investigators to assess clinically for development of DVT/PE and if necessary to recommend either D-dimer, V/Q Scan or venous duplex ultrasound of the lower extremities.

Venous thromboembolism included both deep venous thrombosis and pulmonary embolism. Suspected deep venous thrombosis included unilateral leg swelling developing after prolonged bedrest and known associated risk for DVT. It is proven DVT if venous duplex ultrasound shows incompressible or partially compressible deep veins of lower extremities. Suspected pulmonary embolism included cases wherein no primary lung problem can explain sudden deterioration in patients respiration (which may require mechanical ventilation) while admitted in the ICU. Proven pulmonary embolism included those with positive high resolution lung CT scan and/or V/Q scan.

Statistical analysis using percentages, mean, standard deviation, 2-tailed Fischers exact test and chi-square or Kruskal-Wallis tests were used accordingly.

Results

The authors were able to collect data from 106 patients admitted in 3 different hospitals (PHC=40; PGH=41; MMC=35). Only patients form medical ICU and neurologic ICU, or its equivalent in the said hospitals, were included in the study. They were subsequently followed up for at least 1 more week or until discharge from ICU or death while in ICU. It was also noted whether the patient developed venous thromboembolism during the study period (whether suspected alone or proven

The mean age is 60.6 years with standard deviation of 18 (22-98 range). The mean BMI is 23.45 with standard deviation of 3.456. Fifty four percent of the subjects were male. Nine patients had active bleeding on admision. Fourteen percent (15/106) had COPD, 15% had CHF (16/106), 15% had ACS. Thirty eight percent (40) had acute lung disease, 37% (39) had cerebrovascular accident (18 infarct, 21 hemorrhage). Sixty one percent (65) had hypertension, 31.1% (33) had diabetes. Thirty five (37) were smokers. Twenty two percent (23) were on mechanical ventilator. Four patients had active cancer, eight had septicemia from other causes (UTI, gynecologic, meningitis, septic arthritis). The average length of hospital stay was 15 days. (Table 1)

Eight patients developed either PE or DVT (suspected or proven). Two patients developed PE during the course of admission (1 admitted for gynecologic septicemia, another with congestive heart failure) proven by lung perfusion scan. One patient developed DVT proven by duplex ultrasound of the lower extremities. The remaining five patients [1 with suspected DVT (symptomatic); 4 with suspected PE based on clinical grounds) were unable to be worked up but otherwise treated as DVT or PE. Around 2.8% (3/106) of the total subjects developed proven DVT or PE.

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Seven out of the eight patients with either suspected or proven PE or DVT had Well's score of more than or equal to two (more than or equal to moderate risk for DVT). The mean Well's score is 1.747 with a standard deviation of 0.719.

All the demographic factors (including hypertension, diabetes, BMI, age, gender, smoking history) specific risk factors (such as acute coronary syndrome, COPD, acute lung disease, congestive heart failure) and presence or absence of DVT prophylaxis were not correlated with either development of PE or DVT. Only the Well's score was significantly correlated with development of positive outcome (either DVT or PE) with a Kruskasl-Wallis H of 4.592 and p value of 0.032. Eleven percent (12 patients) fall under high risk group (with scores of equal to or more than 3 in Well's Scoring). Four patients expired due to their underlying medical condition during the study period.

Out of the 106 patients who satisfied the inclusion criteria, only 57% (60/106) were given DVT prophylaxis. (Figure 1).

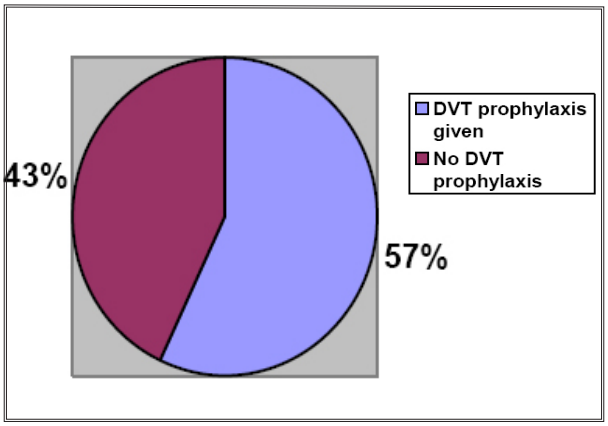

Figure 1. Frequency of Use of DVT Prophylaxis

Of those who had DVT prophylaxis, 38% (21/60) were on LMWH, 47% (29/60) were on mechanical prophylaxis [bandages (8), TED stockings (20), graduated compression stockings (1)], and 6% were unspecified (4/60). Nine out of 60 were on combination of either stockings, LMWH and/or rehabilitation.

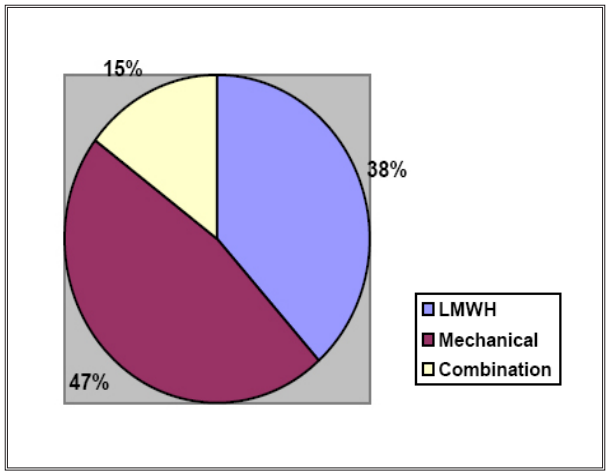

Figure 2. Distribution of DVT Prophylaxis Given (LMWH-low molecular weight heparin, mechanical prophylaxis including graduated compression stockings and TED stockings, and combination of different prophylaxis)

Table 1. Demographic Factors and Associated Illnesses with VTE

Factor	Positive for VTE N=8	Negative for VTE N=96	P Value
Age (mean/SD)	55.25/ 21.3	61/17.8	0.386
BMI (mean/SD)	24.1/ 2.5	23.4/ 3.55	0.68
Male	3	54	0.462
Female	5	42	
Hypertension	3	103	0.218
Diabetes	4	29	0.25
Smoker	3	34	1.0
DVT prophylaxis	7	53	0.13
COPD	1	14	1.0
CHF	2	13	0.63
Acute lung disease	5	3	0.15

*All not significant

Fifteen percent (16/106) were already on either UFH (unfractionated heparin) or LMWH for primary treatment of ACS or cardioembolic disease. Of those on LMWH for VTE (DVT and PE) prophylaxis, 81% received enoxaparin 40 mg sq OD. Nine percent each received 60 mg and 20 mg SQ enoxaparin.

Out of the 57% who received VTE prophylaxis, only 62% (37/60) were deemed appropriate for risk stratification. Appropriate means that the recommended ACCP prophylaxis corresponding to risk stratification was followed accordingly. For moderate risk group of patients totalling 96, only 40 received prophylaxis and only 35 were appropriate. And as for the high risk group only 2 out of 10 received appropriate prophylaxis.

Only 12% (7/60) had regular monitoring for complications of prophylaxis (CBC with platelet count, PT and PTT).

Two out of 29 patients on LMWH (or 7%) had significant bleeding requiring transfusion. One was diagnosed to have heparin-induced thrombocytopenia (defined as a 50% drop in platelet count from baseline occurring between days 4-12 after being exposed to heparin). One had hemorrhagic transformation of cerebral infarction. All four stopped heparin and were shifted on anti-embolic stockings alone or graduated compression stockings.

Out of the 27 fellows from PHC who answered the questionnaire, 78% believed that the incidence of DVT in the Philippines is as common as in the West. Seventy four percent believed that the primary indication for using DVT prophylaxis was history of previous DVT/PE. Seventy one percent use DVT prophylaxis selectively as opposed to routine. (Figure 3).

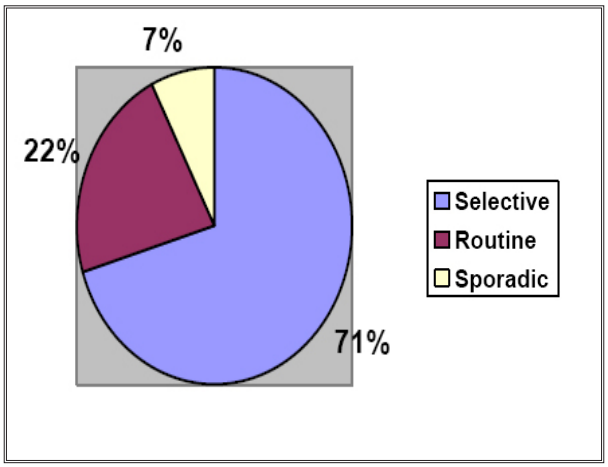

Figure 3. Distribution of Fellow's response Regarding use of DVT Prophylaxis

Among those who used it selectively, forty percent do so due to risk of bleeding and the same percentage find it expensive. (Figure 4).

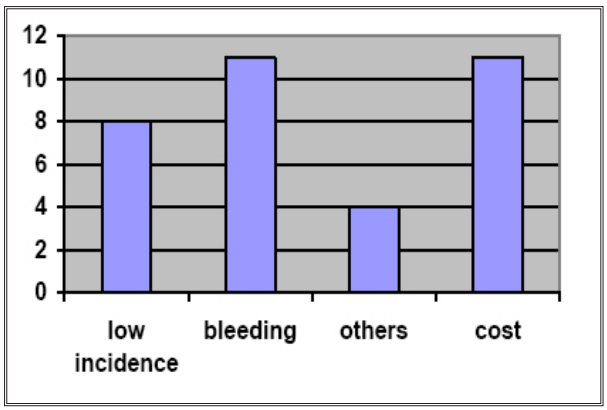

Figure 4. Reasons for Sporadic or Selective Use of DVT Prophylaxis

Almost all use LMWH as method of prophylaxis while 70% also use compression stockings and 7% used pneumatic compression. (Figure 5).

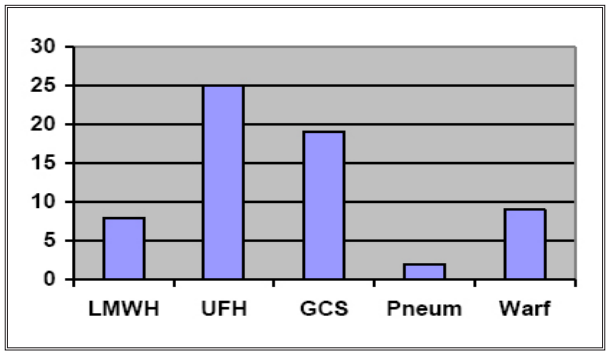

Figure 5. Type of DVT Prophylaxis Used (GCS- graduated compression stockins; pneum- intermittent pneumatic compression; warf- warfarin)

Only 44 % admitted using a protocol for DVT prophylaxis and this was mostly true for pulmonology fellows compared to cardiology fellows. Sixty percent have seen mortality and 70% reported seeing morbidity due to development of DVT and PE, 75% of which were not on any thromboprophylaxis. Most (70%) learned about DVT prophylaxis during residency and fellowship.

Discussion

It has been established that venous thromboembolism (VTE) remains a major cause of morbidity and mortality among hospitalized patients. Even in the industrialized countries where venous thromboprophylaxis in surgical patients is widely practised, this approach has not been broadly implemented in hospitalized medical patients. What apparently limits the accurate assessment of overall burden of VTE in medical patients lies in their greater heterogeneity. In the absence of a structured and intitutional protocol with convenient risk-stratification, identifying individual medical patients at high risk for VTE may seem daunting to practitioners.[4]

Considering that admission to an intensive care unit is already associated with higher risk of VTE , the risk being at least moderate due to multiplicity of risk factors (including expected prolonged bed rest) the use of VTE prophylaxis (heparin and mechanical prophylaxis) remains low in the three institutions studied which in total is around 57%. And only 62% of which followed the appropriate recommendation for VTE prophylaxis. Compared to the France and Canada with a usage of around 63.9% of LMWH or UFH for VTE prophylaxis, usage among the participating institutions showed a significantly lower rate (20% of patients in both MICU and NICU).[5-6] Also mechanical prophylaxis remains low (27%) even with the absence of attendant risk of bleeding. In PGH in

particular, elastic bandages were used more frequently as an alternative to more expensive TED stockings (which is almost excusively the compression therapy of choice in mechanical prophylaxis compared to more effective graduated compression stockings). Heparin usage and VTE prophylaxis in general may be low due to several factors including lack of awareness among physicians of necessity of giving thromboprophylaxis, lack of institutional guidelines to be implemented, lack of confidence in prescribing prophylaxis to MICU and NICU patients, fear of complications like bleeding, cost of prophylaxis and belief of low prevalence of VTE.[7-8]

The absence of association of presence or absence of DVT prophylaxis with the reduction or increase of VTE (PE and DVT, proven or suspected) is probably due to the late administration of prophylaxis among the patients who did receive DVT/VTE prophylaxis (average of 6 days post ICU admission). This provides an important information to us since VTE prophylaxis should be instituted early to provide necessary protection. The rather higher rate of bleeding complications among MICU and NICU compared to other subset of patients may be partly explained again by the multiplicity of co-existing illnesses that may increase the risk for bleeding (e.i. renal failure, septicemia, etc.) and also the low rates of surveillance for complications of DVT prophylaxis among the patients.[9] The same is true for finding no association between the known demographic factors like age, BMI and associated illness like congestive heart failure, acute lung disease, COPD and development of PE or DVT.[10] The sample size is also limited. There is also underutilisation of established non invasive reliable methods for diagnosis of DVT and PE, like duplex ultrasound of the lower extremities. However a Well's score of two or more (which is moderate to more than moderate risk for DVT) was significantly correlated with development of PE and DVT.

The limitation of the of this study is inherent in the study group (the heterogeneity of subjects). The number of participants was also rather limited and they were only followed up to a maximum of 4 weeks. Another limita tion is inability to diagnose the asymptomatic cases of DVT and PE (which to some authors may not be clinically relevant especially the distal DVT) because of lack of screening duplex ultrasound of lower extremities which was used in the MEDENOX, PREVENT and ARTEMIS studies. However, the clinical relevance of asymptomatic VTE is still not well-established.

Conclusion

Despite the growing body of evidence that thrombophylaxis among medical and neurologic ICU patients being safe and effective, there is a general gap between knowledge and actual practice. In our country specifically in the institutions studied, there is a low usage of DVT prophylaxis among both neurologic and medical ICU patients. In fact even in United States of America, hospitalized medical patients seem to be the last frontier in DVT prophylaxis owing to the fact of general indifference to its perceived effectiveness, risk of bleeding and cost.[11] But due to the larger population of medical patients compared to for example orthopedic or surgical patients, an equivalent larger benefit may be achieved. As long as pulmonary embolism still remains the most common preventable cause of death in hospitalized patients, the coming years may bring about wider and more appropriate use of anticoagulants to prevent potentially fatal complications of VTE. The rather dismal use of DVT prophylaxis in medical and neurologic ICUs is no different in our country wherein cost issues may be more important. Even in those who receive thromboprophylaxis, there is a lack knowledge in the appropriate type and intensity of prophylaxis (e.g. for very high risk both LMWH and mechanical prophylaxis is appropriate), surveillance of complications of VTE and complications of prophylaxis itself. The apparent late initiation of prophylaxis among these patients appears to be self-defeating and might be heavily leaning on waiting for symptoms to develop before starting thrombophrophylaxis. Which brings us to the pitfall of using only Well's criteria for risk stratification (many of the scores being garnered from symptomatic DVT). In fact it may be more helpful to use the 'stepwise approach to thromboprophylaxis for acutely ill medical patients' for risk assessment on admission to the hospital particularly the intensive care units similar to the protocol use by MEDENOX (prophylaxis in MEDical patients with ENOXaparin study This type of stepwise approach is easy to follow and can be done on admission of any acutely ill medical patient whether they are admitted in the ICU or in the wards. This eliminates the burden and difficulty of identifying risk of individual hospitalized medical patients. This must be coupled with strong and steady implementation of an instutional based protocol to prevent VTE.[12-13]

For future studies, it is recommended that weekly DVT screening using duplex ultrasound be employed for all patients included in the study to detect also asymptomatic DVT. A larger sample size is also ideal. Other risk stratification modalities or protocols can also be used besides Well's scoring. Since neurologic patients may have inherent differences from medical ICU patients with regards to risk of VTE, it may also be intersting to compare the practices between the two groups. Another area of research is to look into factors that will improve implementation of VTE protocols (e.g. after lectures or round table discussions, checklist of risk factors in every chart, etc).

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Outcome of Patients Who Underwent Coronary Artery Bypass Graft With Concomitant Valve Surgery in Philippine Heart Center

Ronald P. Galicio, MD; Frederick Vicente, MD.

Background --- The Philippine Heart Center (PHC) is the center of cardiovascular care in the country, catering to patients from all walks of life. The annual statistics of patients undergoing coronary artery bypass graft (CABG) surgery is 500 to 600 and there has been a comparable mortality rate in our institution with the foreign data, 3.69% vs. 2.5%, respectively. However, mortality rate significantly increases when CABG is done with concomitant valve surgery and/or in the presence of other identified risk factors. This study was conducted to present the institution's experience regarding coronary artery bypass graft surgery with concomitant valve surgery.

Methods --- Surgery department census from January 1, 2005 to December 31, 2006 was reviewed for all the cases of CABG with concomitant valve surgery. The data collection was complemented by accessing the hospital's electronic medical records (EMR). Variables identified as risk factors by Fortinez JT and Edwards et al. in their CABG with valve surgery model, and in PHC Risk Index and American College of Cardiology/American Heart Association (ACC/AHA) Practice Guidelines for CABG surgery were extracted and combined.

Results --- Total incidence of outcomes was measured and reoperation for bleeding was the most frequent complication followed by renal failure, cerebrovascular disease, deep sternal infection, and lastly reoperation for post-pericardiotomy syndrome. The mortality rate was 14.6%. We also measured outcomes against specific concomitant valve surgeries and yielded multiple valve surgery as the one with the highest mortality rate of 28.57%, followed by mitral valve and aortic valve surgeries. Concomitant multiple valve surgery also had the highest incidence of complications such as reoperation for bleeding, renal failure and deep sternal infection. Concomitant mitral valve surgery, however, had the highest incidence for postoperative cerebrovascular disease and had the longest total and postoperative length of hospital stay

Conclusion --- The results of this study, having a small population size, could not in any way be compared with the results observed internationally. However, this study gave us some insights on the characteristics, complications and mortality of this subset of patients being operated on in our own institution. This may somehow pave the way to large scale studies in our country, involving multiple centers who handle this subset of patients. ***Phil Heart Center J 2007; 13(2):119-123.***

Key Words: Coronary artery bypass graft surgery ■ valve surgery ■ mortality, complications ■cerebrovascular disease

The Philippine Heart Center (PHC) is the center of cardiovascular care in the country cater ing to patients from all walks of life. A large volume of patients is being admitted in this hospital, either due to medical management or procedural intervention. The annual statistics of patients undergoing coronary artery bypass graft (CABG) surgery is 500 to 600 and there has been a comparable mortality rate in our institution with the foreign data, 3.69% vs. 2.5%, respectively.[1,13] However, mortality rate significantly increases when CABG is done with concomitant valve surgery and/or in the presence of other identified risk factors.[1-4]

The PHC CABG registry aims to provide us significant information on the quality of care, procedural outcome and other possible risk factors innate in our own set of patients. Risk stratification models of patients who underwent CABG and valve surgeries had been made in the past both internationally and locally,[1-11] but the information on the subgroup of patients who underwent CABG with valve surgery in our institution has been minimal and not really been put into focus. This study was conducted to determine the outcomes, such as in-hospital mortality and morbidities, of patients who underwent CABG with concomitant valve surgery.

Methods

Surgery department census from January 1, 2005 to December 31, 2006 was reviewed for all the cases of CABG with concomitant valve surgery. The data collection was complemented by accessing the hospital's electronic medical records (EMR). Variables identified as risk factors by Fortinez JT and Edwards et al. in their

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CABG with valve surgery model, and in PHC Risk Index and American College of Cardiology/American Heart Association (ACC/AHA) Practice Guidelines for CABG surgery were extracted and combined.[1,3-5,9,13] These are pulmonary artery systolic pressure (PASP), bypass time (BT), ischemic time (IT), previous cardiac operation, serum creatinine of >2 mg%, operative status whether emergency, urgent or elective, age, diabetes mellitus (DM), gender, dialysis-dependent renal failure (DDRF), three-vessel CAD (3VD), preoperative intra-aortic balloon pump (IABP) or inotropes, NYHA class IV, body surface area (BSA), left ventricular ejection fraction (EF), myocardial infarction (MI), hypertension (HPN) and case category. Other risk factors identified by Edwards et al.[9] such as chronic lung and peripheral vascular diseases were not included since they were consistently found to be insignificantly correlated with mortality in previous local studies.[1,5,7] Immunosuppressive therapy which was also identified as one of the risk factors by Edwards et al.[9] was not included since the details of this variable's inclusion was not clear to the author. Outcomes such as mortality, complications and length of hospitalization were obtained from the medical records. Mortality is defined as death occurring at anytime during the same hospitalization. Complications such as cerebrovascular disease (CVD) is either infarct or bleed, while deep sternal infection (DSI) is surgical site infection of the anterior chest post-open heart surgery, necessitating debridement. Renal failure is the need for any form of dialysis post-operatively or as defined in RIFLE classification.[12] Valve surgery is either replacement or repair of native or prosthetic valve. Multiple valve surgery (MLVS) is surgery involving any combination of valves.

Statistical Analysis

Frequency and percentage were used to characterize the categorical variables, while mean and standard deviation were used to present continuous variables. The data gathered were analyzed using Chi square. The small population size was addressed by using Fisher's Exact Probability Test for significance and finally determined by t-test.

Results

Fifty-three patients were identified and out of which only 41 (77%) medical charts were available for review. Of the 41 medical charts retrieved, 1 had missing data on BT, IT and echocardiographic report while 2 more charts had no echocardiographic data.

Table 1 illustrates the clinico-demographic characteristics of the included patients. The mean age of patients does 58.9 years, with males comprise majority of the population. Mitral valve surgery was the most common concomitant valve surgery and almost half of the population had 3-vessel disease and hypertension. Neither any body was operated on an emergency basis nor was there a patient in dialysis-dependent renal failure. A small number of patients came in with diabetes, moderately severe pulmonary arterial systolic pressure, an ejection action of less than 40%, in severe heart failure and with a history of myocardial infarction within seven days. Majority were private cases. Likewise, majority had prolonged bypass and cross-clamp time.

Table 2 shows the outcomes of the patients who underwent CABG with concomitant valve surgery. Reoperation for bleeding was the most frequent complication, followed by renal failure, cerebrovascular disease, deep sternal infection, and lastly reoperation for post-pericardiotomy syndrome. The in-hospital mortality rate was 15%.

Table 1. Clinico-Demographic Characteristics of the patients included

Characteristic	Frequency*	%
Age in years		
Mean (SD)	58.9 (9.5)	
Gender		
M	28	68
F	13	32
Concomitant Valve Surgery		
Aortic	11	27
Mitral	23	56
Multiple	7	17
DM	6	15
HPN	20	49
Previous Cardiac Operation	2	5
3 Vessel Disease	18	44
Serum Creatinine >2mg%	2	5
Operative Status		
Emergency	0	0
Urgent	14	34
Elective	27	66
Preoperative IABP/Inotropes	11	27
NYHA class IV	1	2
PASP ≥60 mmHg (n=38)	7	18
Myocardial Infarction within		
24 hrs	0	0
7 days	3	7
>7 days or no MI	38	93
EF (n= 38)		
≥40%	34	89
<40%	4	11
BT (n= 40)		
>180 mins	26	65
≤180 mins	14	35
IT (n= 40)		
>120 mins	32	80
60-120 mins	7	18
<60 mins	1	2
Case category:		
Private	36	88
Service	5	12

*n=41, unless otherwise specified

Among the risk factors identified, it was only the gender difference which showed statistically significant relationship with the outcome in this study, with the female being at risk of developing postoperative acute renal failure (p=0.028). A number of variables however, showed trends of association with the outcome. Concomitant valve surgery and ischemic time were not statistically measured since the small number of population did not allow analysis. Tables 3.1 and 3.2 show all the risk factors as measured against the outcomes.

We also measured outcomes against specific concomitant valve surgeries. Multiple valve surgery yielded the highest mortality rate of 29%, followed by mitral valve and aortic valve surgeries. Concomitant multiple valve surgery also had the highest incidence of complications such as reoperation for bleeding, renal failure and deep sternal infection. Concomitant mitral valve surgery however, had the highest incidence for postoperative cerebrovascular disease and had the longest total and postoperative length of hospital stay (Table 4).

Table 2. Incidence of outcomes observed among patients who underwent CABG with concomitant valve surgery

Outcome	Frequency	%
Death	6	15
CVD	4	10
Reoperation for PPS	1	2
Reoperation for Bleeding	7	17
Renal Failure	5	12
Deep Sternal Infection	2	5

Table 3.1. Association of Risk Factors to Outcomes of Mortality, CVD and Renal Failure

Risk Factors		Mortality					CVD					Renal Failure				
		Survived N=35		Died N=6		*p*	No N=37		Yes N=4		*p*	No N=36		Yes N=5		*p*
Age (mean, SD)		58.2 (8.7)		63 (13.5)			58.4(9.4)		63.8(12.4)			58.2(9.5)		63.8 (12.4)		
		n	**%**	**n**	**%**		**n**	**%**	**n**	**%**		**n**	**%**	**n**	**%**	
Gender	M	26	93	2	7	0.07	26	93	2	7	0.58	27	96	1	4	***0.03***
	F	9	69	4	31		11	85	2	15		9	69	4	31	
DM	+	29	83	6	17	0.57	32	91	3	9	0.48	30	86	5	14	1.0
	-	6	100	0	0		5	83	1	17		6	100	0	0	
HPN	+	17	81	4	19	0.66	20	95	1	5	0.34	17	81	4	19	0.66
	-	18	90	2	10		17	85	3	15		19	95	1	5	
BSA	≥1.4	31	84	6	16	1.0	34	92	3	8	0.35	32	86	5	14	0.58
	<1.4	4	100	0	0		3	75	1	25		4	100	0	0	
Previous Cardiac Surgery	+	2	100	0	0	1.0	2	100	0	0	1.0	2	100	0	0	1.0
	-	33	85	6	15		35	90	4	10		34	87	5	13	
3 vessel disease	+	14	78	4	22	0.38	16	89	2	11	1.0	15	83	3	17	0.64
	-	21	91	2	9		21	91	2	9		21	91	2	9	
Serum Creatinine > 2mg%	+	2	100	0	0	1.0	1	50	1	50	0.19	1	50	1	50	0.19
	-	33	85	6	15		36	92	3	8		35	90	4	10	
Operative Status	Elective	23	85	4	15	1.0	24	89	3	11	1.0	23	85	4	15	0.65
	Urgent	12	86	2	14		13	93	1	7		13	93	1	7	
Pre-op IABP/ Inotropes	+	10	91	1	9	1.0	19	91	1	9	1.0	10	91	1	9	1.0
	-	25	83	5	17		27	90	3	10		26	87	4	13	
NYHA Class IV	+	1	100	0	0	1.0	1	100	0	0	1.0	1	100	0	0	1.0
	-	34	85	6	15		36	90	4	10		35	88	5	12	
PA SP ≥ 60 mmHg (n=38)	+	5	71	2	29	0.30	6	86	1	14	1.0	6	86	1	14	1.0
	-	27	87	4	13		28	90	3	10		27	87	4	13	
MI within 7 days	+	3	100	0	0	1.0	2	67	1	33	0.27	3	100	0	0	1.0
	-	32	84	6	16		35	92	3	8		33	87	5	13	
EF (n=38)	*<40%*	4	100	0	0	1.0	4	100	0	0	1.0	4	100	0	0	1.0
	≥40%	28	82	6	18		30	88	4	12		29	85	5	15	
Bleeding Time	*>180 min*	23	88	3	12	0.65	24	92	2	8	0.60	24	92	2	8	0.32
	≤ 180 min	11	79	3	21		12	86	2	14		11	79	3	21	
Case Category	PVT	30	83	6	17	1.0	32	89	4	11	1.0	31	86	5	14	1.0
	SVC	5	100	0	0		5	100	0	0		5	100	0	0	

Table 3.1. Association of Risk Factors to Outcomes of Reoperation and Deep Sternal Infection

Risk Factors	Reoperation for PPS					Reoperation for Bleeding					Deep Sternal Infection				
	No N=40		Yes N=1		p	No N=34		Yes N=7		p	No N=39		Yes N=2		p
Age (mean, SD)	--		-		-	59.1 (9.5)		58.1 (10.2)		0.82	--		--		-
	n	%	n	%		n	%	n	%		n	%	n	%	
Gender															
M	27	96%	1	4%	1.0	22	79%	6	21%	0.40	27	96%	1	4%	0.54
F	13	100%	0	0%		12	92%	1	8%		12	92%	1	8%	
DM															
without	34	97%	1	3%	1.0	29	83%	6	17%	1.0	33	94%	2	6%	1.0
with	6	100%	0	0%		5	83%	1	17%		6	100%	0	0%	
HPN															
without	20	95%	1	5%	1.0	16	76%	5	24%	0.41	20	95%	1	5%	1.0
with	20	100%	0	0%		18	90%	2	10%		19	95%	1	5%	
BSA															
≥1.4	36	97%	1	3%	1.0	30	81%	7	19%	1.0	35	95%	2	5%	1.0
<1.4	4	100%	0	0%		4	100%	0	0%		4	100%	0	0%	
Previous Cardiac Surgery															
without	38	97%	6	3%	1.0	33	85%	6	15%	0.31	37	95%	2	5%	1.0
with	2	100%	0	0%		1	50%	1	50%		2	100%	0	0%	
3VD															
without	23	100%	0	0%	0.43	18	78%	5	22%	0.43	22	96%	1	4%	1.0
with	17	94%	1	6%		16	89%	2	11%		17	95%	1	5%	
Serum Crea >2mg%															
without	38	97%	1	3%	1.0	32	82%	7	18%	1.0	37	95%	2	5%	1.0
with	2	100%	0	0%		2	100%	0	0%		2	100%	0	0%	
Operative Status															
Urgent	13	93%	1	7%	0.34	13	93%	1	7%	0.38	14	100%	0	0%	0.54
Elective	27	100%	0	0%		21	78%	6	22%		25	93%	2	7%	
Pre-op IABP/Inotropes															
without	29	97%	1	3%	1.0	27	90%	3	10%	0.06	29	97%	1	3%	0.47
with	11	100%	0	0%		7	64%	4	36%		10	91%	1	9%	
NYHA class IV															
no	39	98%	1	2%	1.0	34	85%	6	15%	0.17	38	95%	2	5%	1.0
yes	1	100%	0	0%		0	0%	1	100%		1	100%	0	0%	
PASP ≥60 mmHg (n=38)															
no	30	97%	1	3%	1.0	25	81%	6	19%	1.0	29	94%	2	6%	1.0
yes	7	100%	0	0%		6	86%	1	14%		7	100%	0	0%	
MI															1.0
within 7 days	2	67%	1	33%	0.07	3	100%	0	0%	1.0	3	100%	0	0%	
>7 days or no MI	38	100%	0	0%		31	82%	7	18%		36	95%	2	5%	
EF (n= 38)															
≥40%	33	97%	1	3%	1.0	29	85%	5	15%	0.14	33	97%	1	3%	0.20
<40%	4	100%	0	0%		2	50%	2	50%		3	75%	1	25%	
BT (n= 40)															
>180 mins	26	100%	0	0%	0.35	22	85%	4	15%	0.67	24	92%	2	8%	0.53
≤180 mins	13	93%	1	7%		11	79%	3	21%		14	100%	0	0%	
Case category:															
Private	36	100%	0	0%	0.12	30	83%	6	17%	1.0	34	94%	2	6%	1.0
Service	4	80%	0	20%		4	80%	1	20%		5	100%	0	0%	

Table 4. Frequency of Outcome According to Concomitant Valve Surgery

Outcome	Aortic Valve Surgery N=11	Mitral Valve Surgery N=23	Multiple Valve Surgery N=7
Mortality (n,%)	1 (9)	3 (13)	2 (29)
CVD (n,%)	1 (9)	3 (13)	0
Reoperation for PPS (n,%)	0	1 (2)	0
Reoperation for Bleeding (n,%)	0	4 (17)	3 (43)
Renal failure (n,%)	1 (9)	2 (9)	2 (29)
Deep Sternal Infection (n,%)	1 (9)	0	0
Length of Hospital Stay (LOHS), days (mean ± SD)	20±8	27.7±20.1	20.4±12.5
Post-operative LOHS, days (mean ± SD)	13.4±7.6	18.6±13.1	15.6±.5

Discussion

This is the first study in our institution that focused on the subset of patients who had coronary artery bypass graft with concomitant valve surgery. Internationally, the study done by Edwards et al.[9] was somehow similar but it only included patients with concomitant valve repair and also did not take into consideration those patients who had concomitant multiple valve surgery. The statistically calculated non-significance of the variables in this study may be attributed to a small sample size and could be strengthened by increasing the population. Nonetheless, being a female still significantly exemplified the risk for complication. The mortality rate that we have observed here almost doubled what was observed in the study of Fortinez JT on valve surgeries and almost four time that of Milo et al.'s study on CABG surgery.1,5 This suggests that the combined operative risks of these patients significantly increase mortality and complications than patients who undergo any individual CABG or valve surgeries combined. But again, this has to be proven statistically.

Conclusion

The results of this study, having a small population size, could not in anyway be compared with the results observed internationally.[8-10] However, this study may give us some insight on the characteristics, complications and mortality of this subset of patients being operated on in our own institution and may somehow pave the way to a large scale studies here in our country. It is therefore recommended that a larger population be studied to verify and somehow confirm what have already been at hand.

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Echocardiographic Assessment of Right Ventricular Diastolic Function After Tetralogy of Fallot Correction

Flerida L. Teodoro, MD; Corazon Estevanez, MD; Benito R. Gonzales R. Gonzales, RMT

Background --- Literature has shown that there is a development of right ventricular dysfunction in some patients after the total repair of Tetralogy of Fallot. Right ventricular diastolic function has been recently observed to show signs of impairment with a diverse behavior in different phases of the postoperative follow-up. The incidence of right diastolic dysfunction in literature after TOF repair ranges from 28 to 52%. This study was aimed to quantitate right ventricular diastolic dysfunction in early postoperative phase of tetralogy of fallot and to correlate it with the type of surgical procedure and clinical parameters.

Methods --- This was a prospective cohort study involving Tetralogy of Fallot patients who underwent total repair from May to November 2006 at the Philippine Heart Center. Clinico-demographics as well as echocardiographic studies with emphasis on the right ventricular function were obtained. RV diastolic indices, such as Tricuspid Inflow E Velocity, A velocity, E/A ratio, Tricuspid deceleration Time, Isovolumic relaxation time and Superior Vena Cavae velocities, were obtained from the study population and compared with normal values. Post-operative clinical parameters were then correlated with the RV diastolic indices.

Results --- There were 10 patients included in the study. The mean age of the patients was 9.78 +/- 5.3 years old There were six male and four female. There were seven patients who had VSD closure with RVOT patching while the remaining three patients had VSD closure with infundibulectomy. All the above RV diastolic indices measured from the patients have a significant difference as compared to normal values (P value < 0.05) except to E wave velocity of tricuspid inflow during inspiration. This means that most of the patients developed RV diastolic dysfunction in early postoperative period.

Conclusion --- Right ventricular diastolic dysfunction can develop in early post-operative period after TOF correction. The RV diastolic indices such as Tricuspid E wave velocity, Tricuspid E/A ratio, deceleration time, isovolumic relaxation time and Superior Vena Cavae Velocities are good parameters to determine the RV diastolic dysfunction. Age prior to surgery, ECG findings, and O2 saturation are good predictors of outcome of TOF correction. Surgical technique and duration of bypass time did not show significant correlation with our results in patients who had RV diastolic dysfunction. Almost all patients who developed right ventricular dysfunction have elevated central venous pressure, prolonged ICU stay and prolonged inotropic supports. ***Phil Heart Center J 2007;13(2):124-129.***

Key Words: Congenital Heart Disease ■Tetralogy of Fallot ■ Echocardiography ■ Right Ventricle, Diastolic Dysfunction

Diastole is a period of ventricular relaxation incorporating periods of isovolumetric relaxation and early and late diastolic filling. Impaired diastolic function with relative preservation of systolic function is an early feature of right and left ventricular disease.

The literature has shown that there is a development of right ventricular dysfunction in some patients after the total repair of tetralogy of fallot. Right ventricular diastolic function has been recently observed to show signs of impairment with a diverse behavior in different phases of the postoperative follow-up. The incidence of right diastolic dysfunction in literature after TOF repair ranges from 28 to 52%.[6]

In the study of Cardoso et al, restrictive right ventricular physiology was detected on the follow-up of most patients who underwent repair of tetralogy of Fallot.[8] A significant number of their patients(63.3%) with restrictive physiology had a longer post-operative period, a longer duration of QRS complex, and a lower E/A ratio in inspiration.

In our institution, there were some of patients who underwent TOF repair had a complicated post-operative course. In order to give optimal patient management perioperatively, we would like to objectively assess the right ventricular diastolic function after Tetralogy of Fallot repair. This can be of clinical use and can provide accurate prognostic information.

This study was conducted to identify right ventricular diastolic dysfunction in early postoperative phase of tetralogy of fallot and to correlate it with the type of

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surgical procedure and clinical parameters.

Methods

This was a prospective cohort study involving children less than 19 y/o that underwent TOF correction from May to November 2006. TOF patients with pulmonary arteries are confluent and good sized (Mcgoons: >/= 1.5) and with good RV and LV systolic function were included. Exclusion Criteria are as follows: presence of pulmonary valve atresia with ventricular septal defect (VSD), double-outlet right ventricle (DORV), associated complex congenital heart disease such as TOF with atrio-ventricular septal defect (AVSD), TOF with absent pulmonic valve, Coronary abnormalities, Malposition of great arteries, Genetic abnormalities(Down's Syndrome), and Cardiomyopathy.

Selected patients were identified and informed consent was obtained from all the parents. Clinical data was taken from their medical chart. We also recorded the age, sex, oxygen saturation, pertinent pre-operative ECG finding, surgical technique used for TOF correction, bypass time, central venous pressure, ICU stay and duration of inotropic support. These clinical parameters were recorded to correlate with the RV diastolic indices of the patients.

Echocardiogram was done at Non-invasive Cardiovascular Medicine Division of Philippine Heart Center from May 2006- November 2006. Detailed echocardiogram, which was done after a week or more postoperatively (when the patient was discharged from ICU), was obtained by one adult echo technologist who is well-trained in diastology. After doing the echocardiogram, patients were group into two:

Group 1 – Good Outcome (those who have normal right ventricular diastolic function indices post-operatively)

Group 2- Poor Outcome (those who have abnormal right ventricular diastolic function indices post-operatively)

The ICU stay and prolonged inotropic support was not used as a basis of good and poor outcome because patients were managed by different doctors.

Echocardiography

Transthoracic echocardiography was performed with an Acuson machine using 3.5 MHz transducer. Spectral Doppler recordings were obtained from the pulmonary artery (PA), Tricuspid valve, and Superior Venue Cavae inflow. These are the following techniques to measure Right Ventricular Diastolic Indices (by pulsed doppler study using apical four-chamber view):

1. Tricuspid Peak E velocity – a peak velocity during rapid right ventricular early filling; by using a pulse wave Doppler, place the cursor just below the tricuspid valves opening and when the E wave and A wave are identified, we can measure the peak E velocity by measuring the height of the E wave.
2. Tricuspid Peak A velocity – a peak velocity during rapid right ventricular late filling; by using a pulse wave Doppler, place the cursor just below the tricuspid valves opening and when the E wave and A wave are identified, we can measure the peak A velocity by measuring the height of the A wave.
3. E/A ratio- ratio of the Peak E velocity and Peak A velocity
4. Right Ventricular Isovolumic relaxation time- can be measured from the pulmonic closing component of the second heart sound to the onset of flow on the tricuspid Doppler tracings.
5. Deceleration Time can be measured as the slope of a straight line drawn from the peak E velocity to the point where peak E decreases by half of the descending limb of the early diastolic inflow. Ten tricuspid peak E wave velocities (inspiratory and expiratory) were recorded in every study and we got the average and compared it with the normal.

Other RV diastolic indices

1. Superior vena cavae velocity can be recorded from the suprasternal notch or subcostal positions. From the suprasternal position, forward flow in the superior vena cava is directed away from the transducer. (Suprasternal approach was used in our study). Normal superior vena caval flow is characterized by three distinct waveforms. The largest waveform is the S wave, which represents forward flow in the superior vena cava caused by relaxation of the right atrium and descent of the tricuspid annulus during right ventricular systole. The D wave, a second forward flow, occurs during rapid ventricular filling when the tricuspid valve opens. A third waveform is the A wave represents the reverse flow associated with right atrial contraction.
2. Diastolic Pulmonary Artery forward flow can be investigated by pulsed-wave doppler using parasternal short axis view. Velocities of PA systolic and diastolic forward flow were measured. Diastolic pulmonary artery forward flow is a premature opening of the pulmonic valve. It is believed to occur when RV diastolic pressure equals or exceeds diastolic pulmonary artery pressure. Recordings were made with simultaneous ECG, phonocardiogram, and a respiratory tracing. All patients were in sinus rhythm and without inotropic support during the doppler recordings.

Results

There were 10 patients included in the study. The age of the patients in the study is 9.78 +/- 5.3 years old (Table 1) Four patients were above 10 years old and the rest were below 10 years old. Among the ten, 6 were male and 4 were female. The ECG findings of these patients showed that those with prolonged PR interval and ST depression on right chest leads were ages 12 years old and above.

And those below 10 years old did not have prolonged PR or ST depression. Those patients with ST depression on ECG also have oxygen saturation of 85% and below. These same group of patients have increased hematocrit (>/= 0.58) as compared to those below 10 years old.

Table 1. Pre-operative clinical data of TOF patients included in the study.

Patient	Age/Sex	CLINICAL FINDINGS		
		O2 Sat	Hematocrit	ECG findings
1	3 / M	92%	0.50	(-) ST depression on R chest leads
2	9 / M	83%	0.52	(-) ST depression on R chest leads
3	12 / M	74%	0.60	PR: prolonged
4	5 / F	88%	0.59	(-) ST depression on R chest leads
5	15 / F	83%	0.58	(+) ST depression on R chest leads
6	16 / M	76%	0.74	(+) ST depression on R chest leads
7	9 / M	89%	0.56	(-) ST depression on R chest leads
8	3 / F	88 %	0.50	(-) ST depression on R chest leads
9	16 / M	85%	0.63	(+) ST depression on R chest leads
10	5 / F	87%	0.52	(-) ST depression on R chest leads

The operative and post-operative characteristics of the patients are presented in Table 2. There were seven patients who had VSD closure with RVOT patching while the remaining three patients had VSD closure with infundibulectomy. Five patients had a bypass time of 1'30" or more while the remaining had a bypass time of <1'30." Perioperatively, among the ten patients, six of them have elevated central venous pressure. Three of these patients with elevated CVP were above 10 years of age. Six patients stayed in the ICU more than seven days while the remaining four stayed in the ICU less than seven days.

Table 3.1 showed the statistical analysis done on each of the echocardiographic parameters of the patients. These standard Normal Values was done by Snider. All the above RV diastolic indices measured from the patients have a significant difference as compared to normal values (P value < 0.05) except to E wave velocity of tricuspid inflow during inspiration. This means that most of the patients developed RV diastolic dysfunction in early postoperative period.

Table 2. Operative and Post-Operative Characteristics of Included Patients

Patients	Surgical Procedure	Bypass time	Central Venous Pressure	ICU stay	Duration of Inotropic Supports
1	VSD patch closure w/ savage; transannular patching with pericardium and monocusp	1' 50"	13 mmHg	18 days	15 days
2	VSD patch closure, Infundibulectomy and MPA patching	1' 51"	14 mmHg	7 days	3 days
3	VSD patch closure and RVOT patching	2" 11'	13 mmHg	11 days	8 days
4	VSD patch closure and Infundibulectomy	1" 16'	10 mmHg	6 days	4 days
5	VSD closure and RVOT patching	1" 50'	15 mmHg	10 days	9 days
6	VSD patch closure and RVOT patching	1' 45"	9 mmHg	9 days	7 days
7	VSD patch closure and RVOT patching	1' 20"	8 mmHg	6 days	5 days
8	VSD closure and RVOT patching	1' 10"	9 mmHg	5 days	4 days
9	VSD patch closure and RVOT patching	1'01"	19 mmHg	9 days	9 days
10	VSD closure and Infundibulectomy	1" 40'	8 mmHg	5 days	4 days

Table 3. Post-operative Right Ventricular Diastolic Indices by Doppler Echocardiography

Patient	1	2	3	4	5	6	7	8	9	10
Tricuspid inflow E wave (inspiration)	0.584	0.924	0.64	1.06	0.574	0.413	0.67	0.94	0.59	0.83
Tricuspid inflow E wave (expiration)	0.924	0.826	0.528	0.99	0.565	0.407	0.58	0.854	0.442	0.66
E/A ratio	0.596	0.832	0.45	3.87	0.843	1.387	1.09	2.2	0.81	1.4
Tricuspid deceleration time	0.239	0.239	0.218	0.143	0.266	0.160	0.201	0.167	0.253	0.14
SVC										
S	0.42	0.27	0.25	0.54	0.20	0.28	0.64	0.27	0.57	0.15
D	0.73	0.26	0.15	0.18	0.34	0.25	0.75	0.53	1.17	0.63
A	0.112	0.120	0.080	0.10	0.088	0.191	0.116	0.140	0.112	0.072
IVRT	112	96	56	80	104	80	88	104	128	72
DPAFF	(-)	(-)	(-)	(-)	(-)	(+)	(-)	(-)	(+)	(-)

SVC = Superior venae cava velocity S,
D, A= Superior Vena Cava waveforms
IVRT = Isovolumic Relaxation Time
DPAFF = Diastolic Pulmonary Artery Forward Flow

Table 3.1. Doppler Echocardiography of Patients After TOF repair

PARAMETER	OBSERVED (PATIENTS) Mean +/- SD	NORMAL VALUE	P VALUE
E WAVE (Inspiration)	0.722 +/- 0.204	0.62 +/- 0.13	NS
E WAVE (Expiration)	0.628 +/- 0.202	0.49 +/- 0.12	0.031
E/A ratio	1.351 +/- 1.021	2.56 +/- 1.29	0.000
Isovolumic Relaxation Time	89.78 +/- 21.08	55 +/- 10	0.000
Deceleration Time	0.208 +/- 0.055	0.14 +/- 0.02	0.000
SVC			
S	0.305 +/- 0.118	0.532 +/- 0.097	0.000
D	0.383 +/- 0.194	0.337 +/- 0.086	0.453
R	0.115 +/- 0.035	0.337 +/- 0.86	0.000

Note: Refer to Normal Values on Table 3.1. All the results of RV diastolic indices of these 3 patients were normal or almost near the normal values. This means that they did not develop Right Ventricular Diastolic Dysfunction.

Table 3.2. Group II Bad Outcome (No RV Diastolic Dysfunction)

Group II	E wave(exp)	E/A	IVRT	DT	SVC S	SVC D	SVC R
Patient							
1	0.427	0.596	80	0.239	0.42	0.73	0.112
2	0.826	0.832	96	0.297	0.27	0.26	0.120
3	0.528	0.45	56	0.218	0.25	0.15	0.80
5	0.565	0.843	104	0.266	0.20	0.34	0.088
6	0.407	1.387	80	0.160	0.28	0.25	0.191
7	0.576	1.088	88	0.201	0.42	0.43	0.112
9	0.442	0.81	128	0.253	0.25	0.33	0.136

Note: Refer to Normal Values on Table 3.1. All the patients in this group have abnormal RV diastolic indices. This means that they developed Right Ventricular Diastolic Dysfunction.

Discussion

Surgical repair of tetralogy of fallot in our center (Philippine Heart Center) has markedly improved and our concern now is to decrease the early and late morbidity of TOF repair. There are many studies done by different regarding right ventricular diastolic function in TOF by showing diverse results. We therefore want to present the results and outcome of our surgical repair of tetralogy of fallot.

Clinical Characteristics

Demographic data was presented in Table 1. It showed that those patients' ages 12 years old and above (4 out of 10) manifested ischemic changes in preoperative ECG, most likely secondary to prolonged hypoxemia and chronic pressure overload. These same patients have an oxygen saturation below 85% and increased in hematocrit (>0.56) as compared with those below 12 years old with oxygen saturation of above 85% and hematocrit of below 0.56. With regards to our operative and perioperative characteristics of the TOF patients, there was no correlation between the surgical technique done and the development of RV diastolic dysfunction after repair. In the study of Gunnar et al (9), transannular patching (TAP) or without transannular patching of RVOT can have restrictive RV physiology. Similarly, our results showed that not all who underwent TAP (7 out of 10 patients) had RV diastolic dysfunction or restrictive RV physiology Five

patients have a cardiopulmonary bypass time of > 1' 30" and the rest were less than 1' 30". Correlating the bypass time with the RV diastolic indices of the respective patients, there is no significant correlation between the bypass time and development of RV diastolic dysfunction after TOF repair. There was a patient with shorter bypass time (patient 9 with bypass time of 1' 01") and still developed RV diastolic dysfunction. And some of the patients with prolonged bypass time didn't developed RV diastolic dysfunction. (Table 2)

Echocardiographic Findings (Table 3 – 3.1, 3.2)

We grouped the patients into two groups. The group 1 has a good outcome which means that there was no development of RV diastolic dysfunction after TOF repair, while group 2 has a bad outcome which means that there was a development of RV diastolic dysfunction after the surgical procedure (Table 3.2).

Following our criteria in grouping the patients, we compared the RV diastolic indices of each patient with the standard normal value by Snider (2). Those with good outcome were patient 4, 8 and 10. These three patients were ages 3 to 5 years old, with good oxygen saturation of 87-88% and no ischemic changes on ECG (Table 1). This indicates that age at the time of surgery , oxygen saturation and ECG findings are good preoperative clinical parameters that can predict the outcome of the TOF correction. These group of patients also have normal central venous pressure perioperatively, shorter ICU stay (5-6 days) and shorter duration of inotropic supports (4 days) (Table 2).

There was an exception in one patient (Patient 1) aged 3 years old who still developed RV diastolic dysfunction. This is probably because the patient underwent TOF correction with transannular patching and monocusp and therefore the bypass time was prolonged. There are no other clinical findings that can contribute to the development of RV diastolic dysfunction. The patient had good oxygen saturation (92%) prior to surgery; with no signs of ischemic changes on ECG and no increased in hematocrit. Patient 1 had also elevated central venous pressure perioperatively. The ICU stay and duration of inotropic supports of this patient were prolonged.

Those with bad outcome (w/ RV diastolic dysfunction after TOF correction) were patient 1,2,3, 5,6, 7 and 9(Table 3-3.2). Patient 1 was discussed above, then patient 3, 5, 6 and 9 were aged 12 years old up to 16 years old. These four patients have signs of ischemic changes on ECG prior to surgery and with increased hematocrit (>/= 0.58) (Table 1). Perioperatively, they have elevated central venous pressure (> 12 mmHg), prolonged ICU stay (>/= 9 days) and prolonged inotropic supports (>/= 7 days) (Table 2). Other patients who developed RV diastolic dysfunction after TOF repair were patient 2 and 7. Both of them were 9 years of age but they didn't have ischemic changes on ECG. Patient 2 had an oxygen saturation of 83%. This could be one of the factors for the development of RV diastolic dysfunction, a prolonged ischemia other than an older age prior to surgery (9 years old). Patient 7 had a good oxygen saturation of 89% but age prior to surgery was his risk factor (9 years old).

Among those who developed RV diastolic dysfunction, there were two patients (Patient 6 and 9) who had restrictive physiology on doppler study. They have diastolic pulmonary artery forward flow on echocardiogram post-operatively. Both patients were 16 years of age. The mechanism of the diastolic pulmonary artery forward flow is speculated to occur when the RV pressure equals or exceeds the diastolic PA pressure. The right ventricle appeared to be fairly non-compliant or non-distensible in these patients probably because of the chronic myocardial hypertrophy or pressure overload. These decreased RV compliance and increased RV diastolic volume (after surgery) created diastolic forward flow.[10]

Conclusion

We therefore conclude that right ventricular diastolic dysfunction can develop in early post-operative period after TOF correction. The RV diastolic indices such as Tricuspid E wave velocity, Tricuspid E/A ratio, deceleration time, isovolumic relaxation time and Superior Vena Cavae Velocities are good parameters to determine the RV diastolic dysfunction. Age prior to surgery, ECG findings, and O2 saturation are good predictors of outcome of TOF correction. Surgical technique and duration of bypass time did not show significant correlation with our results in patients who had RV diastolic dysfunction. Almost all patients who developed right ventricular dysfunction have elevated central venous pressure, prolonged ICU stay and prolonged inotropic supports.

Recommendation

We recommend to further study on the preoperative echocardiographic assessment of RV diastolic function in all tetralogy of fallot and correlate with the post-operative echocardiographic findings.

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Congenital Cystic Malformations of the lung: A 30-year Review of Cases at the Philippine Heart Center (1975-2005)

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Background --- Congenital cystic lung malformations are uncommon but potentially life-threatening anomalies of infants and children.

Methods and Results --- A 30-year retrospective review of 20 patients with congenital cystic lung malformation was done. Histopathologic examination revealed the following: congenital cystic adenomatoid malformation (n= 9) accounted for 45%, congenital lobar emphysema (n= 5) 25%, bronchogenic cyst (n=3) 15% and pulmonary sequestration (n= 3) 15%. Twelve patients were under 1 year of age 5 of whom where neonates. There was no sex preponderance in all four diseases. Most common symptoms were dyspnea, acute respiratory tract infection, fever and cyanosis while tachypnea, intercostals retractions, decreased breath sounds and tachycardia were the most common physical findings. The duration of illness ranged from 2 days to 6 years. Dyspnea was noted in 80% of patients. Lobectomy was done in 70% of patients. Immediate post-operative complication in decreasing frequency were pneumonia, atelectasis, pneumothorax, septicemia, bronchopleural fistula and bleeding were noted in 80% of patients. There was no significant correlation between survival and the number of lobes resected. Poor post-operative outcome was not associated with the types of congenital lung malformation. There was also no significant correlation between presence of post-operative complications and poor outcome. ***Phil Heart Center J 2007; 13(2):130-134.***

Key Words: Congenital Cystic Lung Malformation ■ Congenital Cystic Adenomatoid Malformation (CCAM) ■ Bronchogenic Cysts ■ Pulmonary Sequestration ■ Congenital Lobar Emphysema, Review

Congenital cystic malformations of the lung are rare but fascinating anomalies of lung develop ment that arise from an error in the embryologic development. The lung normally develops from one kind of tissue that becomes the airways arising originally from the upper digestive system, and another kind of tissue that becomes the blood vessels and connective tissue of the lung. These two kinds of tissue must "communicate" clearly with each other to form a normal lung. Errors in communication can lead to one or more of these malformations. They vary considerably in presentation and severity. Four distinct categories of congenital cystic lung malformation can be defined: cystic adenomatoid malformation, lobar emphysema, pulmonary sequestration, and bronchogenic cyst. All may present as abnormal cystic areas within the lung antenatally, in early life or later, although there are differences in clinical course and outcome.

Today, congenital cystic lung malformations are well- known diseases in infants and children because of an obvious increase in number of referrals and admissions in our institution. It is therefore the intent of this study to review patients admitted for congenital cystic lung malformation and to retrospectively evaluate our 30 years of clinical experience with 20 patients. We did a thirty-year retrospective review of medical records of patients diagnosed with congenital cystic lung malformation based on the histopathologic confirmation admitted at Philippine Heart Center between1975-2005. Age at the time of onset of symptoms, age at the time of diagnosis, age at time of treatment, clinical presentation, diagnostic methods, treatment and histopathologic findings were recorded.

Methods

The type of congenital cystic lung malformations and sex distribution are summarized in Table 1. There were nine cases of congenital cystic adenomatoid malformation (CCAM), five cases of congenital lobar emphysema (CLE), three bronchogenic cyst (BC) cases and three cases of pulmonary sequestration (PS). Three out of five cases of CLE were in females. On the other hand, two out of three cases of BC were in males, while in PS, two out of 3 cases were in females.

Results

The type of congenital cystic lung malformations and sex distribution are summarized in Table 1. There were nine cases of congenital cystic adenomatoid malformation (CCAM), five cases of congenital lobar emphysema

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(CLE), three bronchogenic cyst (BC) cases and three cases of pulmonary sequestration (PS). Three out of five cases of CLE were in females. On the other hand, two out of three cases of BC were in males, while in PS, two out of 3 cases were in females.

Table 1. Histologic Types and Sex Distribution of Patients with Congenital Cystic Lung Malformation, PHC, 1975-2005

Disease	Sex		Total
	Male	*Female*	
CCAM	5	4	9
CLE	2	3	5
BC	2	1	3
PS	1	2	3

CCAM- Congenital Cystic Adenomatoid Malformation CLE- Congenital Lobar Emphysema
BC- Bronchogenic Cyst PS- Pulmonary Sequestration

Table 2 summarized the symptoms on presentation of patients with congenital cystic lung malformations. Most common symptoms in decreasing frequency were dyspnea, acute respiratory tract infection, recurrent pneumonia and cyanosis.

Table 2. Presenting Symptoms on Admission of Patients with Congenital Cystic Lung Malformations

Signs	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total
Dyspnea	9	5	1	1	16
AURI	2	1	3	3	9
Fever	1	0	2	0	3
Cyanosis	4	2	0	0	6
Recurrent Pneumonia	0	1	3	3	7
Hemoptysis	0	0	1	1	2

CCAM- Congenital Cystic Adenomatoid Malformation CLE- Congenital Lobar Emphysema
BC- Bronchogenic Cyst PS- Pulmonary Sequestration

Table 3 summarized the signs noted on physical examination. The most common were tachypnea, intercostals retractions, decreased breath sounds and tachycardia.

Table 3. Presenting Signs on Admission of Patients with Congenital Cystic Lung Malformations

Signs	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total
Tachypnea	9	5	1	0	15
Retractions	9	5	1	0	15
Decreased Breath Sounds	5	5	3	3	16
Tachycardia	6	5	2	1	14
Rales	1	1	1	0	3
Alar Flaring	4	3	0	0	7

CCAM- Congenital Cystic Adenomatoid Malformation CLE- Congenital Lobar Emphysema
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The pre-operative diagnosis of congenital cystic lung malformation on chest x-ray showed cystic lucencies in all types and mediastinal shift to opposite side both in patients with CCAM and CLE (Table 4).

Table 4. Chest Radiographic Findings of Patients with Congenital Cystic Lung Malformation

Radiographic Findings	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total
Cystic Lucencies	9	5	3	3	20
Mediastinal Shift to Opposite Side	9	5	0	0	14
Presence of Infiltrates	3	0	1	1	5
Anterior herniation to the Opposite Lung	6	1	0	0	7
Emphysema of the Lobes involved	3	4	0	0	5
Atelectasis of the Adjacent Lobes	5	2	0	0	7

CCAM- Congenital Cystic Adenomatoid Malformation CLE- Congenital Lobar Emphysema
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The left upper lobe was commonly involved in CLE, while CCAM have multiple lobar involvements. The right lower lobe was involved in 2 out of 3 patients with BC. The left lower lobe was involved in all 3 patients with PS. (Table 5)

Table 5. Lobar Distribution of Congenital Cystic Lung Malformation

Lobe/s Involved	CCAM N=9	CLE N=5	BC N=3	PS N=3
Right Upper Lobe (RUL)	2	0	0	0
Right Middle Lobe (RML)	2	0	0	0
Right Lower Lobe (RLL)	3	0	2	0
Left Upper Lobe (LUL)	3	4	0	0
Left Lower Lobe (LLL)	1	0	1	3
RML + RLL	0	1	0	0
RUL + RLL + LLL	1	0	0	0

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Surgical resection was done in all patients consisting of lobectomy and segmentectomy, of which lobectomy was the most common (Table 6).

Table 6. Type of Surgical Resection Done on Patients with Congenital Cystic Lung Malformations

Type of Surgery	CCAM N=9	CLE N=5	BC N=3	PS N=3
Lobectomy	9	3	1	1
Segmentectomy	0	2	2	2

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Out of 20 patients who underwent surgical resection, only one died 9 days after surgery because of respiratory failure involving 2 lobes. Poor post- operative outcome was not associated with the type of congenital cystic lung malformation (Table 7).

Table 7. Post-operative Outcomes of Patients with Congenital Cystic Lung Malformations

Type of Surgery	CCAM N=9	CLE N=5	BC N=3	PS N=3
Alive	8	3	3	3
Dead	1	0	0	0

CCAM- Congenital Cystic Adenomatoid Malformation CLE- Congenital Lobar Emphysema
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Table 8 shows the outcomes according to the number of lobes resected.

Table 8. Surgical Outcomes of Patients with Congenital Cystic Malformation According to Number of Lobes Resected

Number of Lobes	Alive n-19	Dead n-1
One	17	1
Two	2	0

Post-operative complications were noted in the majority of patients with pneumonia as the most common cause in all the congenital cystic lung malformations (Table 9)

Table 9. Post-operative Complications of Patients with Congenital Cystic Lung Malformation

Complications	CCAM N=9	CLE N=5	BC N=3	PS N=3	Total N=20
With complications	8	4	2	2	16
Septicemia	2	0	0	0	2
Pneumonia	5	3	1	2	11
Hypoxemia	6	2	0	0	8
Pneumothorax	4	1	1	2	8
Atelectasis	4	2	0	2	8
Bronchopleural Fistula	2	0	0	0	2
Bleeding	1	0	0	0	1

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The mean age of onset of symptoms, age of diagnosis, and age of intervention are summarized in table 10. All patients with CCAM were less than 1 year of age at the time of onset of symptoms and diagnosis. 80% of patients with CLE were less than 1 year of age at the time of onset of symptoms. However, 40% were diagnosed more than 1 year of age (7 and 14 y/o). 55% presents during the first week of life, most with respiratory distress (CCAM).

Table 10. Mean Age of Onset, Diagnosis and Treatment of Patients with Congenital Cystic Lung Malformations

Disease	Mean Age (days) ± SD		
	Onset of Symptoms	Time of Diagnosis	Time of Surgery
CCAM	35.22 ±55.65	54.33±55.38	68.8 ± 61.0
CLE	450.8±972.34	15.81±2245.91	1141.2 ± 2223.13
BC	2798.33±1281.84	2555.2±1672.64	2918.3 ± 1277.5
PS	516.66±917.08	2798.33±1381.83	2555 ± 1672.6

CCAM- Congenital Cystic Adenomatoid Malformation CLE- Congenital Lobar Emphysema
BC- Bronchogenic Cyst PS- Pulmonary Sequestration

Discussion

During the development of the embryo, separation of the trachea and esophagus occurs, and migration of the early lung bud takes place. The lung tissue shows further differentiation thereafter into airway epithelium and alveolar cells. In this developmental stage, numerous abnormalities can take place. Bronchopulmonary foregut malformations are combinations of these forms of disordered lung growth such as dysplasia, hypoplasia, or hyperplasia involving one or more structural component of the lung.[13] Any abnormality involving the structural component of the lung would give rise to the different types of congenital cystic lung malformation.

Congenital cystic lung malformation consists of pulmonary sequestration (PS), cystic adenomatoid malformation (CAM). Congenital lobar emphysema (CLE), and bronchogenic cyst (BC).[3,6,7,8,9,10,11,13] All may present as abnormal cystic areas within the lung antenatally , in early life or later, although there are differences in clinical course and outcome. A wide variety of symptoms can lead to the differential diagnosis of congenital cystic malformation of the lung, including respiratory distress, cough, stridor, recurrent pulmonary infections, hemoptysis, dysphagia, pneumothorax, or life-threatening event with respiratory failure. Common presenting symptoms are respiratory distress in early life as was found in CCAM and CLE. This may be due to the pressure effects caused by the lung cyst compressing the surrounding mediastinal structure. The same findings were also seen in this study. Recurrent pulmonary infections and persistent radiographic abnormalities in older children were noted in intralobar PS and BC as was found in this study. It is similar to the cases reported by Gustafson et al.[12]

CCAM may present at birth, or most commonly, in the neonatal period. Only 10% of cases present after the

first year of life. Rarely, presentation may be delayed until later childhood when episodes of recurrent infection, continued slow growth or serendipitous discovery reveal the lesion.

CCAM has no clear sexual or racial predilection. The lesion is unilateral as was found in eight out of nine patients in this study. Occasionally multilobar involvement has been reported which was found in one of the patient in this study who eventually succumb to death because of respiratory failure. Right and left sided involvements occur with equal frequency. In a review of literature, the oldest patient reported was 14 years old at the time of diagnosis. Three patients, aged 35, 24, 7 years, are reported. The 35 and 7 years old patients presented with episodes of recurrent infection while a 24 year old patient, a preoperative chest radiograph was done prior to surgical repair of a facial fracture.[3] There is a debate about the advisability of segmental resection versus lobectomy for CCAM. Segmental resection has been promoted as a lung tissue preserving surgical management of CCAM. However segmental resection has a higher complication rate and repeat surgery for lobectomy due to incomplete removal of abnormal lung tissue is not infrequently required. In this study, a right lower lobe lobectomy was done in one of the patient with involvement of three lobes for the reason that involvement of the right upper lobe and left lower lobe were just minimal. However, after nine days, patient died because of respiratory failure. Lobectomy has been shown to be a more safe and effective procedure. This was done in all patients with CCAM in this study. If necessary, resection of more than one involved lobe is possible, although compromised long-term physical activity can be expected.

CLE is mainly a disease of infancy and always involves one lobe, with rates of occurrence as follows: LUL- 41%, RML- 34%, and RUL- 21%. The left upper lobe distribution in our cases was similar to those in the literature and previous studies.[1, 2] However patient can show multilobar involvement but is rare as was found in one patient in this study. Rarely, CLE may be discovered as an incidental finding in an asymptomatic older child or an adult. The traditional treatment of CLE is lobectomy of the involved lobe or lobes. This was done in three patients with CLE in this study. Segmentectomy was done in two patients. A few patients with exhibited mild symptoms were reported as treated conservatively with medical treatment.

PS is an uncommon congenital anomaly consisting of a mass of dysplastic lung tissue that has no normal connection with the tracheobronchial tree and the pulmonary arteries. The anomalous arterial blood supply usually comes from the abdominal and thoracic aorta with equal frequency. Sequestration are found in two forms: (1) intralobar sequestration, in which the sequestered part of lung lies within normal pulmonary visceral pleura; and (2) extralobar sequestration, in which the abnormal segment of lung is completely separate and enclosed in its own pleural investment. In our cases, intralobar sequestration was found. The usual radiographic appearance is that of a solid or cystic mass in the base of one lung. Almost invariably, symptoms are related to the presence of an airway communication, as demonstrated in 23 out of 32 patients from the review of files of three Army Medical Centers, the largest single series in the literature.[4] No patient with an aerated sequestrum was without marked symptoms. Conversely, few patients with a non-aerated sequestrum exhibited noticeable symptoms. Recurrent fever, chills, and purulent sputum were far the most commons. Less common, but related to chronic infection, are hemoptysis and massive intrapleural hemorrhage. Any indolent process seen on chest roentgenogram should raise suspicion of sequestration, especially if the posterior basilar region is involved. The findings of posterior basilar involvement were also similar in this study. Aortography may be helpful, especially in the patient with an asymptomatic mass noted on routine chest roentgenogram. If the sequestrum is non-aerated and aortography is pathognomonic, then consideration can be given to a non-operative approach. If at any time the patient becomes symptomatic, resection can be done as was done in this study. Simple excision is always adequate for extralobar sequestration. Lobectomy is usually necessary for intralobar sequestration which was done in one of the patient in this study. Occasionally, however, basilar segmentectomy can be performed. Two patients underwent segmentectomy in this study.

BC develop from an abnormal budding of the ventral foregut between the 26th and 40th week of gestation. As such, they are often more appropriately termed foregut duplication cysts. The frequency of BC is unknown presumably because most patients are asymptomatic. Though usually an incidental finding, morbidity from BC has been reported from the cyst becoming secondarily infected or from post-obstructive pneumonia. Dysphagia and dyspnea have resulted from compression of a large cyst on the esophagus and airways. Cases have been reported of cyst rupture and hemorrhage within the cyst. The frequency in different races is unknown. Frequency in each sex is also unknown. In this study, male: female ratio was 2:1. Large cysts may present in the pediatric population because of compression of the esophagus or trachea or because of infection as was seen in this study manifested as pleural effusion and pneumonia. In adults, the cysts typically present as an incidental mass in either the mediastinum or the lung. BC is located most commonly in the mediastinum (85%). Common locations include precarinal, paratracheal, and retrocardiac sites. Intrapulmonary BC is less common (15%) however this was found in this study. Chest radiograph is usually adequate

is usually adequate for detecting larger mediastinal or lung masses; however, it is limited in differentiating solid from fluid. This typically shows a sharply demarcated spherical mass of variable size, most commonly located in the middle mediastinum around the carina. When the cysts is infected or contains secretions, it may appear as a solid tumor or may demonstrate an air fluid level as found in this series. CT findings are characteristic when the lesion demonstrates water density. If the lesion demonstrates soft tissue density, differentiating the cysts from lymph nodes or other solid lesions is difficult. MRI findings are usually diagnostic for mediastinal cysts. In this study, a chest radiograph was done to support preoperative diagnosis and was confirmed by histologic findings.

In summary, we presented 20 cases of congenital cystic lung malformation and compared to the literature and previous studies. Findings in 20 cases showed CCAM as the most common, followed by CLE, BC and PS. In patients with CCAM and CLE, cystic lesions were discovered by respiratory distress. Signs of infection was a core clinical feature in patients with BC and PS. As to the diagnostic modality, diagnosis of congenital cystic lung malformation was based initially on chest x-ray which serves as a starting point for diagnostic evaluation in this study. Two patients with CCAM, one with BC and one with CLE were diagnosed by CT scan. In all of the cases, pulmonary resection is indicated as soon as the diagnosis is made.

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Comparison of CPIS (clinical pulmonary infection score) and Clinical Criteria in the Diagnosis of Ventilator-associated Pneumonia in ICU Complex Patients

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Background --- Accurate data on the epidemiology of ventilator-associated pneumonia (VAP) are limited by the lack of standardized criteria for its diagnosis. The difficulties of diagnosis are mostly a results of the following factors: possibility of multiple other causes of systemic inflammatory reactions, pre-existing antibiotic usage in ICU patients and the absence of a standard test to detect and diagnose VAP. The accuracy of clinical criteria (infiltrates on the chest radiograph and 2 of the following: leukocytosis, fever, purulent secretions) for the diagnosis of pneumonia was reasonable with sensitivity of 69% and specificity of 75%. On the other hand, the Clinical Pulmonary Infection Score (CPIS), which combined the clinical signs recorded on the day of the clinical suspicion of VAP to the tracheal aspirate gram stain and culture and PaO2/Fio2 ratio, proved to achieve 72% sensitivity and 85% specificity. This study evaluated the validity of the CPIS and Clinical criteria in the diagnosis of VAP in ICU complex patients and determined the length of ICU stay and mortality rate of patients who had VAP.

Methods --- A prospective cohort study was conducted involving patients who had been under mechanical ventilation for more than 48 hours, suspected for VAP and admitted in the ICU complex of the Philippine Heart Center from July 2006 to January 2007. The criteria for diagnosis of VAP using the clinical criteria as well as the CPIS were applied to them. Patients were followed up for occurrence of death until discharge.

Results --- Forty patients admitted at ICU complex were enrolled. The mean age of the subjects was 59.6 + 14.8 years. Length of ICU stay was 19.2 + 14.5 days with mean duration of mechanical ventilation of 13.6 + 12.3 days. Sensitivity showed 35.3% and 78.3% on the 1st and 3rd day of referral respectively. Specificity revealed 95.7% and 81.3% on the 1st and 3rd day of referral respectively. Five patients (13%) died, all of them were females. The causes of death were arrhythmia (3 patients) and septic shock (2 patients).

Conclusion --- This study would still recommend the use of the clinical criteria over CPIS in the diagnosis of VAP. However, VAP continues to be an important challenge to the critical care physician and it is difficult to diagnose accurately, and a high index of suspicion is required. ***Phil Heart Center J 2007;13(2):135-138.***

Key Words: Ventilator-associated Pneumonia ■ diagnostic criteria ■ validation study ■ Clinical Pulmonary Infection Score

Ventilator associated pneumonia (VAP) is an important form of hospital acquired pneumonia (HAP), specifically developing in a mechanically ventilated patient more than 48 hours after tracheal intubation.[1] Despite major advances in techniques for the management of VAP and the routing use of effective procedures to disinfect respiratory equipment, VAP continues to complicate the course of 8 to 28% of the patients receiving mechanical ventilation.[2] Pulmonary complications are common after surgical procedures, accounting for nearly one of every four deaths that occur in the first post-operative week. In the intensive care unit, pneumonia accounts for 28 to 47% of all nosocomial infections. The single greatest risk factor for VAP is related to the duration of mechanical ventilation. The risk peaks at day 5 on the ventilator, plateaus after day 15, and then declines significantly, with the result that VAP is uncommon in patients on long term mechanical ventilation.[8] The risk of VAP is highest early in the course of hospital stay, and is estimated to be three percent per day during the first five days of ventilation, two percent per day during days 5 to 10 of ventilation, and one percent per day after this.[3] Accurate data on the epidemiology of VAP are limited by the lack of standardized criteria for its diagnosis. The absence of a gold standard continues to fuel controversy about the adequacy and relevance studies in this field.[2] In 1991, Pugin and colleagues proposed to combine the clinical signs recorded on the day of the clinical suspicion of VAP to the tracheal aspirate gram stain and culture and PaO2/FiO2 ratio into a CPIS as a diagnostic tool of pneumonia. The score varied from 0 to 12 points with a CPIS of more than six being associated with a high likelihood of pneumonia.[4] (Table 1). The score proved to

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achieve 72% sensitivity and 85% specificity.[9] These results do not indicate a superiority of CPIS to Johansson's criteria, and given that the CPIS is more time consuming to calculate, there is no evidence to recommend this score in routine clinical practice. The accuracy of clinical criteria (infiltrates on the chest radiograph and 2 of the following: leukocytosis, fever, purulent secretions) for the diagnosis of pneumonia was reasonable with sensitivity of 69% and specificity of 75%.5 (Table 2). Thus, available evidence indicates that clinical diagnosis of VAP is associated with around 30-35% false-negative and 20-25% false-positive results. The high rate of false-positive results is probably due to alternative diagnoses that may cause pulmonary infiltrates mimicking VAP such as alveolar hemorrhage, atelectasis, pulmonary infarction and the fibroproliferative phase of acute respiratory distress syndrome (ARDS). False-negative results may result from initial phases of pneumonia not detected on chest radiograph.[9] Noninvasive (TBA) and invasive (PSB, BAL, protected BAL) sampling techniques were not superior to these clinical criteria.[5] Recently, several studies have suggested that the use of quantitative cultures of endotracheal aspirate may have similar diagnostic value compared with invasive techniques, such as protected specimen brush (PSB) and bronchoalveolar lavage (BAL). The advantage of quantitative endotracheal aspirates is its reliance on the simplicity and cost effectiveness of the method, as well as the lack of side effects. In fact, it has been suggested that using lavage in mechanically ventilated patients with pneumonia can lead to systemic and sepsis-like effects. Furthermore, deterioration of blood gas exchange has been described.[10] The difficulties of diagnosis are mostly a results of the following factors: possibility of multiple other causes of systemic inflammatory reactions, pre-existing antibiotic usage in ICU patients and the absence of a standard test to detect and diagnose VAP.[6] This study aimed to validate CPIS and clinical criteria in the diagnosis of VAP in ICU complex (RR, SICU, MICU, CCU) patients. Specifically, it aimed to evaluate the sensitivity and specificity of clinical criteria and CPIS on patients suspected of VAP as well as to determine the length of ICU stay and mortality rate of patients who had VAP.

Table 1. CPIS (clinical pulmonary infection score)

Criteria		Points
Temperature (°C)		
	>or equal to 36.5 and < or equal to 38.4	0
	>or equal to 38.5 and < or equal to 38.9	1
	>or equal to 39 and < or equal to 36	2
Blood leukocytes, mm³		
	>or equal to 4,000 and < or equal to 11,000	0
	< 4,000 or > 11,000	1
	< 4,000 or > 11,000 + band forms> equal to 50%	2
Tracheal secretions		
	Absence of tracheal secretions	0
	Presence of non purulent tracheal secretions	1
	Presence of purulent tracheal secretions	2
Oxygenation:PaO2/FIO2, mmHg		
	>240 or ARDS (ARDS defined as PaO2/FIO2 ≤ 200), pulmonary arterial wedge pressure ≤ or equal to 18 mmHg and acute bilateral infiltrates)	0
	≤ 240 and no ARDS	2
Pulmonary radiography		
	No infiltrate	0
	Diffuse (or patchy) infiltrate	1
	Localized infiltrate	2
Progression of pulmonary infiltrate		
	No radiographic progression	0
	Radiographic progression (after CHF and ARDS excluded)	2
Culture of tracheal aspirate		
	Negative	0
	Positive	2

NOTE: score of > 6 is considered suggestive of pneumonia. 7

Table 2. Clinical Criteria

1.) New infiltrate on chest radiograph (or radiographically confirmed worsening of pre-existing infiltrate) and
2.) At least 2 of the following:
- Leukocytosis (>12,000/mm3)
- Leucopenia (< 4,000/mm3)
- Fever (>38 0 C)
- Hypothermia (< 35 oC)
- Purulent tracheal secretions

Methods

This was a prospective study of patients who were admitted in ICU complex (RR, SICU, MICU, CCU) of Philippine Heart Center between July 2006 to January 2007. All patients had been under mechanical ventilator for more than 48 hrs and were suspected of having contracted VAP and were subsequently referred to pulmonary service. Patients with immunosuppression (organ transplantation, HIV infection and AIDS, severe neutropenia < 1.0 x 10 9/l, steroid therapy equivalent to prednisone in a dose of >20 mg/day) were excluded. Data gathering includes age, sex, type of surgical procedure, duration of mechanical ventilation, length of stay and co-morbidities were recorded. Each patient was then scored by clinical criteria and CPIS on the day of the referral as baseline and was repeated 72 hours after for reassessment. Clinical and laboratory evaluation. All clinical (body temperature and endotracheal secretion) and laboratory (CBC, Chest radiograph, arterial blood gas and microbiological assay of endotracheal secretion) were recorded. Chest radiograph were also reviewed by one of the investigators and an independent radiologist. The endotracheal aspirate (ETA) was collected using French size 60 cm suction catheter with mucus trap and introduced through the endotracheal tube for approximately 24 cm. Gentle aspiration was then performed without instilling saline and the catheter was withdrawn from

the endotracheal tube. Sample was immediately taken to the laboratory for processing. The result of the gram stain was obtained within 24 hours and quantitative culture was obtained within the following 48 to 72 hours.

Microbiological processing

Sample was then inoculated into different culture media (blood agar plate and MacConkey by Biomerauex). The plates were incubated within 18-24 hours at 370°C. After initial characteristics of the isolates by colony morphology and gram stain, species identification and susceptibility testing were done using the disc diffusion method.

Results

Forty patients admitted at ICU complex (RR, SICU, MICU, and CCU) of the Philippine Heart Center were enrolled in this study from July 2006 to January 2007. Table 1 shows that the mean age was 59.6 years. The average number of days of referral and ICU stay were 7.0 days and 19.2 days, respectively. More than half of the patients were male (58%). Five patients (13%) died, all of them were females. The causes of death were arrhythmia (3 patients) and septic shock (2 patients).

Table 3. Clinical Characteristics of Patients Included in the Study

Characteristics	N(%) or mean (SD)
Age, years	59.6 ± 14.8
Day(s) of referral	7.0 ± 8.7
Length of ICU stay (days)	19.2 ± 14.5
Duration of Mechanical Ventilation, days	13.6 ± 12.3
Gender	
Male	23 (57.5)
Female	17 (42.5)
Mortality	
Expired	5 (13.2)
Recovered	33 (86.8)

*Data are presented as mean ± SD or No. (%) unless otherwise indicated

For the first-day diagnosis, the sensitivity of clinical pulmonary infection score method was 35.3%. That means that 35.3% of those with ventilator associated pneumonia, as diagnosed by clinical criteria, were detected using clinical pulmonary infection score. On the 3rd day diagnosis, the sensitivity went up to 78.3%. Its specificity on the 1st and 3rd day diagnosis was 95.7% and 81.3%, respectively. Thus, on the 1st and 3rd day diagnosis, 95.7% and 81.3%, respectively, of those without VAP were identified as such using CPIS. Positive predictive values were the same for the 1st and 3rd day diagnosis. Among those identified by CPIS as positive, the likelihood that they really have the disease was 85.7%. On the other hand, the negative predictive values were 66.7% and 72.2% for the 1st and 3rd day, respectively. Those with negative CPIS result, the likelihood that they do not have VAP were 66.7% and 72.2% during the 1st and 3rd day, respectively. ROC curve had area under the curve of 0.655 and 0.798 on the 1st and 3rd day diagnosis, respectively. This showed that the VAP determination of CPIS is better in the 3rd day diagnosis than the 1st day. One patient was transferred to another hospital, thus, a decrease to 39 patients on the 3rd day diagnosis from 40 patients on the 1st day diagnosis. (Table 4 and 5)

Table 4. Sensitivity and Specificity of CPIS in Detecting VAP on Day One

CPIS	Clinical Criteria		Total
	Positive	Negative	
Positive	6	1	7
Negative	11	22	33
Total	17	23	40

Sensitivity 35.3, Specificity 95.7

Positive Predictive Value. 85.7, Negative Predictive Value 66.7 AUC 0.655

Table 5. Sensitivity and Specificity of CPIS in Detecting VAP on Day Three

CPIS	Clinical Criteria		Total
	Positive	Negative	
Positive	19	3	21
Negative	5	13	18
Total	23	16	39

Sensitivity 78.3, Specificity 81.3

Positive Predictive Value. 85.7, Negative Predictive Value 72.2 AUC 0.798

Discussion

VAP (ventilator associated pneumonia) is a common and serious infection in the Intensive Care Unit patients, and is often difficult to diagnose. The difficulties of diagnosis are mostly a result of the following factors: the possibility of multiple other causes of systemic inflammatory reactions in these patients, pre-existing antibiotic usage in ICU patients and the absence of a standard test to detect and diagnose VAP.[13] There is no doubt that the best diagnostic strategy in patients with suspected ventilator associated pneumonia (VAP) remains contentious. The central problem is the difficulty in striking a balance between avoiding a delay in starting antibiotics when they are required and reducing inappropriate use of broad-spectrum antibiotics.[11] In this study, we have evaluated the clinical diagnosis of ventilator associated pneumonia, assessed on either the routine clinical criteria on the first day and on the 3rd of referral and the CPIS (clinical pulmonary infection score) and the contribution of the respiratory specimens gram stains result to the diagnosis of VAP, taking endotracheal aspirate culture as the reference test.[4] The mortality rate of ventilator-associated pneumonia (VAP) was 13% in this study, which is

secondary to cardiac arrhythmia and septic shock. However, the mortality rate has been reported to be 30%.[12] In the study by Nieto et al, the mortality of ventilator associate pneumonia (VAP) ranges from 20-70%. The sensitivity and specificity of clinical criteria in diagnosing ventilator-associated pneumonia were noted to be 35.3%, 78.3% and 95.7%, 81.3% on the first and third day of referral respectively. This showed a comparable result in terms in the diagnosis of VAP especially on the third day of diagnosis. In the study of Fabregas et al, this result was reasonable with sensitivity of 69% and specificity of 75%.[5] In another study by Fagon et al, found that clinical predictors about the presence or absence of definite and probable VAP were accurate in 62% and 84% of VAP patients respectively.[8] Disappointingly the use of scoring systems, such as the clinical pulmonary infection score, seems to add little to diagnostic acccuracy.[14] The positive predictive values were 85.7% and 85.7% on the first and third day of referral respectively. However, In the study by Fagon et al, this was contradictory because the clinical diagnosis of VAP is associated with around 20-25% false positive results.[8] Many investigators have claimed that the incidence of VAP may be overestimated when clinical criteria alone are used. In a recent postmortem study the combination of infiltrates on the chest radiographs and at least 2 of 3 clinical criteria (fever, leukocytosis, and purulent secretions) had a sensitivity of 69% and a specificity of 75% for diagnosing VAP. Moreover, there have been studies that demonstrated a similar diagnostic yield with invasive and noninvasive techniques and similar patient outcomes in terms of mortality, ICU stay, and duration of mechanical ventilation. However, the VAP rates in the various studies cannot be compared because of differences in survey methods, lack of uniform diagnosis criteria, different length of ICU stay, and the lack of an adequate system to compare illness severity and invasive diagnostic or therapeutic procedures.[15] Prognostic factors for a poor outcome from nosocomial pneumonia include inappropriate antibiotic treatment.[10] This study would recommend that clinical criteria could be used as a tool in the diagnosis of ventilator associated pneumonia and reassess on the third day if antibiotic could be withhold. CPIS has a lot of variable, which include endotracheal aspirate and arterial blood gas that could further add expenses on the part of the patient. However, endotracheal aspirate is an important part in the diagnosis of ventilator-associated pneumonia which is very important in the diagnosis as well as therapeutic option in the management of ventilator-associated pneumonia. And because clinical suspicion alone is overly sensitive and lack of specificity, further diagnostic tests are required for optimal management. Ideally, microbiological data should be obtained before the start of antibiotic therapy.[14] The main drawbacks of the CPIS are that all of its elements are weighted equally (for example, the presence of an infiltrate is given the same weight as a WBC count of 11,000/mm3, even though it is substantially more suggestive of pneumonia) and that assessment of chest x-rays and sputum production is necessarily subjective, meaning that an equivocal CPIS could lead to an inappropriate treatment decision. VAP continues to be an important challenge to the critical care physician and is the most common nosocomial acquired infection among patients with acute respiratory failure. It is difficult to diagnose accurately, and a high index of suspicion is required.[14]

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A Prospective Cohort Study on the Effects of Pulmonary Rehabilitation on Non-COPD Lung Disease

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Background --- Pulmonary rehabilitation is described as a multidisciplinary program of care that is individually tailored and designed to optimize physical and social performance and autonomy. The effects of pulmonary rehabilitation on COPD patients are well documented. However studies are limited on the role of pulmonary rehabilitation in patients with chronic lung diseases other than COPD. This study therefore aimed to determine the effects of the program on patients with non-COPD lung disease.

Methods --- This was a prospective cohort study involving non-COPD patients as well as COPD patients (which serves as comparator group) enrolled in the pulmonary rehabilitation program of the Philippine Heart Center. Six minute walk test as well as symptom-limited exercise testing was done at baseline and at the end of the eight week program.

Results --- There were 48 patients, predominantly female (31 females, 17 males), with a mean age of 62.3 years, with various pulmonary problems (kyphoscoliosis, asthma; bronchiectasis, and sequelae of tuberculosis), who were recruited in the pulmonary rehabilitation program. The mean FEV1 was 1.1 liters and the mean FVC was 1.7 liters. Ten of these patients were on oxygen therapy, using a mean of 2 lpm. After an 8 week rehabilitation program, results showed an improvement in exercise tolerance in the study population. An increase in the 6 minute walk distance covered and workload tolerated in the incremental symptom limited exercise testing on a treadmill were observed. A greater improvement among non-COPD lung patients was also noted when compared with the COPD group in the following parameters: the 6 minute walk distance test (p=0.000), the incremental symptom limited exercise testing (p=0.007) and the perceived breathlessness (p=0.015) and muscle fatigue (p=0.005) using the Modified Borg's scale in the post –rehabilitation 6 minute walk distance test.

Conclusion --- In conclusion, this study showed a significant improvement in exercise capacity, shortness of breath and muscle fatigue, in patients with pulmonary diseases other than COPD after undergoing pulmonary rehabilitation. Improvements demonstrated by these patients were observed to be significantly better than the COPD patients. Phil *Heart Center J 2007;13(2):139-143.*

Key Words: Pulmonary Rehabilitation ■ COPD ■ non-COPD ■ six-minute walk test ■ exercise testing ■ exercise training

Pulmonary rehabilitation is defined as an "evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decrease daily life activities. Integrated into the individualized treatment of the patient, pulmonary rehabilitation is designed to reduce symptoms, optimize functional status, increase participation, and reduce healthcare costs through stabilizing or reversing systemic manifestations of the disease.[1] The goal of pulmonary rehabilitation is to allow patients to work toward exploring the boundaries that ventilatory limitation places on them from physical, cognitive and emotional perspectives. Most published studies focus on pulmonary rehabilitation in chronic obstructive pulmonary disease (COPD) in comparison with asthma, cystic fibrosis, and pre- or post-lung transplantation. Pulmonary rehabilitation can offer much to patients with ventilatory limitation from other causes as it does in COPD.[2] In the study conducted by Foster and co-workers,[3] there was a significant improvement in the distance covered during the six minute walk test in both non-COPD patients and COPD patients. Non-COPD indications for pulmonary rehabilitation, include: asthma; chest wall disease ; cystic fibrosis; interstitial lung disease, including post ARDS pulmonary fibrosis; lung cancer; selected neuromuscular diseases; peri-operative states; post-polio syndrome; pre-lung and post-lung transplantation; pre-lung and post-lung volume reduction surgery. A prospective non-randomized open trial conducted over a 9 week period on patients with post tuberculosis by Ando 4 showed that there was an increase in the 6 minute walk distance after rehabilitation in both the post-tuberculosis group and COPD group by as much as 42m vs. 47m ($p<0.01$) respectively. In patient with

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idiopathic pulmonary fibrosis, the impairment of the quality of life areas, "physical health" and "level of independence" are important issues. Rehabilitation programs were found to enhance the quality of life of these patients.[5] The benefits achieved from rehabilitation programs extend beyond an increase in exercise ability. It includes a reduction of dyspnea and an improvement in health status. Comprehensive pulmonary rehabilitation is a standard of care in COPD patients. Similar benefits which include improvement in exercise capacity and shortness of breath can be observed in patients with chronic respiratory disease other COPD. This study therefore aimed to determine the effects and benefits of pulmonary rehabilitation on patients with non-COPD lung disease. Specifically, the study aimed to determine the effect of pulmonary rehabilitation on the distance covered during 6 minute walk test as well as the maximum workload tolerated during exercise testing. Also, the study compared the effects of pulmonary rehabilitation on non-COPD lung disease with COPD patients.

Methods

This is a prospective cohort study which included all non-COPD patients recruited in the pulmonary rehabilitation program of the Philippine Heart Center from January 1991 to December 2005. Entry criteria included the following: (a) Clinical diagnosis of non- COPD lung disease confirmed by history, physical examination, spirometry and chest roentgenogram; (b) stable condition for 2 weeks while receiving an acceptable medical regimen prior to entry, and (c) no unstable cardiac disease or other medical problem that would hinder a patient's participation in the program.

COPD patients enrolled in the pulmonary rehabilitation program the Philippine Heart Center were also included in the study for comparison. Entry criteria were as follows: (a) clinical diagnosis of COPD lung disease confirmed by history, physical examination, spirometry and chest roentgenogram; (b) stable condition for 2 weeks while receiving an acceptable medical regimen prior to entry; and (c) no unstable cardiac disease or other medical problem that would hinder a patient's participation in the program.

Baseline test

Each patient underwent pre-rehabilitation testing which included arterial blood gas analysis, six minute walk distance test and incremental symptom limited exercise testing using the treadmill.

Exercise Training

Rehabilitation sessions were done three times a week for 8 weeks. Upper body exercise training included unsupported upper arm exercises using the Qi-Gong (a Chinese arm exercise) done for 3 cycles and 6 repetitions and the upper body cycle ergometer. The lower body exercises included supervised walking on a treadmill with goal of walking continuously for 30 minutes and home walking exercises to the level similar to the treadmill. Perceived breathlessness and muscle fatigue were rated using Modified Borg's scale.[21]

Education

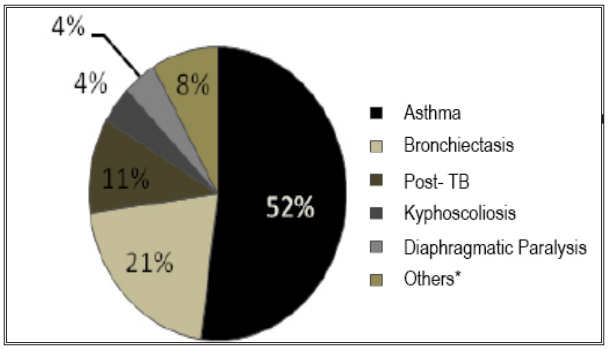
The education sessions consisted of lectures and discussions on the following topics: breathing strategies; normal lung function and pathophysiology of lung disease; proper use of medications, including oxygen; bronchial hygiene techniques; benefits of maintaining physical activities; energy conservation and work simplification techniques; nutrition; avoiding irritants and smoking cessation; indications for calling health provider; anxiety and panic control, including relaxation techniques and stress management and leisure, travel and sexuality; with the help of visual aids, slides, and videotapes. The assigned member of the rehabilitation staff (which includes the pulmonary physician, respiratory therapist, psychiatrist, and nutritionist) conducted the lectures for an hour twice a week.

Follow-up

At the end of the eight week program, each patient performed the six minute walk distance and the incremental symptom limited exercise testing utilizing identical protocols done at baseline. At the end of each test, perceived breathlessness and muscle fatigue were rated using the Modified Borg's scale.

Result

There were 48 non-COPD patients included in the study, 31 were females and 17 were males. Eighty two COPD patients were also recruited from the same pulmonary rehabilitation program to be a part of the investigation for comparison with the non-COPD population. Figure 1 shows the distribution of the diagnoses of the non-COPD patients.



**thymoma, post-cardiac surgery, pulmonary malignancy*

Figure 1. Distribution of Non-COPD paients according to lung pathology (n=48)

Table 1. Baseline Characteristics of included patients

Characteristics	Non-COPD Mean ± SD n=48	COPD Mean ± SD n=82	p-value
Age	62.3 ± 13.8	67.1 ± 10.3	***0.040***
Smoking(No. of pack years)	18.5 ± 28.4	38.8 ± 19.8	***0.004***
FEV1	56.3 ± 28.8	49.0 ± 23.7	0.159
FEV1 (liters)	1.1 ± 0.6	1.1 ± 0.6	0.893
FVC (liters)	1.7 ± 0.7	1.9 ± 0.7	0.198
FEV1/FVC	67.3 ± 18.3	58.6 ± 18.2	***0.020***

In comparison to the COPD group, the non-COPD group was relatively younger (p=0.040), had greater FEV1/FVC ratio (p=0.020), and with a smoking history that was shorter in duration (p=0.004). No significant difference was noted between the 2 groups except for the smoking history and the FEV1/FVC ratio (Table 1). There were 10 non-COPD who were on oxygen therapy utilizing a mean of 2lpm, while there were 9 COPD patients utilizing a mean of 1 lpm. No significant difference was noted between the 2 groups in terms of O^2 consumption. (p=0.307)

There was an increase in the workload tolerated using the incremental symptom limited exercise test using the treadmill in both the non-COPD and COPD group. Statistical analysis of the perceived breathlessness and fatigue did show significant change despite increase in the workload post- rehabilitation. This may be attributed to the improvement in exercise endurance (Table 2).

Table 2. Comparison between the pre- and post- rehabilitation treadmill exercise test parameters among the COPD and non-COPD groups

	Pre-rehabilitation Mean ± SD	Post-rehabilitation Mean ± SD	p-value
NON-COPD			
METS	5.0 ± 3.1	6.0 ± 3.6	*0.021*
Modified Borgs:			
Perceived breathlessness	3.3 ± 1.2	2.7 ± 1.3	0.061
Perceived muscle fatigue	2.7 ± 1.7	2.7 ± 1.4	1.00
COPD			
METS	3.3 ± 1.3	4.8 ± 2.0	*0.000*
Modified Borgs:			
Perceived breathlessness	2.9 ± 1.5	2.8 ± 1.3	0.835
Perceived Muscle Fatigue	2.6 ± 1.1	2.7 ± 1.3	0.950

A significant improvement in the six minute walk distance for both Non-COPD and COPD group post rehabilitation (p=0.00) was also noted, from a baseline of 293m to 578m post rehabilitation, and from a baseline of 294m to 372m post rehabilitation, respectively. (Figure 2). A significant improvement was also observed in perceived breathlessness using the Borg's scale in the non-COPD group (p= 0.039) which was not observed in the COPD group.

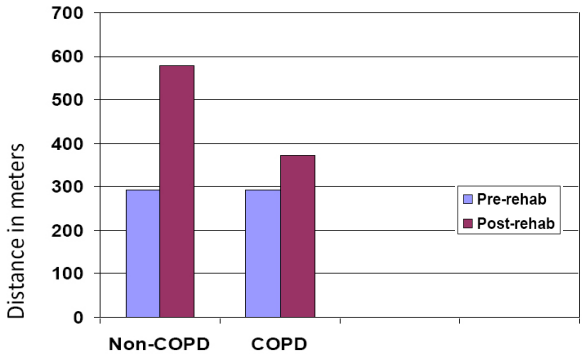


Figure 2. Six minute walk test results of the COPD and non-COPD groups, pre-rehabilitation and post-rehabilitation

Table 3. Comparison of the Incremental Symptom limited exercise testing on a treadmill between Non-COPD group and COPD group

	Non-COPD Mean ± SD	COPD Mean ± SD	p-value
Pre-Rehabilitation:			
METS	4.5 ± 3.2	3.3 ± 1.3	***0.007***
Modified Borg's:			
Perceived breathlessness	3.3 ± 1.3	3.0 ± 1.5	0.319
Perceived muscle fatigue	2.6 ± 1.6	2.8 ± 1.3	0.427
Post-rehabilitation:			
METS	6.2 ± 3.1	4.7 ± 2.1	***0.029***
Modified Borg's			
Perceived breathlessness	2.7 ± 1.3	2.9 ± 1.3	0.635
Perceived muscle fatigue	2.7 ± 1.4	2.7 ± 1.3	0.913

Comparing the two groups, the Non- COPD group performed better than the COPD group in the incremental symptom limited exercise test on a treadmill pre- rehabilitation and post rehabilitation.

On the other hand, the pre-rehabilitation 6 minute walk test was comparable between the 2 groups. But post rehabilitation, the non-COPD improved better than the COPD group in terms of distance covered (p=0.000), perceived breathlessness (p=0.015) and perceived muscle fatigue (p=0.005).

Discussion

Pulmonary rehabilitation is regarded as an important treatment modality in the management of patients with COPD. The beneficial effects of Pulmonary Rehabilitation had been well documented. It is widely accepted that Pulmonary Rehabilitation is beneficial in various non-COPD lung disorders, which includes cystic fibrosis, pulmonary fibrosis and restrictive thoracic disease. The American thoracic society cited the following non-COPD conditions as indication for pulmonary rehabilitation: asthma, chest wall diseases; cystic fibrosis interstitial lung disease, including post ARDS pulmonary fibrosis; lung cancer; selected neuromuscular diseases;

peri operative states; post-polio syndrome; pre-lung and post-lung transplantation; and pre-lung and post-lung volume reduction surgery. However, little evidence is available to indicate whether pulmonary rehabilitation is truly effective in the treatment of these lung disorders.[4]

The results of this study showed a significant difference between the non-COPD and COPD groups in terms of age and airflow obstruction. The non-COPD groups were younger, with less severe airflow obstruction. A significant improvement in the exercise performance post rehabilitation of the non-COPD patients in both exercise testing and the six-minute walk test. The results of the exercise tests of the non-COPD group improved significantly than the post rehabilitation results of the COPD patients. Foster and Thomas[3] compared the effect of pulmonary rehabilitation among COPD and non-COPD patients. He concluded that post rehabilitation, there was an improvement in exercise tolerance in non-COPD patients. The non-COPD group was very heterogeneous, which included neuromuscular disease, whose exercise tolerance could be limited by the disease itself. Crouch and MacIntyre[11] reported a similar comparison and also showed equivalent benefits of pulmonary rehabilitation among those patients. The study of Morihide Ando4 on patients with post tuberculosis lung disorder, were relatively homogeneous. Results also demonstrated the efficacy of pulmonary rehabilitation in non-COPD patients.

Our study, however, manifested more improvement in the non-COPD patients. The mean difference of the distanced walked pre- and post rehabilitation was 72.2 m. for the COPD group and 285.7 m. for the non-COPD group. A change of 54m had been suggested to be the minimum needed for clinical significance in a properly conducted 6MWT.[7] This could be ascribed to the fact that about 52% of the non-COPD subjects were diagnosed asthmatics and may not be severely impaired and are younger than the COPD group. On the other hand, COPD patients are limited primarily by ventilation limitation, physical deconditioning, brought about by their sedentary lifestyle, which affected their exercise capacity.

An improvement in exercise performance and a decrease in dyspnea using the Modified Borg's scale were demonstrated on post- rehabilitation testing. Of the various components of a pulmonary rehabilitation program, exercise training is the only one demonstrated in controlled clinical trials to enhance exercise endurance, dyspnea and quality of life.[1]

Improvements in exercise tolerance can be attributed to one or more of the following mechanisms: physiologic changes, improved efficiency, better coordination of neuromuscular activity and desensitization to dyspnea. [12] The patients in this study underwent maximum intensity exercises. This advocates training intensity targets near the maximally tolerated work rate for patients, which was about 80% of their maximum peak work rate. Patients with chronic lung disease are limited by their ability, and not by limits of muscle metabolism. It was postulated that, in order to be effective, a training program must involve exercise intensities associated with lactic acidosis. Patients who exercise at high intensities associated with lactic acidosis demonstrated greater evidence of a physiologic training effect.[13] The level of the lactic acidosis in our non-COPD patients was not determined. Further studies in the future may be recommended to provide data on this matter.

A patient's level of exertional dyspnea is markedly reduced after exercise training. Previously, the benefits gained were thought to be purely psychological. In patients with COPD, dyspnea correlates better with general health status than with the degree of airflow obstruction,[14] suggesting this symptom is complex and probably modulated by non-physiologic as well as physiologic factors. It has been shown that anxiety, depression, hysteria, degree of social support, grief, anger, frustration, fear, and past-life experiences may all affect perception.[15] KC Ong showed that patients have "desensitized" to their symptoms with frequent episodes of breathlessness while undergoing exercise training. A measure of dyspnea of fatigue (VAS or Borg) alongside is considered to increase the sensitivity of exercise measurements.

The limitations that could be cited in our study include heterogeneity of the non-COPD study population and non-rehabilitation of control patients could not be made for ethical reasons. The proponents of the study recommend a prospective randomized controlled study to be undertaken, and ideally, a study with large sample size is recommended for non-COPD, wherein each non-COPD disorder is well represented, to show statistical equivalence.

Conclusion

In conclusion, this study showed a significant improvement in exercise capacity using the incremental symptom limited exercise tolerance test and six minute walk test as outcome measure in patients with pulmonary diseases other than COPD after undergoing pulmonary rehabilitation. Improvements demonstrated by the Non-COPD lung disease patients were observed to better than the COPD patients.

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Pre-flight Testing of Children and Adolescent with Asthma

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Background --- Commercial aircraft cabins provide a "hostile" environment for children and adolescents with underlying respiratory disease. Although there are algorithms and guidelines for predicting in-flight hypoxemia relating to COPD, no data pertaining to bronchial asthma are available to date. The purpose of this study was to evaluate the effect of simulated cabin altitude on subjects with bronchial asthma at rest and during a limited walking task.

Methods --- Forty eight subjects (29 male, 19 female) aged 6 years to 18 years old with bronchial asthma, mild persistent disease category and forty two control subjects (20 male, 22 female) were recruited for the study. All had baseline oxygen saturation of more than 95%. Subjects underwent a standardized Hypoxia Altitude Simulation Test using 100% nitrogen while at rest and during limited walking exercise.

Results --- There is reduction on oxygen saturation and increase of heart rate in the control group. On the other hand, the asthmatic patients grouped into two: ages 6 to 12 years old and adolescents with ages 13 to 18 years old showed a statistically significant greater oxygen desaturation (p=0.00, p=0.007, respectively) and tachycardia (p=0.00, p=0.00, respectively) during the testing. There were no clinically noticeable ill effects at the level of oxygen saturation decline in all subjects.

Conclusion --- Patients with mild persistent bronchial asthma, when subjected to pre flight evaluation such as Hypoxia Altitude Simulation Test (HAST), showed a significant decline in oxygen saturation and increase in heart rate. None of the subjects involved in the study experienced any untoward reactions like shortness of breath, palpitations, and lightheadedness. A limitation of the study is its small sample size. A larger study is needed to validate its findings to other more severe forms of asthma. ***Phil Heart Center J 2007;13(2):144-148.***

Key Words: Bronchial asthma ■ Hypoxia Altitude Stimulation Test (HAST) ■ Pre-flight Testing

The number of people, including children, using commercial aircraft to travel is increasing. Most commercial aircraft generally cruise between 9150 and 13000 meters above sea level.[1] At cruising altitudes, most commercial airlines are pressurized to maintain pressure cabin equivalent to 1530-2440 meters. As the height increases the partial pressure of oxygen in the atmosphere falls, so passengers in aircraft at cruising altitude are breathing equivalent of 15% to 16% Fi02. This low oxygen environment elicits little or no clinically relevant effects in healthy adults but may result in lowered arterial hemoglobin oxygen saturation.[2] In a study done by Lee et al.[3] healthy children during air travel was noted to have desaturation as low as 94-95% during travel without notable clinical symptoms.

However, patients with pre-existing respiratory conditions such Chronic Obstructive Pulmonary Disease, cystic fibrosis, neonatal chronic lung disease, or other chronic lung diseases may develop hypoxia related respiratory distress leading to symptom exacerbation, altitude related illnesses, or even death during flights.[2]

The Hypoxia Altitude Simulation Test is a simple method of demonstrating a passenger's need for supplemental oxygen during flight and for determining in-flight oxygen requirements.[4] Data on the use of hypoxia test among infants and older children are sparse. This test predicted cases of oxygen desaturation during flight in children with cystic fibrosis. Two existing studies used hypoxia tests in infants and young children. Parkins and co workers5 performed sleep studies in 34 healthy infants aged 1-6 months during prolonged hypoxia test reported that the mean Sp02 (oxygen saturation) declined from 97.6% to 92.8%. More recently, Buchdahl, et al.,6 reported the use of hypoxia tests in 20 young children with a history of respiratory disease; 6 patients with Sp02 > 95% in room air desaturated below 90% when performing hypoxia test.

In the recent statement from the British Thoracic Society, guidelines were identified relating to professional aircrew and potential recruits with asthma, none were found relating to passengers. Surprisingly these guidelines do not mention avoidance of flying during acute asthma exacerbations.[1] The flight environment experienced by commercial passengers should

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not pose a problem for most patients with asthma. QANTAS airlines, in a review of all consecutive in-flights medical incidents reported 454 significant medical incidents, 9% of which were reported as respiratory tract infection or asthma.[7] A review of incidents on US commercial aircraft where an enhanced medical kit was used found that 10% of 362 episodes were due to asthma, lung disease or breathlessness.[8]

There are a number of environmental changes that arise from altitude, including fall in humidity, irradiation, temperature, atmospheric pressure and partial pressure of oxygen.[9] Low cabin humidity may present a theoretical risk of bronchospasm as a result of water loss from bronchial mucosa. To our knowledge, no study of this nature has been done, to this date among asthmatic children and adolescents. It is therefore useful to know physiologic effects of high altitude especially among asthmatic children and adolescents. This study was conducted to determine the effect of simulated cabin altitude on asthmatic children and adolescent at rest and during

Methods

This is a case control study involving asthmatic children and adolescents, ages 6 years to 18 years old with mild persistent disease category, which include one or more of the following: a) daytime symptoms of more than once a week, b) nighttime symptoms of more than twice a month, accompanied by c) a normal peak expiratory flow (PEF) and force expiratory volume in one second (FEV1) and a peak expiratory flow (PEF) variability of 20-30% based on the Philippine Consensus for the Management of Childhood Asthma. Subjects are in stable condition and with no modification of anti asthma treatment for at least 2 weeks. Excluded were subjects with other co morbid conditions, have respiratory symptoms (coughing, sneezing, chest tightness) of more than 2 weeks in duration and in asthma exacerbation and are unable to follow instructions for the pulmonary function test. Children and adolescents aged 6-18 years old who have no respiratory signs and symptoms two weeks prior to testing and are able to follow instructions for the pulmonary function test served as control of the study.

Hypoxia Altitude Simulation Test (HAST) was conducted at the Pulmonary Rehabilitation - Preflight Evaluation Clinic of the Philippine Heart Center. Voluntary informed consent was obtained from the parent and/or guardian.

The investigator conducted an interview and physical examination of all children and adolescent upon enrollment of the study. A standardized questionnaire was used to assess the clinical signs and symptoms of bronchial asthma based on the Philippine Consensus in the Management of Childhood Asthma.

The prediction of arterial oxygen tension in-flight was done using the hypoxia altitude simulation test (HAST) at constant barometric pressure. This method involved inhalation of hypoxic gas mixtures, allowing measurement of oxygen saturation at simulated in-flight cabin altitude. It utilized the Vohra and Klocke technique using the Venturi delivery system with a face mask covering the nose and mouth.[10] A Venturi jet was connected to a mask by a corrugated tubing to attain Fraction of Inspired Oxygen (Fi02=35%). With a nitrogen source, the Venturi device delivered an Fi02 of 16.5% to 16.9% as measured by a mini oxygen analyzer (Mini Ox 1, MSA Catalyst Research). The subjects were placed on a comfortable sitting position. Nasal cannulas connected to oxygen tank were provided. Venturi mask was tightly fitted over the face. One henudred percent (100%) Nitrogen gas was given at six liters/min for 20 minutes to allow equilibration. Heart rate was recorded every five minutes. Oxygen saturation was continuously monitored using pulse oximeter (BCI Fingerprint, BCI International, Wisconsin). While inhaling the same gas mixture, the subject was asked to stand and walk on a 5-flight of stairs in 3 minutes. Oxygen supplementation was provided when oxygen saturation fell less than 92%. Spirometric studies (pre and post bronchodilation) was done and referred to sea level.

The subjects was grouped according to age. The tables presented descriptive data as mean + SD. Paired sample correlation was done to determine the differences

Results

Fifty two (52) known asthmatic children and adolescents (30 male and 22 female), ages 6 years to 18 years old with mild persistent disease category were recruited to the study. Four subjects had respiratory symptoms of cough and coryza with pneumonia on chest xray, thus, were excluded. A control group of forty two (42) non-asthmatic children and adolescent were likewise recruited. The asthmatic group and control group were further stratified according to age: Asthmatic group 1 (6 years to 12 years old) and Asthmatic group 2 (13 years to 18 years old); Control group 1 (6 years to 12 years old) and Control group 2 (13 to 18 years old). The demographic and pulmonary function data of the study and control subjects are shown in Table 1.

All subjects studied had baseline SpO2 >95% (range = 95-100%). Of the 90 subjects studied, no one experienced feeling of shortness of breath, palpitations or lightheadedness throughout the testing. The mean oxygen saturation of the asthmatic group 1 declined from a mean sea level saturation of 97.3+1.2% to 93.5+2.3% during the test while sitting down (p value=0.002) and to 93.9+2.4 during light exercise (p value=0.017). On the other hand, significant oxygen desaturation of the asthmatic group 2 was demonstrated by a decline of the mean oxygen saturation from 97.2+1.3% to 96.3+2.7% during the test while sitting down (p value=0.05) and no

desaturation during light exercise. The mean heart rate in beats per minute (BPM) at baseline increased from 90/minute to 93/minute during the test while sitting down (p value=0.026) and to 107/minute during light exercise (p value=0.026). The results are summarized in Tables 2A, 2B, 2C and 2D.

When comparing the oxygen saturation and heart rate during the hypoxia testing, oxygen saturation and heart rate differences between the study and control groups were statistically significant for children aged 6 years to 12 years old. However, oxygen saturation and heart rate differences among adolescents aged 13 years to 18 years old did not reach statistical significance due to smaller sample size and variable results. In general, all age groups (6 to 12 years old, 13 to 18 years old) showed significant oxygen desaturation during the testing. Children age 6 to 12 years old and adolescents age 13 to 18 years old demonstrate considerable heart rate increases during the testing. The age group results are stratified in Table 3.

Table 1. Comparison of the demographic profile and pulmonary function test of four groups

Variables	6-12 years old Mild Persistent n=39	6-12 years old Control n=30	p-value	13-18 years old Mild Persistent n=9	13-18 years old Control n=12	p-value
Male	24 (61.5%)	12 (40%)		5 (55.6%)	8 (66.7%)	
Female	15 (38.5%)	18 (60%)		4 (44.4%)	4 (33.3%)	
Age (yrs)*	8.15 ±2.1	8.63 ±2.1	0.36	14.13±1.8	14.11 ±1.1	0.84
Height (cm*)	123.5±14.2	123.58±12.5	0.99	153±6.7	152.14±11.0	0.83
Weight (kg)*	26.85±12.5	23.49±7.5	0.19	45.1±9.1	39.88±8.1	0.16
BMI (kg/m2)*	16.89±4.0	15.04±2	0.016	19.25±3.4	17.11±1.9	0.074
FVC *±	95.38±15.4	94.89±1.2	0.41	99.08±7.9	87.55±11.3	0.02
FEV1*±	99.28±15.2	99.32±14.2	0.99	98.62±11.6	96.77±14.8	0.76
FEV1/FVC* ±	95.78±10.7	95.66±4.9	0.24	94.01±17.0	96.35±3.4	0.71

*Data for continuous variable expressed as mean± SD; other data expressed as n (%).

± % predicted

p value refers to comparisons of patient characteristics by age, height, weight and spirometric studies

Table 2A. Result of Hypoxia Altitude Simulation Test among asthmatic patients (Group 1) Mild Persistent (6-12 years old)

Variable Heart rate	Sea Level beats/min Mean ±SD	HAST (Sitting) beats/min Mean ±SD	HAST (Exercise) beats/min Mean ± SD
Asthmatic	90.9±13.9	93.1±13.7*	107.3±13.4*
Control	83.2±11.7	85.8±12.7*	99.4±15.1*
p value	0.017*	0.026*	0.026*

Table 2B. Result of Hypoxia Altitude Simulation Test among asthmatic patients (Group 1) Mild Persistent (6-12 years old)

Variable SpO2	Sea Level Sp02 Mean±SD	HAST (Sitting) Sp02 Mean ±SD	HAST (Exercise) Sp02 Mean ±SD
Asthmatic	97.3±1.2	93.5±2.3*	93.9±2.4*
Control	97.8±1.2	95.3±2.3*	95.2±1.9*
p value	0.066 NS	0.002*	0.015*

Table 2C. Result of Hypoxia Altitude Simulation Test among asthmatic patients (Group 2) Mild Persistent (13-

Variable Heart Rate	Sea Level beats/min Mean±SD	HAST (Sitting) beats/min Mean±SD	HAST (Exercise) beats/min Mean±SD
Asthmatic	82.5±23.2	86.6±17.4*	103.8±21.5*
Control	78.4±8.0	78.8±8.2*	98.8±12.0*
p value	0.017*	0.161 NS	0.478 NS

Table 2D. Result of Hypoxia Altitude Simulation Test among asthmatic subjects (Group 2) Mild Persistent (13-

Variable Sp02	Sea Level Sp02 Mean±SD	HAST (Sitting) Sp02 Mean±SD	HAST (Exercise) Sp02 Mean±SD
Asthmatic	97.2±1.3	96.3±2.7*	94.5±2.0
Control	97.7±1.5	96.2±1.9	96.3±1.5
p value	0.066 NS	0.962 NS	0.026*

Table 3. Correlation of heart rate and s02 at sea level and Hypoxia Altitude Simulation Test (sitting and exercise)

GROUP	Variable	Sea Level Mean±SD	HAST (Mean±SD) Sitting	HAST (Mean±SD) Exercise	p value
Asthmatic					
6-12 y.o.	HEART RATE	90.9±13.9	93.1±13.7	107.3±13.4	0.00*
	SpO2	97.3±1.2	93.5±2.3	93.9±2.4	0.00*
13-18 y.o.	HEARTRATE	82.5±23.2	86.6±6	103.9±21.5	0.00*
	SpO2	97.2±1.3	96.3±2.8	94.6±2.0	0.007*
Control					
6-12 y.o.	HEART RATE	83.2±11.7	85.8±12.7	99.4±15.1	0.00*
	SpO2	97.8±1.2	95.3±2.3	95.2±1.9	0.00*
13-18 y.o.	HEART RATE	78.4±8.0	78.8±8.2	98.8±12.0	0.00*
	SpO2	97.7±1.5	96.2±1.9	96.3±1.5	0.033*

Discussion

Predicting adverse consequences associated with hypoxia during commercial flight is important. Patients with lung diseases have potential health risks during air travel. The ascent to high altitude results in reduced inspired oxygen pressure with associated decrease in Pa02. The falling barometric pressure is responsible for the reduction in oxygen tension.

A previous study by Lee and co workers3 involving 80 healthy children aged 6 months to 14 years old were studied during their eight flights between Honolulu, Hawaii and Taipei, Taiwan. Oxygen saturation declined and heart rate increased significantly after 3 hours and 7 hours with reduced aircraft cabin pressure. There were no clinically noticeable ill effects noted at the level of oxygen desaturation.

Our study, involving children who are known asthmatic, showed that a high proportion of children aged 6-12 years old and 13-18 years old exhibit significant oxygen desaturation below 95% when breathing hypoxic gas mixture (Fi02=16.5%-16.9%).

The British Thoracic Society guidelines recommend that in-flight oxygen is not required in adults in

whom sea level Sp02 is >95% or 92-95%, depending on the absence and presence of additional risk factors.[1] In a study done by Buchdahl and co workers,[6] they reported their experience of preflight hypoxia testing in 20 young children with various chronic lung diseases. Eighteen infants and young children had normal baseline Sp02. Of these, six patients exhibited oxygen desaturation below 90% with one infant recording Sp02 of <85% during exposure to 15% Fi02. The present study support these earlier findings and suggest that a normal Sp02 in room air of children with bronchial asthma at sea level may be insufficient to determine the safety of this patient group in the low oxygen environment encountered during flight or at high altitude.

In the present study, 80% of asthmatic children and adolescent had inhaled corticosteroids and long acting beta 2 agonist as maintenance medications. In addition, all asthmatic children and adolescent had normal spirometric studies. The reasons why these children are more susceptible to hypoxia are not clear but may be due to the relative immaturity of the respiratory system leading to increased ventilation-perfusion mismatch.[11] Studies in children in high altitude regions of the world (>3000m) had shown them to have higher minute ventilation (VE), tidal volume (VT), expiratory duration, vital capacity (VC), lung compliance, oxygen extraction, hematocrit and hemoglobin levels and to maintain pulmonary vascular reactivity.[9] In a study done by Wagner and co workers13, thirty 5 to 7 year old children were exposed to 12% oxygen for 10 minutes; 7 of 10 whose oxygen saturation fell <88% had histories of reactive airways disease. Desaturation was a better predictor for reactive airways disease and had a sensitivity of 100% for reactive airways disease. This suggests that small airways disease contributes to the susceptibility to desaturate with exposure to hypoxia. This may be because airway/alveolar hypoxia induces bronchoconstriction.

When comparing oxygen saturation differences between study group and control group during hypoxia testing, there was statistical significance noted among children age 6 to 12 years old and 13 to 18 years old. Considering these asthmatics to have a normal pulmonary function test while undergoing the preflight testing, we are therefore cautious about extrapolating conclusions from our observations to asthmatic children and adolescent in general.

In the recent British Thoracic Society recommendations in managing passengers with respiratory disease planning air travel, there are three current procedures that was used to assess whether the patients are fit to fly namely: the 50 meter walk, predicting hypoxemia from equations and the hypoxia challenge test.[1] We routinely use a 20 minute hypoxia challenge test using the 35% Venturi device with nitrogen as source gas that effectively lowers the Fi02 to 16.5% equivalent to an altitude of 6,700 feet. Because of the lower density of nitrogen, less air is entrained by the Venturi device lowering the delivered Fi02. Briefly, acute hypoxia in normal individuals initiate reflex responses that reduce oxygen gradient between the atmosphere and body tissues and prevent a large fall in Pa02. Hyperventilation is the primary physiologic response to acute hypoxia and maximizes alveolar P02 and Pa02, assuming that oxygen consumption is stable. Minute ventilation increases, primarily as a result of increased tidal volume rather than tachypnea. Blood flow and oxygen delivery to the heart and brain organs with high oxygen requirements are normally maintained during acute hypoxia. Cardiac output characteristically increases initially with hypoxia in a dose dependent fashion, primarily due to tachycardia.[10] This observation was evident on all study and control subjects while doing the hypoxia altitude simulation testing (HAST). Although the degree of oxygen desaturation is statistically significant, the lack of acute symptoms from this in both asthmatic and control subjects suggest that this degree of oxygen saturation decline may not be clinically important.

A limitation of the study is its small sample size especially among adolescents aged 13 years to 18 years old. These observations suggest that larger studies, involving stable and poorly controlled asthmatics undergoing hypoxia testing.

In addition, children with preexisting acute or chronic cardiopulmonary conditions (e.g. asthma in acute exacerbation, pneumonia, bronchopulmonary dysplasia, congenital heart disease) who may already be mildly hypoxemic are the patients most likely to seek medical advice about whether to fly.[17,19,20] These patients with pre existing anemia or cardiopulmonary diseases are likely to sustain greater degrees of clinical compromise with similar degrees of oxygen desaturation and may result at greater risk of developing acute symptoms. While it may be possible to predict hypoxia among stable asthmatic during flight, there are no means of predicting symptoms or actual risk of harm during air travel.[18] Further information is required to determine the effects of hypoxia testing on poorly controlled asthmatics and the clinical significance of hypoxia testing among stable asthmatics.genital heart disease) who may already be mildly hypoxemic are the patients most likely to seek medical advice about whether to fly.[17,19,20] These patients with pre existing anemia or cardiopulmonary diseases are likely to sustain greater degrees of clinical compromise with similar degrees of oxygen desaturation and may result at greater risk of developing acute symptoms. While it may be possible to predict hypoxia among stable asthmatic during flight, there are no means of predicting symptoms or actual risk of harm during air travel.[18] Further information is required to determine the effects of hypoxia testing on poorly controlled asthmatics and the clinical

significance of hypoxia testing among stable asthmatics.

Conclusion

In conclusion, patients with mild persistent bronchial asthma when subjected to pre flight evaluation such as Hypoxia Altitude Simulation Test (HAST) showed a significant decline in oxygen saturation and increase in heart rate. None of the subjects involved in the study experienced any untoward reactions like shortness of breath, palpitations and lightheadedness. A limitation of the study is its small sample size. A larger study is needed to validate its findings to other more severe forms of

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Comparative Assessment of Asthma Control Test (ACT) and GINA Classification including FEV1 in predicting asthma severity

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Background --- The gold standard in classifying severity of asthma is the GINA classification, however, the numeric cut-off values of frequency and intensity symptoms and parameters of physiologic dysfunction used to classify asthma severity are artificial and transitory. Currently, asthma questionnaires, such as the Asthma Control Test (ACT), provides a more simplified assessment of control by not requiring FEV1. It is the aim of this study to compare the Asthma Control Test (ACT) and GINA classification, including FEV1, in assessing asthma severity and validate ACT as a screening tool for asthma severity.

Methods --- This is a prospective cohort study involving adult asthmatic patients who were classified based on their ACT scores into controlled asthma (ACT>19) and uncontrolled asthma (ACT < 19). They were then classified accordingly to their GINA asthma symptom severity. After which, FEV1 and peak expiratory flow rate (PEFR) were recorded. Correlation as well as measures of validity were obtained, with level of significance set at 0.05.

Results --- Among the 86 patients included in this study, 62 have ACT scores < 20. The prevalence rate of uncontrolled asthmatics was 72% with majority classified as moderate persistent. Significant association between ACT and GINA classification (p-value 0.00), ACT and FEV1 in liter (p-value 0.013), ACT and FEV1 as % predicted (p-value 0.023) and ACT and PEFR in % predicted (p-value 0.037) were observed. There appeared to be an association between a lower ACT score and a more severe symptom severity. ACT was 92.3% sensitive and 90.5% specific with AUC of 0.972. The positive predictive value was 98% and the negative predictive value is 79%.

Conclusion --- With its high sensitivity, specificity and positive predictive value, ACT can served as an alternative diagnostic tool in assessing asthma severity even without an aid of a spirometer or a peak flow meter. An ACT score of at least 20 can classify patient as intermittent or controlled asthmatic while an ACT score < 20 can classify the patient as in persistent or uncontrolled asthmatics. ***Phil Heart Center J 2007;13(2):149-154.***

Key Words: Asthma ■ GINA ■ Severity ■ Validation Study ■ Asthma Control Test ■ FEV1

Asthma is a worldwide disease which affects all ages, sex and racial groups. In the Philippines, limited reports showed a prevalence rate of 12% in children aged 13-14 years old and 12-22% in older age groups.[2] In spite of the recent advances in the detection and treatment of the condition, asthma remains a cause of significant morbidity and economic burden.

Despite the availability of national and international guidelines, asthma management is grossly suboptimal worldwide. The Asthma Insights and Reality in Asia-Pacific (AIRIAP) survey, involving asthma subjects from eight areas including the Philippines, has demonstrated that the disease causes substantial morbidity, utilization of healthcare resources and absence from work/school, especially in those with more severe disease.[1]

Asthma severity and asthma control are distinct yet related concepts. Asthma severity describes the underlying disease in the absence of therapy and is ideally defined without concurrent treatment confounding its assessment. The in trinsic intensity of the disease, which can change, but does so only slowly over time. In the presence of the appropriate intervention, including education, environmental control, and pharmacotherapy, many of the characteristics of disease that we used to describe severity may be changed or absent.[3]

More recently, the concept of asthma control has been introduced to describe better the status of disease in the presence of intervention. Asthma control describes the clinical status of disease with medical intervention. It can rapidly change in response to triggers or therapy. However, the individual parameters by which we define asthma severity and asthma control overlap significantly.[3]

The therapeutic goal is to achieve uncontrolled

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asthmatics to well-controlled then ultimately total controlled. This require aggressive therapy/intervention to achieve adequate control especially in severe persistent compared to a mild disease.[2] A well-controlled asthmatic should have no or minimal symptoms or use of rescue medication, no significant limitation in activity and (near) normal lung function.[3] The gold standard in classifying severity is the GINA classification of asthma symptom severity which includes daytime and nocturnal symptoms, objective parameters using the FEV1 and PEF variability.[2]

Long term mental retention and adherence to the classification details have not been satisfactory. Because asthma is a chronic inflammatory disease, the severity of its chronic state exists in a continuum. Numeric cut-off values of frequency and intensity symptoms and parameters of physiologic dysfunction currently used to classify asthma in different levels of severity are artificial and transitory.[2] Furthermore, the availability as well as the affordability of the spirometry is not readily met by all patients.

Concurrently, many asthma questionnaires were formulated to make the assessment of asthma severity and control easy. The most recent and the most simplified questionnaire done by Nathan, et al was the Asthma Control Test (ACT). As a screening tool, the overall agreement between ACT and the specialist's rating ranged from 71% to 78% and the AUC was 0.77. The ACT provides a more simplified assessment of control by not requiring FEV1 and by providing a meaningful and easy to use scoring method, which is simpler than the other previous asthma questionnaires but comprehensive enough to evaluate the range of asthma control. Still, the best measure of control would be the use of a FEV1.[10]

Objectives

General Objectives

1. To compare the Asthma Control Test (ACT) and GINA classification including FEV1 in assessing asthma severity.
2. To determine the frequency of uncontrolled asthmatics through Asthma Control Test (ACT).

Specific Objectives

1. To determine the validity of Asthma Control Test (ACT) as a screening tool in
assessing asthma severity
2. To determine if there is an association between Asthma Control Test (ACT) and GINA classification of asthma severity.
3. To determine the association of Asthma Control Test (ACT) with forced expiratory volume in 1 sec - FEV1(L and %predicted) and Peak Flow Meter Rate – PEFR (L/min and %predicted).

Methods

This was a prospective cohort study which included mainly adult asthmatic patients who have been and had been taking asthmatic medications. Patients younger than 18 years old and with concomitant lung pathology such as emphysema, bronchiectasis, bronchitis and tuberculosis were excluded.

The Asthma Control Test (ACT), a validated 5-item self-administered survey designed to assess asthma control, was administered to the subjects. ACT is scored on a scale of 5-25 with the higher scores reflective of better asthma control. An ACT score of >19 suggests controlled asthma while ACT score of less than or equal to 19 suggests uncontrolled asthma.

After the Asthma Control Test (ACT), patients had an interview wherein they were classified according to the GINA symptom severity. The GINA classification of symptom severity includes 4 categories – mild intermittent, mild persistent, moderate persistent, and severe persistent. This is based on clinical symptoms including daytime and nocturnal shortness of breath, spirometric studies with FEV1 and PEF variability.

After which, spirometric studies and peak expiratory flow rate were done. They were instructed to blow first on the Peak Flow Meter or the Mini-Wright followed by the portable ventilometer or the Microloop. The recorded FEV1 (L and % predicted) and PEFR (L/min and % predicted) were taken as the best of three satisfactory results.

Statistical Analysis: Fisher's Exact Test and Chi-squared test were used to determine association between variables. Pearson Correlation coefficient was utilized to determine correlation between FEV 1 and PEFR. ROC was used to calculate the specificity and sensitivity of ACT as a screening tool. The level of significance was set at 0.05.

Results

A total of 86 asthmatic patients were seen at the Out-Patient Department. Of these, 62 patients have ACT score of less than 20, giving a 72% prevalence rate of uncontrolled asthmatic patients or patients with persistent asthma. On the other hand, 28% of the study population showed ACT score of at least 20, which falls into the category of intermittent asthma. Table 1 shows that there was a significant difference between the mean FEV 1 in L (p: 0.013) and in % (p: 0.023) of patients with ACT score of less than 20 and patients with ACT score of at least 20. FEV1 < 2L or <80% predicted were associated with ACT score of <20 while FEV1 >2L or >80% predicted were associated with ACT score of at least 20.

There was also an association between GINA classification of asthma symptom severity and ACT score

Table 1. Characteristics of eligible patients grouped based on their ACT scores

Clinical and Demographic Characteristics	ACT Score (≤ 19) N=62	ACT Score (>19) N=24	p-value
Age, y (mean, SD)	40.0 (10.5)	38.5 (10.6)	0.540
Sex			
male, n(%)	14 (23)	9 (38)	0.130
female, n(%)	48 (77)	15 (62)	
Smoking History			
Smoker, n(%)	3 (5)	3 (12)	0.211
Non smoker, n(%)	59 (95)	21 (88)	
Presence of Allergic Rhinitis			
With, n(%)	9 (14)	7 (29)	0.106
Without, n(%)	53 (86)	17 (71)	
GINA classification (n,%)			
Mild Intermittent	2 (3)	19 (79)	
Mild Persistent	15 (24)	1 (4)	0.000*
Moderate Persistent	32 (52)	2 (8)	
Severe Persistent	13 (21)	2 (8)	
FEV 1, L (mean, SD)	1.9 (0.6)	2.2 (0.6)	0.013*
% (mean, SD)	76.0 (18.0)	83.9 (12.4)	0.023*
PEFR , L/min (mean, SD)	344.5 (95.8)	382.3 (93.5)	0.102

*significant

Table 2. Derived Asthma Control Test (ACT) scores and asthma symptom severity using the GINA classification

GINA Classification of Asthma Severity	ACT Score (5-14)	ACT Score (15-19)	ACT Score (20-25)	Total
Mild Intermittent	0 (0.0)	2 (4.5)	19 (79.2)	21(25)
Mild Persistent	0 (0.0)	15 (34.1)	1 (4.2)	16(18)
Moderate Persistent	8 (44)	24 (54.5)	2 (8.3)	34(40)
Severe Persistent	10 (56)	3 (6.8)	2 (8.3)	15(17)
TOTAL	18(21%)	44(51%)	24(28%)	86

(p value: 0.00). However, no association were noted with sex, smoking history and allergic rhinitis and the ACT score. Both group exhibited almost the same population characteristics; the age ranged between 30 -40 y/o, > 50% of the subject population were females, majority were non-smoker(>70%) and a small proportion of asthmatics has concomitant allergic rhinitis (7%).

In Table 2, we could see the breakdown of the different ACT Score in conjunction with the GINA classification of asthma severity. The derived ACT scores were based on the AIRIAP study by Lai, et.al.[9]

In our study, 51% of the patient had ACT score of 15-19, which signifies not controlled asthmatic and 21% had scores below ACT 15 or classified as poorly controlled asthmatics. Based on the GINA classification of asthma symptom severity, majority of the asthmatics were moderate persistent(40%), followed by mild persistent(18%) and severe persistent(17%) and lastly, the mild intermittent(25%). There appeared to be an association between a lower derived ACT score and a more severe symptom severity. Although, there was an overlapping of ACT score for moderate persistent from

Table 3. Comparison of the derived ACT score level with GINA Classification of Asthma Symptom Severity, FEV1, PEFR (% predicted)

	ACT Score (5-14)	ACT Score (15-19)	ACT Score (20-25)	p-value
GINA Classification of Asthma Severity (n,%)				0.000*
Intermittent	0 (0.0)	2 (4)	19 (79)	
Persistent	18 (100.0)	42 (96)	5 (21)	
FEV1, L (mean, SD)	1.7 (0.6)	1.9 (0.6)	2.2 (0.6)	0.022*
FEV1, % (mean, SD)	71.4 (17.6)	77.8 (18.0)	83.9 (12.4)	0.057
PEFR (n,%)				0.037*
> 80% predicted	7 (38.9)	28 (63.6)	19 (79.2)	
60 – 80% predicted	7 (38.9)	14 (31.8)	4 (16.7)	
< 60% predicted	4 (22.2)	2 (4.5)	1 (4.2)	

Table 4. Sensitivity and Specificity of ACT as a screening tool in assessing asthma severity

ACT Score	GINA Classification Persistent	GINA Classification Intermittent	SN	SP	PPV	NPV	Area Under the Curve
≤ 19	60	2	92.3%	90.5%	98%	79%	0.972
> 19	5	19					

ACT 5 to 19, again, it can be classified generally as not controlled asthmatics..

As we compared the derived ACT score with the GINA classification and the FEV1, it almost showed the same association as in Table 1.; ACT scores of 5-14 and 15-19 falls in persistent asthma with a FEV1 <2L while ACT scores above 20 falls in intermittent asthma with a FEV1 >2L(Table 3) except for the FEV1(%).

In our study, PEFR (% predicted) was shown to be associated with the derived ACT scores but not the actual value of PEFR(L/min). As the ACT scores fall, the PEFR (% predicted) also fall <60% (Table 3). ACT score is 92.3% sensitive and 90.5% specific with area under the curve of 0.972 (97.2%). The positive predictive value is 98% and the negative predictive value is 79%. In consequence, ACT score is an excellent diagnostic tool for screening asthma severity with its high sensitivity and positive predictive value.

Discussion

Based on NIH(1997), Asthma is now considered as a disease of airway inflammation. The incessant release of the inflammatory mediators from eosinophils and mast cells results in persistent bronchial inflammation of the airways. Obviously, the airways undergo structural abnormalities resulting in the following: fibrosis, increase in mass of the smooth muscle and mucus glands, epithelial shedding, thickening of the reticular basement membrane and fibronectin deposition in the subepithelial layer. Histological sections show thickening of the airways by 50-300% of normal.

Airway remodeling results in the following physiologic consequences: 1) increase in airway hyperre

sponsiveness 2) non-reversibility of airway obstruction and residual obstruction after bronchodilator and anti-inflammatory therapy and 3) accelerated decline in the FEV1 in a subset of asthmatic patients.[2]

Asthma is diagnosed by a combination of history (positive family history), clinical findings: 1)cough which worsens at night, 2) wheeze, 3) dif ficulty of breathing, 4) chest tightness. In addition, objective measurements of variable airflow obstruction using spirometry(FEV1) and peak flow meter(PEFR). However, in some cases, the medical history and PE may not be reliable in diagnosing asthma. Furthermore, the physical examination maybe normal as asthma symptoms are characteristically episodic especially in children. An objective measure is needed to diagnose asthma accurately(GRADE A).[2]

Asthma can be classified according to: 1) etiology 2) severity (clinical condition on presentation whether the patient is in acute or in a chronic state). The first classification is limited as no environmental cause can be identified. For identification of the specific etiology will guide both the physician and the patient on the use of avoidance strategies in management.[2]

The second classification is based on the severity of the disease. It is important to put emphasis on patient who are in acute exacerbation such could be fatal if not treated appropriately.

Even patient with chronic asthma, however mild, may have an acute exacerbation. Any patient, even with mild symptoms, should be considered as having asthma exacerbation if there is: 1) history of life threatening acute attacks, 2) hospitalization within previous year, 3) psychosocial problem, 4) history of intubation for asthma, 5) recent reductions or cessation of glucocorticoid therapy, and 6) noncompliance with recommended medical therapy. These clinical conditions are associated with a higher risk of asthma mortality. Since acute exacerbation demands an urgent need to intervene and modify existing treatment.[2]

Crockcroft and Swystun have suggested that the only measure that can distinguish asthma severity and asthma control is the minimal amount of controller medication required to achieve adequate control. However, this measure is an accurate reflection of disease severity only when optimal control has been achieved. Unfortunately, optimal control is not routinely achieved among the general population which limits the usefulness of such measure. Therefore, efforts are made to develop measures that accurately classify asthma severity and asthma control.[3]

Fuhlbrigge, et.al. assessed asthma burden in the US using 3 components: Short-term symptom burden(4-week recall), Long-term symptom burden(past year) and Functional impact(activity limitation). In this study, there is a discordance in the pattern of the asthma symptoms by individuals. Also seen by Colice, et.al., evaluation of the asthma severity utilizing individual component of disease may lead to inadequate treatment of asthma . Hence, no single variable can give a complete picture of the clinical status of disease. Accurate assessment requires a combination of parameters.[4]

Eventually, validated instruments such as questionnaire has developed to evaluate asthma control. The Asthma Therapy Assessment Questionnaire (ATAQ) by Vollmer, et.al. showed a significant association between the level of control and healthcare utilization5. The Asthma Control Questionnaire (ACQ) by Juniper, et.al. has demonstrated high evaluative and discriminative properties. Recent evidence showed ACQ compared to the composite measure based by GINA/NIH criteria showed significant association with the ACQ score and the severity of the disease.[6]

The Asthma Control Test, a five item self administered survey which scored from 0 -5; Recent analysis compared it with the specialist assessment showed a specificity of 76.2% and a sensitivity of 68.4%7. Nathan, et al . studied the overall agreement between ACT and the specialist's rating ranged from 71% to 78% and the AUC was 0.77.[10]

All questionnaires focus on patient-oriented features of the disease.[4] All 3 describe the impact of asthma on daily activities, sleep disrupted by asthma and the need for rescue medication.

Disease severity is not a patient-focused measures, limited by the requirement that it should be assessed prior to use of medication and includes measures of lung function. Unfortunately, these are not performed regularly. In contrast, these 3-survey tools can be assessed in the presence of controller medications, are not dependent on the availability of spirometer and report on asthma control over a longer period of time (1-4wks) depending on the questionnaire used. Disease severity and control have the inherent disconnect of the patient with mild disease that is not well controlled or severe disease who has good contro.[l8]

There is still a continued debate on how to assess asthma control in a way supports management and is easy to use in practice. The ACT questionnaire ask patient to report for the previous 4-weeks(short term recall) regarding: limitations to activities, shortness of breath, night-time awakening, use of rescue medication, perception of control. Completion of the ACT results in a potential score of between 5-25: > or = 20 indicates well controlled and a score < or = 15 suggests poor controlled asthma.[9]

Lai, et al, showed that poorer asthma control, as measured by the derived ACT, was associated with a higher requirement for hospitalization and unscheduled healthcare over the previous year and elevated healthcost based on the questionnaires used in the AIRIAP study.[9]

For ACT of <15, the mean per-patient annual cost

of asthma management was US $861, US $319 for patients with a derived ACT score 15-19 and US $193 for patients with derived ACT score of at least 209. As the ACT scores went down, the expenditure for asthma care went up which connotes an inverse relationship. As asthma is not controlled, the more expenses the patient would incurred.[9]

In our study, only 24 patients(28%) has controlled asthma and the rest were uncontrolled(72%). This substantiates the AIRIAP study which showed that in our part of the world, the Asia-Pacific region, still asthma is not totally contained. This should alert us, the physician, to educate our patient with the nature of the disease that they have incurred. Still, patient education plays an important role in the control of a disease entity.

According to Nathan, et.al., ACT score of < 19 shows that most patients are uncontrolled. ACT is a simple, inexpensive test that has been already been validated10.

Stempel, et al, in his study of 522 subjects showe d that ACT may serve as a useful screening tool in the community to determine whether patients have controlled or uncontrolled asthma.[12]

In our study, there was an association noted between the asthma control test (ACT) and the GINA classification of asthma symptom severity, FEV1(L and %) as well as peak expiratory flow rate (% predicted). The ACT score was able to give a 92.3% sensitive and 90.5% specific with area under the curve of 0.972 (97.2%). Likewise, the positive predictive value is 98% and the negative predictive value is 79%. Consequently, this makes it an excellent diagnostic tool for screening asthma severity. Our findings has corroborated with the above studies.

An ACT score of at least 20 can classify patient as in intermittent or controlled asthmatics with an of FEV1 and PEFR of >80% predicted while an ACT score of less than 20 can classify the patient as in persistent or uncontrolled asthmatics with an FEV1 and PEFR of < 80% predicted.

In the GOAL study, it was designed to assess whether total control or well control status was achievable. This study demonstrated that well or total control of asthma could be attained in the majority of the patients treated with a salmeterol/fluticasone combination. Although control was established at a high threshold, majority of the patients were able to achieve and sustain well or total asthma control. This allows for the establishment of a new goal for assessing asthma outcomes.[13]

In our study, majority of the patients interviewed do not have any controller medication. Only 32 asthmatics(37%) of the study population has used combination beta-agonist and steroids. Not all of them are maintained on a regular basis, some have stopped due to financial constraint, some are still using on a p.r.n. basis and luckily, a few are able sustain its use. Hence, majority of them falls into the category of moderate persistent. Using the patient-oriented concept thru asthma control test (ACT), we hope that detecting uncontrolled asthmatics would be easier, leading to a better adherence to the controller medication and ultimately, a better or total control of asthmatic patients in our country.

Limitations

This study is limited by the relatively small sample size and could lead to variations in values that may not be reflective of the larger, general population specifically the asthmatics. Another is the objectivity analysis of the investigator assessment as the gold standard which is to classify the patients according to the GINA asthma symptom severity. Nonetheless, the magnitude of association flow meter are not readily available. Despite its limitation, this study has demonstrated asthma control test (ACT) with a high positive predictive value as well as high sensitivity and specificity making it a good screening tool in asthmatics. between the asthma control test and GINA classification asthma symptom severity as well as FEV1(L and %) and PEFR(%) indicates that asthma control test (ACT) can be used as a surrogate test in assessing asthma severity especially in places where spirometry as well as peak

Conclusion

With its high sensitivity, specificity and positive predictive value, asthma control test (ACT) can served as an alternative diagnostic tool in assessing asthma severity even with out an aid of a spirometer or a peak flow meter in an out-patient basis or as home based. An ACT score of at least 20 can classify patient as intermittent or controlled asthmatics with an of FEV1 and PEFR of >80% predicted while an ACT score of less than 20 can classify the patient as persistent or uncontrolled asthmatics with an FEV1 and PEFR of < 80% predicted. It can serve as a guide in the case management of asthmatic patients. Therefore, asthma control test (ACT) is a simple, inexpensive tool that can be used especially in our country where financial resources are limited, disabling our patient to do the standard diagnostic test such as the spirometry.

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Predictors of Mortality Based on CT Scan Findings of Patient Admitted Due to Hypertensive Intracerebral Hemorrhage at the Philippine Heart Center

Alma M. Buensuceso MD

Background --- Intracerebral hemorrhage accounts for 10 to 15 percent of all cases of stroke and is associated with the highest mortality rate. Once an ICH occurs, the most efficient way to localize the hemorrhage is Computed Tomography. Hypertensive hemorrhages appear on CT as areas of high density with sharply defined borders. According to previous studies, the mortality rate six months after spontaneous ICH ranges from 23 to 58 percent. A low score on the Glasgow Coma Scale, a large volume of the hematoma, and the presence of ventricular blood on the initial CT scan are factors that have been consistently identified as predictive of a high mortality rate. This study was conducted to determine the predictors of mortality based on the CT scan finding of patient admitted due to hypertensive intracerebral hemorrhage at the Philippine Heart Center.

Methods ---This was a retrospective cohort study involving 124 patients with hypertensive intracerebral hemorrhage (HICH) on their CT scan. Their plates and medical records were reviewed together. The following items were analyzed in each patient in order to determine the predictors of mortality with HICH patient: age, sex, status, occupation, co-morbidities, years of hypertension, blood pressure, hospital stay, management, outcome, presence of midline shift/ herniation, intraventricular and subarachnoid hemorrhage, hydrocephalus and hematoma volume in there ct scan result. Independent predictors of mortality were determined using univariate and multivariate analysis.

Results --- Using univariate analysis the following parameters shows significant result ($p< 0.05$); age, duration of hypertension (years), occupation, hospital stay and the presence of subarachnoid hemorrhage in the CT scan result. We then use the five parameters that give significant result using the multivariate analysis and only one showed significant value which was the presence of subarachnoid hemorrhage in the CT scan ($p=0.0358$), that gives three (3) times higher risk of dying in patient with HICH.

Conclusion --- The presence of subarachnoid hemorrhage in the CT scan findings of patient admitted due to HICH gives three times higher risk of dying to the patient, thus a good predictor of mortality. ***Phil Heart Center J 2007; 13(2):155-160.***

Key Words: Hypertensive Intracerebral hemorrhage ■ Subarachnoid Hemorrhage ■ Hemorrhagic Strokes ■ Computed Tomography, Mortality

The worldwide incidence of intracerebral hemor rhage (ICH) ranges from 10 to 20 cases per 100,000 population 4,8 and increases with age, 90% of them being older than 45 years.[4] Intracerebral hemorrhage is more common in males than females, with males having a 5-20% higher incidence of ICH than females.[4] Certain populations are also predisposed to ICH such as Japanese and black since a higher incidence of hypertension is seen in these people younger than 45 years.[4]

Intracerebral hemorrhage accounts for 10 to 15 percent of all cases of stroke and is associated with the highest mortality rate, with only 38 percent of affected patients surviving the first year. Depending on the underlying cause of bleeding, intracerebral hemorrhage is classified as either primary or secondary. Primary ICH, accounting for 78 to 88 percent of cases, originates from the spontaneous rupture of small vessels damaged by chronic hypertension or amyloid angiopathy. Secondary ICH occurs in a minority of patients in association with vascular abnormalities (such as arteriovenous malformations and aneurysms), tumors, or impaired coagulation.

Hypertensive intracerebral hemorrhage is the most common from ICH. According to the autopsy study of McCormick and Rosenfield, hypertension represents the main causative factor for ICH. The frequency of hypertension in a series of patients with ICHs varies widely from 40 to 89 percent, even in studies applying careful definitions of hypertension. When the blood pressure is chronically high, blood vessels may develop small weakened areas (microaneurysms) from constant pressure on the vessels walls.

These microaneurysms (Charcot-Bouchard aneurysms)

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can leak into the tissues and in time, blood irritates the brain tissues causing swelling (cerebral edema). The blood collects into a mass (hematoma). Both swelling of the brain tissues and the presence of hematoma within put increasing pressure on the brain tissues and eventually destroys them. Bleeding may occur into the ventricles of the brain or into the subarachnoid space (the space between the brain and the membranes covering the brain), causing symptoms of meningeal irritation.

Intracerebral bleeding associated with hypertension occurs most often in the putamen/external capsule (40%), lobar white matter of the cerebral hemispheres (22%), thalamus (15%), pons and cerebellum (8%), and caudate (7%). Notably, hypertension increases the risk of intracerebral hemorrhage, particularly in persons who are not compliant with antihypertensive medication, are 55 years of age or younger, or are smokers. Improved control of hypertensive appears to reduce the incidence of ICH. Typically, active bleeding in hypertensive intracerebral hemorrhage (HICH) is relatively acute and usually lasts less than an hour. Cerebral edema rapidly ensues and progresses for 24 to 48 hours after ictus. Although the clinical course of HICH is highly variable, about 25 percent of patients die within the first 48 hours. Delayed neurologic deterioration occurs in small percentage of cases and is usually due to rapid clot expansion with secondary brain herniation. Delayed hemorrhage usually occurs in patients with persistent hypertension.

Once an ICH occurs, the most efficient way to localize the hemorrhage is Computed Tomography. Hypertensive hemorrhages appear on CT as areas of high density with sharply defined borders. There is typically only a single lesion that tamponades itself thus limiting its size. These areas tend to be homogenous unless there is active bleeding or a coagulopathy as would be seen in a hemorrhage associated with anticoagulant use. Edema develops over the course of days following the initial bleed causing an area of low attenuation to develop around the perimeter of the hemorrhage. Hemorrhages frequently extend into the ventricular system but subarachnoid hemorrhage is occasionally seen.

Patients with large hematoma usually have a decreased level of consciousness as a result of increased intracranial pressure and the direct compression or distortion of the thalamic and brainstem reticular activating system.[10] The presence of a large hematoma and ventricular blood increases the risk of subsequent deterioration and death 10. Similarly, a mass effect (midline shift) which results from the volume of the hematoma, the edematous tissue surrounding the hematoma, and obstructive hydrocephalus with subsequent herniation remains the chief secondary cause of death in the first few days after intracerebral hemorrhage.

According to previous studies, the mortality rate six months after spontaneous ICH ranges from 23 to 58 percent. A low score on the Glasgow Coma Scale, a large volume of the hematoma, and the presence of ventricular blood on the initial CT scan are factors that have been consistently identified as predictive of a high mortality rate.

Broderick et al found that the mortality rate at one month was best predicted by determining the initial score on the Glasgow Coma Scale and the initial volume of the hematoma 9. In their study, patients who initially had a score of less than 9 on the GCS and a hematoma volume of more than 60 ml had a mortality rate of 90 percent at one month, whereas patients with a score of 9 or greater and a hematoma volume of less than 30 ml had a mortality rate of 17 percent.

In another study by Mitra et al , age of more than 60 years, GCS of 6 or less (in a modified Scale of 10) at the time of admission, ICH volume greater than 30 ml, midline shift in CT scan of more than 3 mm and presence of intraventricular hemorrhage (IVH) and hydrocephalus had an adverse impact on outcome. Young age, GCS of more than 8, ICH volume of less than 20 ml, presence of lobar hemorrhage and absence of IVH/Hydrocephalus were associated with relatively favorable outcome.

Surgical treatment of patients with intracerebral hemorrhages must be individualized. Patients with accessible lobar hemorrhages who are deteriorating neurologically will often improve with surgery. Large dominant hemisphere basal ganglia lesions in elderly patients are probably not suitable candidates for surgery.

The decision to operate depends on the patient's neurological deficit, evidence of progression of the deficit, the location of the hemorrhage and an assessment of the neurological prognosis, given all these factors, by the treating physicians.

A meta-analysis of three randomized, controlled trials of supratentorial hemorrhage reported that, as compared with the 126 patients who did not undergo surgery, the 123 patients with an ICH who underwent surgical evacuation through an open craniotomy had a higher rate of death or dependency at six months (83 percent vs. 70 percent). Recent attempts at early craniotomy did not alter the outcome and were usually associated with an increased probability of recurrent bleeding.

This study was conducted to determine the predictors of mortality based on the CT scan finding of patient admitted due to hypertensive intracerebral hemorrhage at the Philippine Heart Center. Specifically, this study aimed to describe the socio-demographic and clinical profile of patients with hypertensive intracerebral hemorrhage as well as determine the association of hematoma volume, midline shift/herniation, intraventricular hemorrhage, subarachnoid hemorrhage and hydrocephalus with mortality among patients with HICH admitted at the PHC.

Definition of Terms

1. Brain edema – represents moderate amount of bulk water within acute hematomas.
2. Computed Tomography – images a section or slice of the patient. This is accomplished by obtaining a series of different angular projections or views of the section. Unlike conventional tomography and radiography, x-rays do not pass through neighboring anatomy, only through the section of interest.
3. Glasgow Coma Scale (GCS) – tests level of consciousness by evaluating eye opening (4), verbal output (5) and motor responses (6). It is most useful for following a patient's neurologic condition over time with serial Glasgow coma scores (total score of 15).
4. Estimated hematoma volume – it is computed by getting the product of Lx W x AP x 0.523 where L is the number of slices showing hematoma on CT scan, W is the greatest transverse diameter of the bleed, AP is the greatest antero-posterior diameter of the hematoma perpendicular to W and 0.523 is a constant factor.
5. Hydrocephalus – refers to ventricular dilatation secondary to obstructed CSF flow, decreased CSF absorption, or a combination of both.
6. Hypertension – elevation of blood pressure. The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure has classified hypertension according to the degree of BP elevation. Stage I patients have a systolic BP of 140 to 159 mm Hg or a diastolic BP of 90 to 90 mm Hg. Stage II individuals have a systolic BP of 160 to 179 mm Hg or a diastolic BP of 100 to 109 mm Hg, whereas Stage III (severe/accelerated hypertension) includes a systolic BP greater than or equal to 180 mm Hg or a diastolic BP greater than or equal to 110 mm Hg.
7. Hypertensive intracerebral hemorrhage – bleeding in the brain caused by high blood pressure.
8. Infarct – refers to subtle loss of gray-white differentiation and/or sulcal effacement on CT (seen in hyperacute stage) which eventually progresses to become a hypodense area (acute/subacute stage) which is limited to the major vascular territory rendered ischemic, with or without involvement of the adjacent border zone.
9. Intraventricular hemorrhage – presence of blood within the ventricular system which can be a complication of hypertensive hemorrhage or it can be due to trauma.
10. Midline shift – is the largest perpendicular distance between distance between an imaginary reference line joining the frontal crest and internal occipital protuberance, and the most shifted point of the septum pellucidum.
11. Subarachnoid hemorrhage – refers to extravasation of blood into the subarachnoid space, 80% of which is caused by ruptured aneurysms.

Methods

This is a retrospective cohort study. The population studied consisted of all patients admitted at the Philippine Heart Center from the period of January 1, 2003 to December 31, 2004, who upon admission, cranial CT scan done revealed findings of hypertensive intracerebral hemorrhage. Included were all charts of patients in this study reveal admitting diagnosis of hypertensive intracerebral hemorrhage either managed medically or with surgical intervention. Excluded were the following: Patients with intracerebral bleed secondary to causes other than hypertension such as trauma, ruptures AV malformation/ aneurysm, tumoral bleed, or impaired coagulation; patients who were initially admitted at our hospital and with cranial CT scan done but eventually transferred to another hospital for further management and patients who were discharged against medical advice.

Prior to collation of data, a data collection form was made with three subdivisions, namely: A. Socio-demographic Profile, containing the name of patient, age, sex, status and occupation; B. Clinical Profile, which included # of years of hypertension, co-morbidities, GCS upon admission, presenting diagnosis at the E.R., management done, length of hospital stay, and outcome of patient, and finally; C. CT Scan Profile, which evaluated presence/absence of midline shift/herniation, estimated hematoma volume, other CT scan findings, serial CT scans (if there are any), and name of the CT reader (Radiologist).

The medical records/charts of 124 patients included in this study were retrieved from the records section of the Philippine Heart Center and by using the data collection form, the following variables were recorded: patient's name, age, sex, status, occupation, # of years of hypertension, co-morbidities, GCS upon admission, presenting diagnosis at the E.R., management done, length of hospital stay, and outcome/status at discharge.

Data Extraction from the CT scan plates

All CT scan plates of 124 patients included in this study were retrieved from the filing area of the Radiology Department of PHC. The following data were collected: estimated hematoma volume, presence/absence of midline shift/herniation, other CT scan findings, serial CT scans done (if there are any), and name of the CT reader.

Estimated Hematoma volume

This is noted from the official CT scan readings and is computed by getting the product of L x W x AP x 0.523

Assessment of Midline Shift

By using a fine-pointed colored pencil (black) and a ruler, midline shift was measured by determining the largest perpendicular distance between an imaginary reference line joining the frontal chest and internal occipital

protuberance, and the most shifted point of the septum pellucidum. By using a piece of paper with a straight edge, measurement was taken and placed parallel to a caliper beside the chosen scanogram and result was recorded. Since manual measurement was done (without the benefit of being exact), the researcher did two trials and she also asked one of her experienced consultant Radiologists to measure the midline shifts in a single trial. Average of the measurements was computed and was recorded in millimeter (mm). All data collected were placed in a master list and eventually used in statistical analysis.

Results

A total of 124 patients' medical charts were reviewed. The socio- demographic and clinical profile is summarized in table 1.The youngest patient was 21 years old female who was a case of a intraparenchymal hemorrhage in the left basal ganglia and the oldest was 97 years old female a case a intracerebral hemorrhage in the right capsulothalamic region.

Table 1. Socio-demographic and Clinical Profile of ICH patients included in the study

Characteristic		Frequency (%)	Mean ± SD
Age			60.161 ± 14.3
Sex			
	Male	71 (57%)	
	Female	53 (43%)	
Status			
	Single	11 (9%)	
	Married	86 (70%)	
	Widow	24 (20%)	
	Separated	2 (2%)	
Occupation			
	Business	26 (27%)	
	Employee	24 (25%)	
	Retired	47 (49%)	
Co-morbidities			
	Absent	42 (33.9%)	
	Present	82 (66.1%)	
Duration of Hypertension			
	Not known HPN	35 (28.2 %)	
	< 2 years	1 (0.8 %)	
	2-5	28 (22.6 %)	
	6-8	7 (5.6 %)	
	9-10	20 (16.1%)	
	>10	33 (26.6%)	
Blood Pressure	(mmHg)		
	Systolic		155.9 ± 37.5
	Diastolic		87.29 ±19.88
Hospital Stay	(days)		10.0 ± 9.26
Management			
	Medical	108 (87.8%)	
	Surgical	15 (12.2%)	
Outcome			
	Recovered	82 (66.1%)	
	Died	42 (33.9%)	

The majority were males (57.3%) than females (42.7%), most were married (69.9%). Mostly were retired(48.5%) while others are employed (24.7%) or self-employed (26.8%). Sixty six percent (66 %) have co-morbidities. Among those with hypertension, the longest duration of hypertension was >10 years (26.6%). Our patients have all clinical diagnosis of hypertensive hemorrhage with a mean hospital stay of 10 + 9 days. There are about 87.8% cases who were managed medically as compared to 12.2 % surgical, with about 66.1% of the total sample remained alive or recovered while 33.9% died. In the CT scan profile (Table 2), we included the radiology findings such as hematoma volume, presence or absence of midline shift/herniation, intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH) and presence of hydrocephalus. We manually computed the hematoma volume and it was found to have a mean of 35.7 ml. Independent predictors of mortality were determined using univariate and multivariate statistical analysis.

Table 2. CT Scan Profile of Patients with Intracerebral Hemorrhage Included in the Study

CT Scan Finding	Frequency (%)	Mean ± SD
Midline Shift/ Herniation		
Present	35 (28.2)	
Absent	89 (71.8)	
Hematoma volume (ml)		35.70 ± 36
Other Findings		
Intracerebral Hemorrhage	15 (30.6)	
Subarachnoid Hemorrhage	24 (49)	
Hydrocephalus	10 (20.4)	

Cranial CT Scan Findings Predictive of Mortality

We recorded the dependent variables as outcome: recovered=0, died=1, and the independent variables such as midline shift: NO=0, YES=1, hematoma volume as 0 =NO, 1=YES, and so with the other CT scan findings of intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH) and hydrocephalus. We entered this variables in a univariate and multivariate analysis to obtain the p value (<0.05 significant result). Results show that among all the CT scan parameters only the presence of subarachnoid hemorrhage is strongly associated with mortality with p-value of 0.039 and Odds Ratio of 3.386.

Table 3. Clinical and CT scan predictors of Mortality among ICH patients

	Recovered N=82	Died N=42	p-value
Age (mean, SD)	58 (13.4)	64 (15.3)	0.033
Male gender	47 (57.3%)	24 (57.1)	NS
Occupation			0.028
Business	17 (20.7%)	9 (21.4%)	
Employee	20 (24.4%)	4 (9.5%)	
Retired	24 (29.3%)	23 (54.8%)	
Presence of Co-morbidities	53 (64.6%)	29 (69%)	NS
Duration of Hypertension (mean, SD)	8.5 (5.7)	10.3 (5.5)	0.029
Systolic BP mmHg (mean, SD)	153 (30.37)	162.2 (48.5)	NS
Diastolic BP mmHg (mean, SD)	87.53 (18.88)	86.8 (22)	NS
Hospital Stay (mean, SD)	12.8 (9.8)	4.57 (4.62)	0.000
Management			NS
Medical	70 (86.4%)	38 (90.5)	
Surgical	11 (13.6%)	4 (9.5%)	
Presence of Midline Shift/ Herniation	21(25.6%)	14 (33.3%)	NS
Volume of Hematoma in mL (mean, SD)	N=19 38.65 (40.58)	N=9 29.44 (24.55)	NS
Other Findings			NS
Intraventricular Hemorrhage	7 (30.4%)	8 (30.8%)	
Subarachnoid Hemorrhage	11 (47.8%)	13 (50%)	
Hydrocephalus	5 (21.7%)	5 (19.2%)	

Discussion

Based on socio-demographic and clinical profile of patients, this study showed that the mean age of the patient population at the Philippine heart center who suffered from hypertensive hemorrhage from the period of January 1, 2005 to April 25, 2006 was 60.2 year. The youngest patient was 21 years old and the oldest patient was 97. Males were noted to be the more affected population than the females with a frequency of 57.3 vs. 42.7, respectively. In related studies, it was shown that 90% of patients with bleed are older than 45 years of age and with a 5-20% higher incidence in males than in females. It was also determined that most of the patients were married (69.9%), retired (48.5%), with co-morbidities (66.1%). Of the co-morbidities present, most of them have long standing hypertension. Chronic hypertension plays a major role since it is a main causative factor for spontaneous intracerebral hemorrhage.

Upon admission, our patient population (based on chart review) had a clinical diagnosis of hypertensive hemorrhage. To confirm the clinical diagnosis, all patient included in this study underwent cranial CT scan procedure with findings of hypertensive intracerebral hemorrhage (HICH) and for which statistical analysis eventually revealed mean hematoma volume of 35.7 ml, 15% intraventricular hemorrhage (IVH) , 19% subarachnoid hemorrhage (SAH) and 8% hydrocephalus. There is a presence of 28.2% midline shift on the sample population with 71.8% having no midline shift at all.

By subjecting the socio-economic and clinical profile of the patient into a univariate analysis (chi-square, p value) for predicting mortality in HICH, it was found out that age (p=0.033), and years of hypertension (p=0.029) are dependent predictors of mortality because both of them have p value <0.05. In the result obtained, although occupation (p=0.028) is statistically significant, it is not a good predictor of mortality because mostly who retired are of old age. Hospital stay (p=0.000) having a significant statistical value however, still is not considered a good predictor because those with shorter stay would likely mean that the patient expired already.

Using the CT scan profile of the patient and subjecting it to a univariate analysis only the presence of SAH (p=0.0358) shows strong association with mortality in HICH patients. Using all the predictors that gives statistically significant result (p=<0.05) in univariate analysis (age, years of hypertension, occupation, hospital stay and SAH) and subjecting it to a multivariate analysis, only the presence of SAH showed a significant result [(p=0.039) Odds Ratio 3.386]. Thus, the presence of SAH in the CT scan findings of the patient with HICH gives a three times higher risk of mortality than those patient without

SAH.

The Glasgow Coma Scale (GCS) was included in the data collection form prior to actual data gathering, however the researcher found out that most of the medical records/ charts of the patients in this study did not contain GCS on admission, hence it was not included in the analysis.

Recommendation

The author wants to emphasize the importance of GCS score of patients who present with neurological deficit at the emergency room be always recorded in the chart for its potential use in the future studies since it is one of the established independent predictors of mortality in HICH.

Conclusion

In conclusion, using the univariate and multivariate analysis, the only strong predictor of mortality on CT scan findings among patient with hypertensive intracerebral hemorrhage admitted at the Philippine heart center is the presence of subarachnoid hemorrhage, having three times higher risk of dying compared to those patients without SAH in the CT scan result.

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Congenital Cystic Adenomatoid Malformation Type II with Associated Cardiac Anomalies

Mary Jane B. Carias, MD, Marissa Orillaza, MD

Many congenital anomalies of the lung in childhood have been described. Included is Congenital Cystic Adenomatoid Malformation also known as Congenital lobar Adenomatosis, Adenomatoid Hamartoma, Pulmonary Adenoma, and Congenital Bronchiolar Malformation in some literature.5 There are nine cases of CCAM diagnosed at the Philippine Heart Center since its establishment. Two of these are rare in as much as they also had associated cardiac anomalies. The first case has an associated Total Anomalous Pulmonary Venous Connection to the Superior Vena Cava and Atrial Septal Defect secundum type while the second case has Atrial Septal Defect, primum type. Both patients underwent lobectomy. The first case also underwent correction of the cardiac anomaly. Both patients were discharged improved. The objective of this paper is to present and describe two unique cases of CCAM with coexisting congenital heart disease in children admitted at the Philippine Heart Center. *Phil Heart Center J 2007;13(2):161-167.*

Key Words: Congenital Cystic Adenomatoid Malformation ■ Congenital heart disease

Congenital Cystic Adenomatoid Malformation of the lung is a multicystic non-functional lung mass accounting for 25% of all congenital lung malformation.[1] Its exact pathogenesis is still uncertain although latest literatures state it is due to fetal maldevelopment of the lung bud between the 6th to 8th weeks of gestation.[2] CCAM has no racial or sexual predilection, although some studies state it is more common in males. It is limited to a single lobe in 95% of cases and bilateral in less than 2% of cases.[3] Eighty percent (80%) are diagnosed before two years of age. The spectrum of this anomaly ranges from asymptomatic lesion to pulmonary compromise. CCAM is usually isolated but in about 10% of cases4 there are associated anomalies, hence, early detection of this entity is very crucial because its prognosis often depends upon the severity of the associated anomaly. Thus, the objective of this paper is to present and describe two unique cases of CCAM with coexisting congenital heart disease in children admitted at the Philippine Heart Center.

Case 1.

The first case is of a one-year old Filipina who presented with dyspnea and cyanosis. She was born preterm to a 32 year old G1P0 mother via caesarean section secondary to myoma uteri. She was tachypneic and dyspneic at birth but was acyanotic. She was confined after birth for two weeks for prematurity and sepsis. She presented with recurrent dyspnea and circumoral cyanosis at three months of age prompting consult with a pediatric cardiologist. Chest X-ray done showed cystic lucencies and bronchopneumonia at the right lower lung (Fig. 1). Chest CT Scan done showed bullous formation at the right lung and shunt anomaly with aberrant vessel connecting to the SVC. Two-dimensional echocardiography revealed Total Anomalous Pulmonary Venous Connection (TAPVC) to the superior vena cava and Atrial Septal Defect (ASD) secundum type. The patient was admitted as a case of Congenital Heart Disease, TAPVC to SVC, ASD secundum type, Bullae right lung field.

On the 13th hospital day, TAPVC correction, ASD patch closure and right lower lung lobectomy were performed. The submitted specimen for histopathology consisted of a spongy lung tissue measuring 8.5 x 2.5x 1 cm with multiple cysts, the largest measuring 2.1 x 2.5 cm (Figure7). Microscopically, it has bronchiolar – like cystic structures lined by ciliated columnar to cuboidal cells (Figure 10). These findings are compatible with Cystic Adenomatoid Malformation of the lung Type II. She was discharged improved and had latest OPD follow – up at 2 years of age, wherein her physical examination was essentially normal except for a faint murmur.

Case 2.

The second case is of a 21 days old boy who presented with dyspnea. He was born to a 34 year old G4P3 (3003), full term via normal spontaneous delivery. At birth, there was note of weak cry and spontaneous respiration.

On his second day of life, patient was noted to have interrupted feeding, tachypnea and severe chest indrawing associated with circumoral cyanosis especially during crying. Due to progressive dyspnea and cyanosis, consideration of a congenital heart disease was made

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upon consultation with a pediatrician. Chest radiograph done revealed cystic lucencies at the right lung with mediastinal structures pushed to the left (Figure 3). He was eventually admitted at East Avenue Medical Center and was placed on mechanical ventilation due to severe dyspnea and cyanosis. He was transferred to the Philippine Heart Center where 2D Echocardiography done showed Atrial septal Defect (ASD), primum type.

On his second hospital day, he underwent right upper lobectomy where intraoperatively, there was a 10 x 8 x 6 cm cystic mass at the right upper lobe occupying almost half of the right hemithorax. The specimen submitted for histopathology revealed a spongy lung lobe with thinned out parenchyma. Cut sections show variably sized cystic spaces, the largest measuring 2.5 x 2.9 cm in diameter. Microscopically, the cysts resemble dilated thin- walled bronchioles separated by normal alveoli (Figure 12). It was signed out as Congenital Cystic Adenomatoid Malformation type II.

On the 5th post-operative day, the patient was extubated but eight hours later, he developed severe tachypnea. He was reintubated and chest tubes were inserted to evacuate hemothorax.

On his 8th post–operative day, patient developed sepsis secondary to ventilator-associated pneumonia. The pneumothorax however was resolved, so the chest tubes were removed. Repeat chest radiograph showed persistence of cystic lucency at the right middle lobe. Abdominal UTZ was done with unremarkable result.

On his 19th post-operative day, he underwent right middle lobectomy, which he tolerated. The specimen submitted for histopathology showed cystic spaces lined by ciliated columnar cells compatible with Congenital Cystic Adenomatoid Malformation Type II (Figure 11). He did not however undergo cardiac anomaly correction. He was discharged improved but was lost to follow–up.

Discussion

CCAM was first described in 1949 by Chin and Tang, but it was Stocker et al. in 1977 who proposed its first classification based upon clinical, gross pathologic and histologic features.6 (Table 1) Stocker has more recently expanded the classification into 5 types7 (Table 2) on the basis of the resemblance to normal anatomical structures from proximal to distal. Internationally, there is only 1 case out of 25,000 – 35,000 births, with only 58 cases seen in an eight year study done in England.8 The US, however, has no data available regarding its frequency. Thorpe – Beeston et al studied 132 cases of CCAM and found that 12% of cases had associated major malformations, and from these 3% had associated cardiac defects.[9] Locally, only two cases were diagnosed with CCAM at the Philippine Children's Medical Center and nine at the Philippine Heart Center. Congenital Cystic Adenomatoid Malformation is seen in the first two years of life in 80% - 85% of cases, [10] but it has also been reported in adults. Although the pathogenesis is still uncertain, it has been postulated that cellular bronchial atresia is the primary event11 while others believe that it is due to maldevelopment of the lung bud in the fetus.

Literatures have conflicting opinions about the association of CCAM and chromosomal abnormalities. While Nyberg, et al. pointed out that CCAM Type II appears to be more associated with other fetal abnormalities and aneuploidy, a recent review of 18 cases of CCAM (9 of whom demonstrated CCAM Type II) by Dumez et al did not reveal a single abnormal karyotype.[12] CCAM is not known to be associated with exposure to teratogens.[13]

CCAM most commonly present with respiratory distress due to the expanding cystic lung mass while others are asymptomatic and later discovered on chest radiograph. Cough, fever, and repeated respiratory infections are the less common presentations. CCAM has no preference for location.[14] Any lobe maybe affected with the following commonly affected in decreasing order of frequency: left lower lobe (LLL), left upper lobe (LUL, right lower lobe (RLL), and right upper lobe (RUL). Some later studies however have observed predilection of the right lung over the left lung for this anomaly.[15] Grossly and microscopically, CCAM presents as cysts of variable sizes composed of terminal respiratory structure of variable sizes which are lined by cuboidal or ciliated columnar epithelium. Table 1 shows the old classification of CCAM by Stocker which is still being used by some researchers in the latest literatures.

Table 1. Comparison of the Three Tyoes of CCAM

CHARACTERISTICS	CCAM Type1	CCAM Type 2	CCAM Type 3
Frequency (%)	75	10 – 15	10
Associated anomalies (%)	8	56	Nil
Cyst size (cm)	3 – 10	0.5 – 3	< 0.5
Mediastinal shift	(+)	Less common	(+)
Predominant epithelium	Ciliated pseudostratified columnar epithelium	Ciliated columnar and cuboidal epithelium	Cuboidal epithelium (minimal ciliation)
Mucous cells	32 %	Nil	Nil
Cartilage	10 %	Nil	Nil
Striated muscle	Nil	12 %	Nil
Presence of intervening pulmonary parenchyma	Yes	Yes	No
Prognosis	Good	Poor	Poor

*Old classification

Recently, Stocker expanded the classification of CCAM mainly based on its resemblance to normal anatomical features.

Table 2. Extended Classification of CCAM by Stocker

Type	Proportional incidence	Gross Appearance	Microscopy	Other features
0 (Bronchial type)	1 – 3 %	Solid; the lungs are small and firm throughout	Bronchial type airways that have cartilage, smooth muscle, and glands that are separated by abundant mesenchymal tissue	Neonates; other malformations; poor prognosis
1 (Bronchial /Bronchiolar type)	60 – 70 %	Large cysts (up to 10 cms.)	The cysts are lined by pseudostratified ciliated cells that are often interspersed with rows of mucous cells	Presentation maybe late; resectable; good prognosis; rare cases show carcinomatous change
2(Bronchiolar)	10 – 15%	Sponge- like composed of multiple small cysts (up to 2 cms) and solid pale, tumor like tissue	The cysts resemble dilated bronchioles separated by normal alveoli; striated muscle in 5%	Neonates; other malformations; poor prognosis
3 (Bronchiolar/ alveolar duct)	5%	Solid	There is an excess of bronchiolar structures separated by air spaces that are small, have a cuboidal lining, and resemble late fetal lung	Neonates; poor prognosis
4 (Peripheral)	15%	Large cysts (up to 10 cms)	The cysts are lined by a flattened epithelium resting on loose mesenchymal tissue	Neonates and infants; good prognosis

Type 0 (most rare) is composed of bronchial-like structures, separated by mesenchymal tissue. It is incompatible with life.[16] Type 1, the large cyst category, presents as a single large cyst frequently with much smaller cyst in the background (Figure 5). It is lined by pseudostratified columnar ciliated epithelium overlying a prominent fibromuscular layer (Figure 8). It is the most common and has the best prognosis.

Type 2 is composed of smaller cysts (Figure 6). It is difficult to distinguish where Type 2 CCAM ends and normal parenchyma begins. The larger cysts are lined by cuboidal to columnar cells; however, most of the lesion is composed of thin–walled bronchiole–like structures (Figure 9). Both the cases presented are comparable with the gross and microscopic description of CCAM Type II (Figure 13). In about 10% of cases, there are associated malformations. Renal anomalies (bilateral renal agenesis), abdominal wall anomalies, CNS defects (hydrocephalus), gastrointestinal anomalies (diaphragmatic hernia, jejunal atresia, tracheoesophageal fistula), and cardiac anomalies and anomalies of the great vessels (VSD, TOF, Truncus arteriosus) are the anomalies associated with CCAM Type II.[16] Of the latest literatures, only one case of CCAM Type II with associated VSD, ASD, and Transposition of the Aorta was reported. This was a case of a patient with Trisomy 18 associated with CCAM Type II.[12] There is no reported case of an associated TAPVC yet. Type II has a worse overall outcome compared to Type I.

Type 3 is the most solid variant. The cysts are innumerable and evenly distributed. They tend to occupy the entire lobe or most of one lung. The microscopic appearance is suggestive of immature lung. It is rare and it carries a poor prognosis due to the hypoplasia frequently involving the other lung segments.

Type IV is a large cyst in the periphery of the lung which is lined by flattened pneumocytes. [17] It has a good prognosis. It is crucial to diagnose the exact type of malformation in order to exclude associated anomalies, as well as the risk of development of malignancy later in life. The two cases presented have clinical and histopathologic findings compatible with CCAM Type II (Table 3).

Table 3. Type II CCAM Compared with The Two Cases

Characteristics	CCAM Type II	Case 1	Case 2
Cyst size (cm)	0.5 – 3	2.5 x 1	2.9 x 2.5 2.9 x 2.5
Associated Anomalies	Yes	TAPVC to SVC ASD, secundum type	ASD, primum type
Mediastinal Shift	Yes	None	Yes
Predominant Epithelium	Ciliated Columnar and Cuboidal Epithelium	Ciliated Columnar and Cuboidal Epithelium	Tall Columnar Epithelium
Cartilage	Nil	None	None
Presence of Intervening Lung Parenchyma	Yes	Yes	Yes
Mucous Cells	Nil	None	None
Prognosis	Poor	Last followed up at 2 years of age	Lost to follow – up

Imaging studies provide a crucial role in the diagnosis of CCAM. Chest X-ray is included in the basic work-up of the child with suspected CCAM. It identifies CCAM of sufficient size to cause clinical problems. The usual appearance is of a mass containing air–filled cysts.[20] (Figure 2) Other radiological signs that maybe evident in

clude mediastinal shift, pleural and pericardial effusions, and pneumothoraces. The two cases presented both had X-ray results fulfilling the radiologic signs of CCAM.

Chest CT scan provides a rapid means of defining the extent of CCAM in all age groups. The typical appearance is of multilocular cystic lesion with thin walls surrounded by normal lung parenchyma.[6] (Figure 4) CT scan of the chest may also outline additional coexisting lesions. In the first case presented, the associated cardiac lesion was appreciated with CT Scan.

MRI is particularly useful in the diagnosis of CCAM. The appearance of the lesion on MRI is determined by the size of the lesion as well as the number and size of the cysts.[20] CCAM usually demonstrates some degree of inhomogeneity due to the multiple cysts. Antenatal UTZ can diagnose CCAM prenatally; however, it cannot distinguish it clearly from other lung lesions such as pulmonary sequestration or lobar emphysema.[20] It is mandatory to perform renal and cerebral UTZ in all newborns with CCAM in order to exclude coexisting renal and CNS anomalies. Echocardiography is also performed in all infants with CCAM to rule out any coexisting cardiac lesions.[20] The two cases presented were referred to PHC primarily due to their coexisting cardiac lesions seen on Echocardiography.

In any child presenting with dyspnea, CCAM is always a strong consideration. However, its signs and symptoms are constitutional and maybe present in other cystic lung diseases. Pulmonary sequestration is among the most common differential diagnosis of CCAM. It is a mass of abnormal lung tissue that does not communicate with the tracheobronchial tree through a normally connected bronchus, and receives its own blood supply from a systemic artery.[18] Congenital Lobar Emphysema is another consideration. This is a localized area of emphysema that presents in early infancy as respiratory distress. Histologically, the parenchyma shows non-specific distention. Bronchogenic cyst is another consideration which is commonly found in the anterior mediastinum or around the hilum. Grossly, the cysts are unilocular , maybe up to 10 cms in diameter and are not in communication with the tracheobronchial tree.[19] Lung abscess is a less common differential diagnosis. It may be difficult to distinguish from any type of lung cyst; however, an abscess often has multiple bronchial communications. Surgical intervention remains the mainstay of therapy for CCAM. The surgical options include fetal surgery, postnatal surgical approaches, and termination of pregnancy. If left untreated, patient can develop pneumothorax, hydrothorax, and recurrent pneumonia leading to demise of the patient. Malignant changes such as rhabdomyosarcoma, pulmonary blastoma, bronchioalveolar carcinoma, and squamous cell carcinoma have also been reported later in life. No specific medical treatment is described for CCAM.[20] Antibiotics are given to children with CCAM complicated by pneumonia. Respiratory support ranging from O2 supplementation to mechanical ventilation maybe required for neonates with respiratory distress. The overall size of the lesion has also been reported as being an important predictor of survival, and one study show 10% to 20% of cases of CCAM can shrink and may even disappear in utero during the 3rd trimester.[21] Poor prognosis is commonly associated with presence of associated anomalies, bilateral lesions, and microcystic lesion. In the absence of any known risk factor, no advice regarding pre-pregnancy preventive measures can be provided. Like with any other child, smoking by and around a child with CCAM is to be avoided.

Table 4. Case Summary of the Two Cases

Case	1	2
Age	1 year old	21 days old
Sex	F	M
Mode of Delivery	CS due to myoma uteri	NSVD
Age of Gestation Completed	Preterm	Full term
Presenting Symptom	Dyspnea	Dyspnea
Lung Involved	RLL	RUL, RML
Associated Cardiac Anomalies	TAPVC to SVC ASD, secundum type	ASD, primum type
Size of Cyst (cm)	2.1 x 2.5	2.9 x 2.5 2.9 x 2.5
Mediastinal Shift	(-)	(+)
Treatment Done	Right Lower Lobe Lobectomy TAPVC Correction	Right Upper Lobe Lobectomy Right Middle Lobe Lobectomy

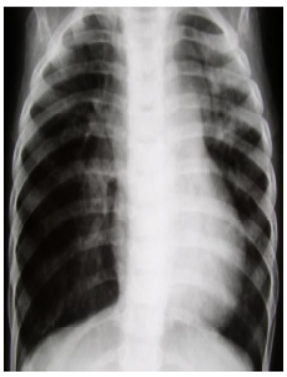


Figure 1. Chest Radiograph of Case 1 showing cystic lucencies in the right lung field

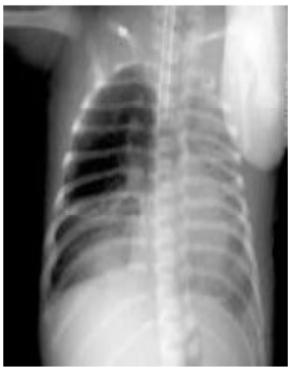


Figure 2. Chest Radiograph of a patient with CCAM. Note the mass containing air – fluid cysts

Conclusion

Congenital Cystic Adenomatoid Malformation, however rare, presents with constitutional signs and symptoms comparable with the more common disease entities. Although rare, it should be entertained in a child who presents with dyspnea and cystic lesion in chest x-ray. Table 4 summarizes the two cases that both presented with dyspnea. With clinical suspicion, radiologic work ups and histopathologic efforts, the more complex anomalies were identified and given proper treatment. Due to the rarity of the reported cases of CCAM Type II, some of the cases may not fit the prototype, yet will still fall under its classification. With early access to imaging modalities and accurate histopathology, cases of CCAM Type II with cardiac anomalies maybe higher than previously reported.

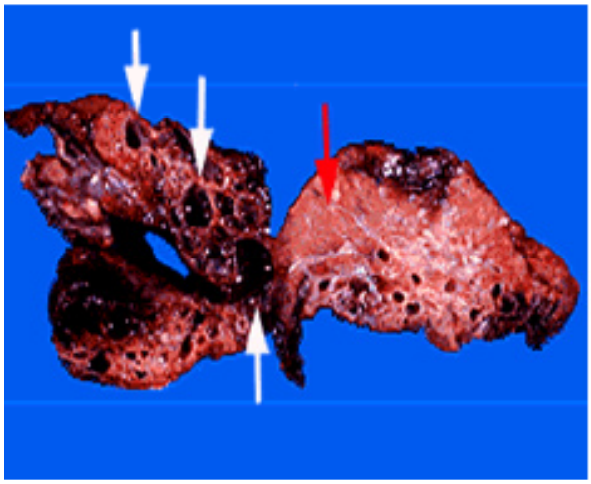


Figure 6. CCAM Type II showing multiple smaller cysts

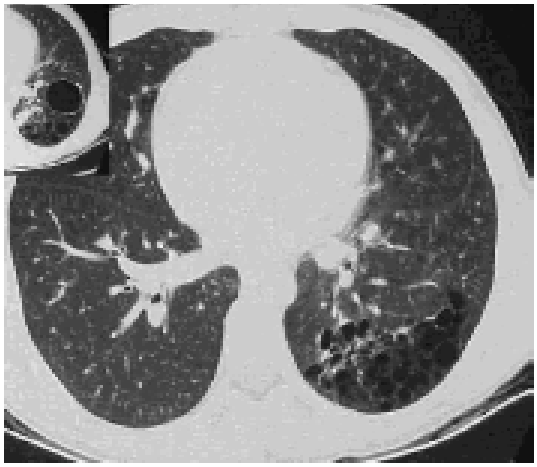


Figure 4. CT Scan of CCAM showing multilocular cysts with thin walls

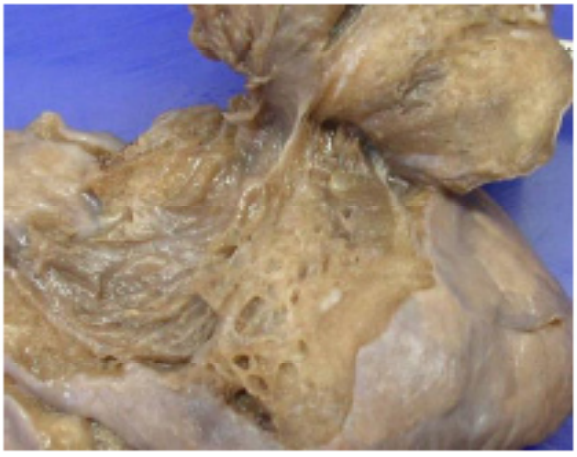


Figure 7. Gross specimen on Case 1 showing multiple smaller cysts

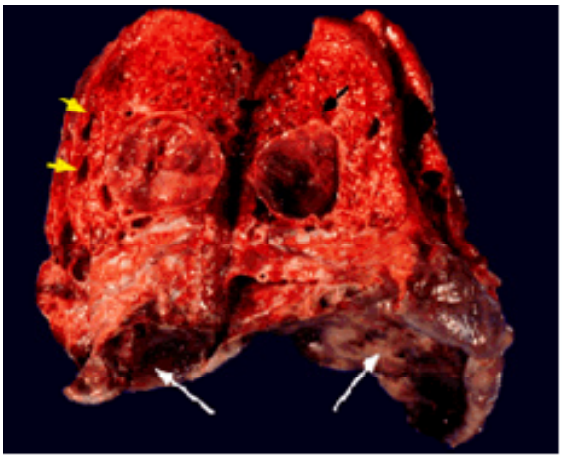


Figure 5. CCAM Type I showing a large cyst surrounded by smaller cysts

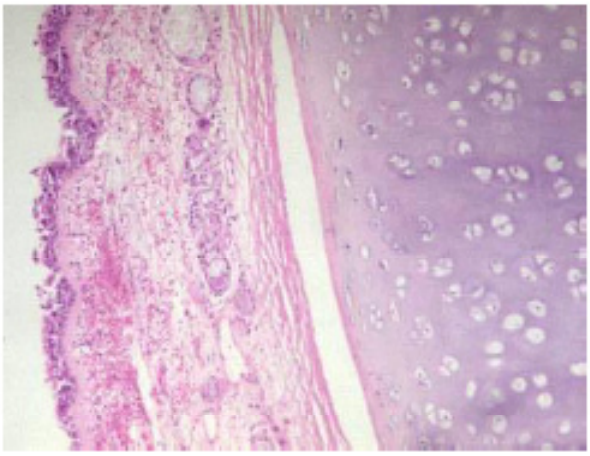


Figure 8. CCAM Type I lined by pseudostratified columnar epithelium and with prominent cartilage (10x magnification)

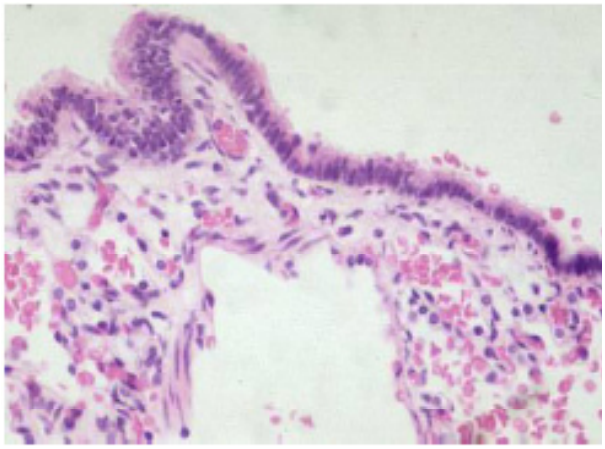
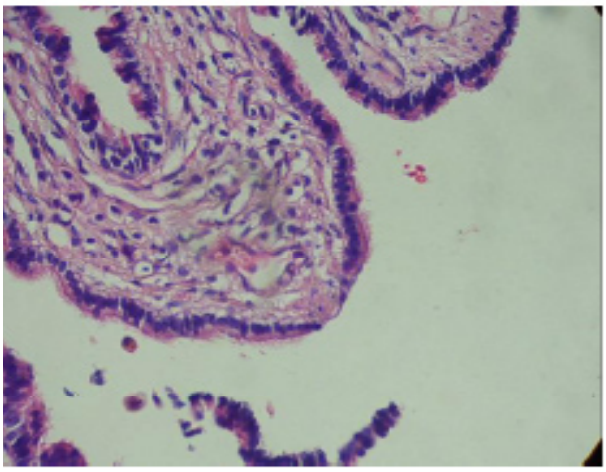


Figure 9. CCAM Type II showing cystic spaces lined by ciliated tall columnar cells (10x magnification)



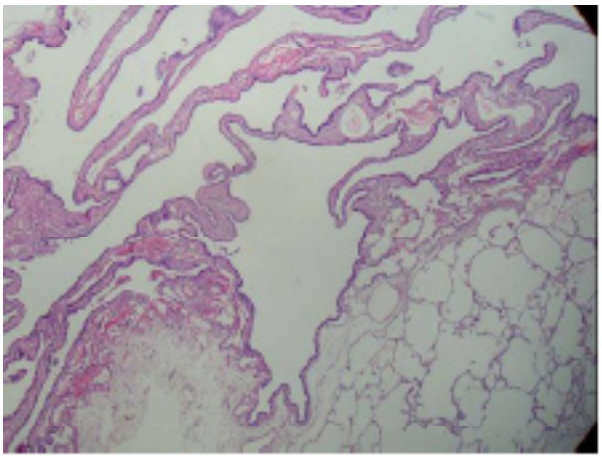


Figure 10. Case 1 showing cystic spaces lined by tall columnar to cuboidal cells (10x magnification)

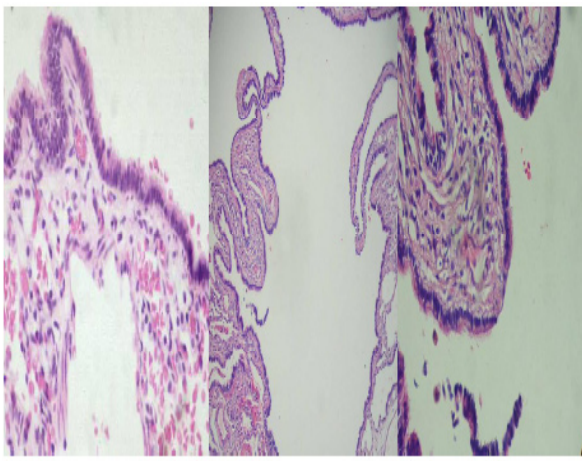


Figure 13. Microscopic Comparison of CCAM Type II and Case1 and 2

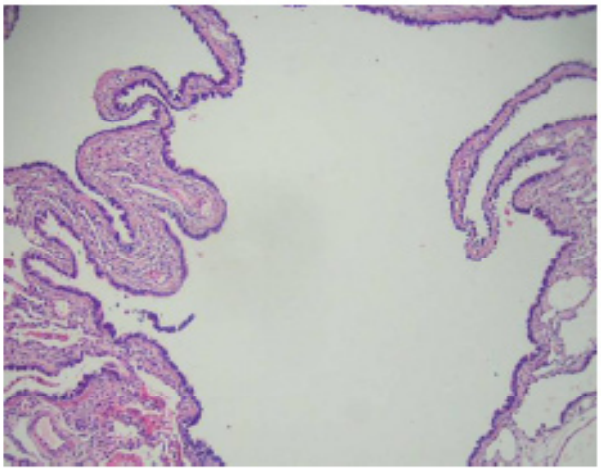


Figure 11. Case 2 taken from R Middle Lobe showing cystic spaces resending dilated bronchioles (10x magnification)

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Recurrent Aortic Graft Infection: Successful Treatment using Omental Flap A Case Report

Melquiedes Marino B. Pua, MD

Recurrent aortic infection graft infection has not previously been reported. We report the case of a 56-year-old male who presented with recurrent fever after aortic graft replacement. A computed tomographic (CT) scan done six months after aortic graft replacement documented a large mediastinal abscess from the brachiocephalic vein down to the subxiphoid process with no signs of leak. A second CT scan was obtained because of recurrent complaints of fever and heart failure symptoms. Evidence of contrast leakage with slight progression in size of the previously noted density in the anterosuperior mediastinum was noted. Aortic graft replacement successfully repaired his aorta, intravenous antibiotics with packing of the cavity around the aorta with omentum eliminated the recurrence of aortic graft infection six months after surgery. *Phil Heart Center J 2007;13(2):168-170.*

Key Words: aortic graft infection ■ omental flap

Case Report

A 56 year old male was admitted due to recurrent episodes of fever after undergoing an emergency aortic valve replacement with placement of aortic graft due to a Thoracic Aortic Aneurysm, Dissecting, De Bakey Type I in 2004. He then had an emergency mediastinal exploration secondary to a massive pericardial effusion with cardiac tamponade six hours after surgery. On the 19th post-op day, he developed surgical site infection for which he underwent debridement of the sternal wound with sternal rewiring. He was discharged on the 33rd post-op day in stable condition with Cotrimoxazole 800mg BID, Amlodipine 10mg/day, and Metoprolol 50mg TID. About three months after discharge, he developed high-grade fever for four days associated with pleuritic chest pain and purulent discharge from the sternotomy site. He underwent sternal wound debridement and was given Vancomycin 500mg q 6hrs for fourteen days. In the succeeding months, he had three other admissions due to the same complaint. Debridement of sternal wound was also done during each admission and IV Vancomycin given. On all these admissions, cultures of blood and wound discharge were positive for Staphylococcus aureus. About one year later, he again had recurrence of high grade fever with discharge from the lower edge of sternotomy site. A thoracic CT scan revealed a large mediastinal abscess. He subsequently underwent mediastinal exploration with extensive debridement of the anterior mediastinum. He was treated with Tazocin 4.5gm q8hrs for 6 weeks with relief of symptoms

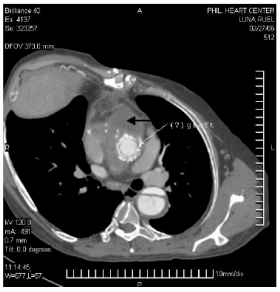

Figure 1

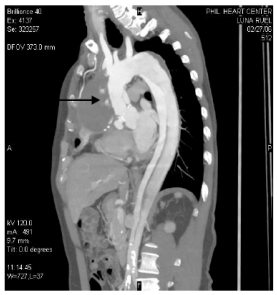

Figure 2

Figure 1 and 2. Large mediastinal abscess overlying the aortic graft from the brachiocephalic vein down to the subxiphoid process

Three weeks after discharge, he had recurrence of fever and wound discharge. Blood and wound cultures were positive for S. aureus. He was treated with Vancomycin IV. He had two other admissions after discharge with the same complaint and all admissions had blood culture growth of S. aureus and treatment with Vancomycin IV done.

Barely ten days after discharge from last admission, fever recurred but now associated with easy fatigability, chest heaviness and shortness of breath. He was readmitted and thoracic CT scan was done which revealed contrast medium leakage with a hematoma formation in the anterosuperior mediastinum measuring 9.8 x 8.5 x 10cm

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in size. He was appraised of a repeat surgical intervention but he refused and hence was continued on Vancomycin 1gm every 12hrs for 8 weeks. He was again discharged afebrile.

Three days prior to admission, he again had fever. Blood culture revealed heavy growth of Staphylococcus aureus. During the course of treatment with vancomycin 1gm IV every 12hours, our patient was blood culture negative by the 7th week. Thoracic CT scan revealed evidence of leakage with progression in size of the previously noted density in the anterosuperior mediastinum.

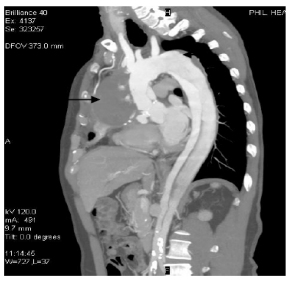

Figure 3

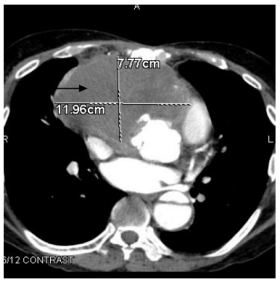

Figure 4

Figure 3 and 4. Dissecting aortic aneurysm (De Bakey1/Stanford A) in the ascending Aorta with evidence of contrast leakage and slight progression in size of the previously noted density over the anterosuperior mediastinum.

He subsequently underwent mediastinal exploration. Intraoperatively, a huge hematoma formation with purulent discharge was noted overlying the aortic graft. Extensive debridement was done, tissue culture later revealed heavy growth of Staphylococcus aureus. Replacement of the infected ascending aorta graft was done, thereafter with placement of an omental flap over the newly implanted aortic graft. The patient recovered fully and was discharge after six weeks of postoperative antibiotics therapy. The patient has remained in good health for six months, with no signs of recurrent graft infection or pseudoaneurysm formation. He then went on to undergo cardiac rehabilitation with no episodes of recurrent infection.

Discussion

The risk of intra-vascular device related infection has increased because of an ever-enlarging pool of patients who have indwelling medical devices implanted for sustaining or improving life. Prosthetic vascular grafts in particular have a long-term incidence between 1 and 6%. Infection risk varies with the location of the graft. The risk of infection for aortic grafts limited to the abdomen is 1% or less. There is no data on the incidence of thoracic aortic graft specifically.

Infection is thought to occur in the intraoperative or peri-operative setting in the majority of infections. Because of this, infection presentation within 2 months of prosthetic graft placement is commonplace. The virulence of the infecting organism may also impact the timing of infection on presentation. In particular, bacteria, such as coagulase-negative Staph may contaminate the graft in the peri-operative period and may not cause symptoms of infection for six months or longer after graft placement. Several risk factors have been identified for vascular graft infection and include emergent surgery, multiple invasive interventions before and after graft placement as was the case with our patient, groin incisions and contiguous infection in the graft area. Disorders of the host are also considered risk factors for graft infection and include diabetes, chronic kidney disease, obesity and immunocompromised conditions.

Fig. 3 and 4. Dissecting aortic aneurysm (De Bakey1/Stanford A) in the ascending Aorta with evidence of contrast leakage and slight progression in size of the previously noted density over the anterosuperior mediastinum.

The management of choice in vascular graft infection remains to be surgery. The optimal method of operative treatment of prosthetic aortic graft infection (PAGI) has been the subject of debate; incidence rates of PAGI are low. Bunt in Cardiovascular Surgery 2001 outlined four tenets that are central to surgical management of graft infections and include: 1.) excision of the graft as a that can potentiate infection, 2.) wide and complete debridement of devitalized, infected tissue, 3) maintain or establish vascular flow to distal bed and 4.) intensive and prolonged antibiotic coverage to prevent secondary graft infection.

Although various strategies have been advocated for mediastinitis following cardiac operations, surgical results for this complication remain a significant concern. The condition is more complicated with replacement of the ascending aorta using a prosthetic graft. Until recently, the role of omental flap transposition in mediastinal infection has been debated. Although no studies have proven its efficacy in ascending aortic graft infection, recent reports on its use in post-operative mediastinal infections have made it a promising approach in the treatment of mediastinitis following graft replacement of the ascending aorta. This case further adds weight to the growing evidence on the use of omental flap transposition in aortic graft infection.

Antimicrobial therapy is a vital adjunct to surgical management. Treatment should be directed against the identified pathogen and guided by the in vitro antimicrobial susceptibility testing results for the isolate. With late-onset infections, current guidelines recommend that antibiotic treatment be deferred until an infective etiology has been confirmed except in the very ill patient. If there is associated bacteremia, particularly if due to S aureus, then a minimum of 14 days antimicrobial treatment is necessary after removal of the device and the first negative blood culture.

In some cases however, no pathogen is recovered and empiric broad-spectrum therapy should be selected to treat many potential nosocomial and skin-colonizing organisms. A regimen including vancomycin is recommended as initial empiric therapy because staphylococci are frequently identified pathogens, and methicillin resistance is common among these strains. Alternative antimicrobial regimens are limited for patients who do not respond or who cannot tolerate vancomycin. Linezolid is a newer agent and offer treatment option for MRSAs and vancomycin-resistant enterococci. Long-term suppressive therapy is a useful treatment option for selected patients who are not candidates for surgery. After a course of parenteral antibiotics, a variety of classes of oral antimicrobials are used. These include beta-lactam antibiotics, Trimethoprim-sulfamethoxazole, fluoroquinolones, clindamycin and fluconazole. A 7% infection relapse was noted in one study.

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Fish Oil Supplementation and the Risk of Ventricular Tachycardia and Ventricular Fibrillation in Patients with Implantable Defibrillators: a meta-analysis

Catherine C. Tan, M.D.

Background --- Sudden cardiac death (SCD) is a very common, and often the first, manifestation of coronary heart disease. Increased attention has been given to the reduced incidence of SCD among people taking omega-3 polyunsaturated fatty acids (omega-3 PUFAs). The protective effect of seems to be due to an anti-arrhythmic effect.

Methods and Results --- This meta-analysis reviewed three journals on the beneficial anti-arrhythmic effect of omega-3 PUFAs in patients with a history of ventricular tachycardia (VT) or ventricular fibrillation (VF) and an implantable cardioverter defibrillator. Three trials involving 1148 patients were included in this review. The population was homogenous. Results of the three studies showed no significant reduction in the number of VF/VT events needing intervention and all-cause mortality. However, there is a trend toward benefit, particularly in the reduction of the mortality rate.

Conclusion --- This meta-analysis supports the provides evidence that a supplement containing long-chain n-3 fatty acids has anti-arrhythmic actions in humans and may reduce the risk of potentially life-threatening arrhythmias in those at risk. ***Phil Heart Center J 2007;13(2):171-173.***

Key Words: Fish oil ■ ventricular arrhythmia ■ sudden cardiac death ■ defibrillator ■ meta-analysis

Sudden cardiac death (SCD) is a very common, and often the first, manifestation of coronary heart disease. The majority are caused by acute ventricular arrhythmias (Brouwer, 2006). A search for preventive measures is needed. During the past years, increased attention has been given to the reduced incidence of SCD among people eating fish or taking supplements of fish oils or very-long-chain n-3 polyunsaturated fatty acids (omega-3 PUFAs). The protective effect of marine omega-3 PUFA on SCD seems to be due to an anti-arrhythmic effect of omega-3 PUFA, an effect mainly demonstrated in in-vitro experiments and in animal studies (Christensen, 2005). In the results of the secondary prevention trial, the Diet And Reinfarction Trial (DART), it showed a significant reduction in total and cardiovascular mortality (both by about 30%) in patients who consumed at least two servings of fatty fish per week after suffering from myocardial infarction. These encouraging reports led us to hypothesize that omega-3 PUFAs might prevent ventricular arrhythmias in high-risk patients.

Objective

The purpose of this meta-analysis was to review whether omega-3 PUFAs has a beneficial anti-arrhythmic effect in patients with a history of ventricular tachycardia (VT) or ventricular fibrillation (VF) and an implantable cardioverter defibrillator, as manifested in decreased need for ICD intervention and decreased mortality.

Criteria For Considering Studies For This Review

Types of studies

Randomized controlled trials (RCTs) in which patients with a history of ventricular tachycardia or ventricular fibrillation were randomized to treatment with fish oil or placebo for the prevention of VF/VT.

Search Methods For Identification Of Studies

We searched the MEDLINE for all articles, journals, and publication from 1985 up to the present, with the search terms "omega-3 fatty acids," "fish oil," "PUFA," "ventricular tachycardia," and "ventricular fibrillation."

Selection Criteria

We have three clinical trials which met the criteria for inclusion. They used omega-3 PUFAs for the prevention of ventricular tachyarrhythmias in patients with a history of ventricular tachycardia or ventricular fibrillation and ICD implantation. All the clinical trials were prospective, randomized, double blind, and placebo-controlled

Data Collection And Analysis

Data was extracted from the studies and recorded. Data included: number of patients enrolled in every group,

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baseline characteristics, inclusion/exclusion criteria, treatment schema and doses, length of follow-up, and the incidence of endpoints. Statistical analyses were performed by statistical package Review Manager 4.2.9,

Data Collection And Analysis

Data was extracted from the studies and recorded. Data included: number of patients enrolled in every group, baseline characteristics, inclusion/exclusion criteria, treatment schema and doses, length of follow-up, and the incidence of endpoints. Statistical analyses were performed by statistical package Review Manager 4.2.9, version 2006. We analyzed dichotomous outcomes using odds ratios with a random effects model.

Results

Three trials involving 1148 patients were included in this review. The population was homogenous. The study by Leaf et al (2005) had the largest proportion of patients noncompliant to the treatment regimen among the three trials. Individually, all three studies showed no significant benefit in either mortality or frequency of ICD intervention. In the study by Leaf et al (2005), those who took fish oil supplement had higher RBC content of EPA plus DHA. There was no significant difference in the number of deaths, but there was a non-significant trend toward a longer time to first ICD event for VT/VF and reduction in total number of confirmed VF/VT events among patients randomized to fish oil compared to placebo. This is also similar to the findings from Brouwer et al (2006) and Raitt et al (2005). Results of the three studies showed no significant reduction in the number of VF/VT events needing intervention and all-cause mortality. However, there is a trend toward benefit, particularly in the reduction of the

Discussion

The result of the three studies did not show a reduction in all-cause mortality and frequency of ICD intervention in high-risk patients for VF/VT, but showed a trend toward benefit. There is evidence that omega-3 PUFAs reduce cardiovascular mortality via an anti-arrhythmic effect. Studies in rats show that a diet high in omega-3 PUFAs reduced the risk of VF during acute ischemia compared with control animals (McLennan, 1993). It changes the spontaneous beating rate of cultured myocardial cells, prevent and terminate drug-induced arrhythmias, and can bind to and inactivate myocardial sodium channels, a class I anti-arrhythmic effect (Kang, 1994). There are four human prospective randomized trials that have shown that supplementation with fish oil is associated with a decreased risk of sudden death without a consistent change in risk of myocardial infarction, the largest of which is the GISSI-Prevenzione trial, which showed significant differences within 4 months in those who were receiving fish oil.

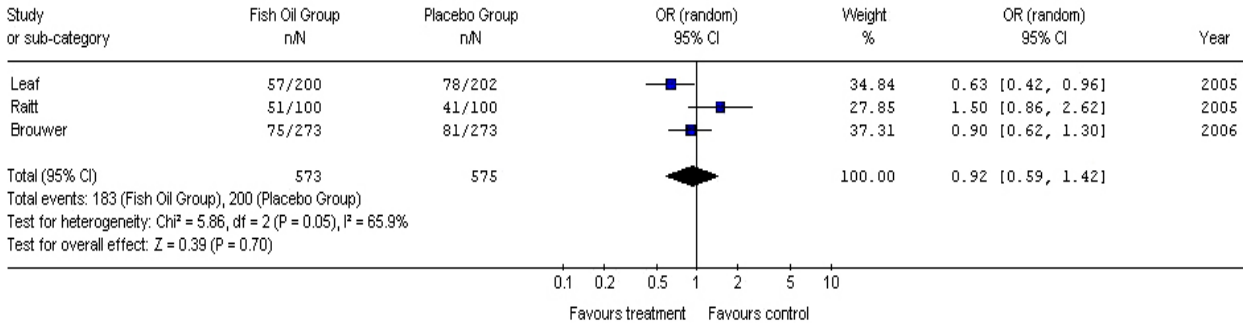

Figure 1. Forrest Plot of Hazard Ratios of Fish Oil Treatment for Frequency of ICD Therapy for VF/VT.

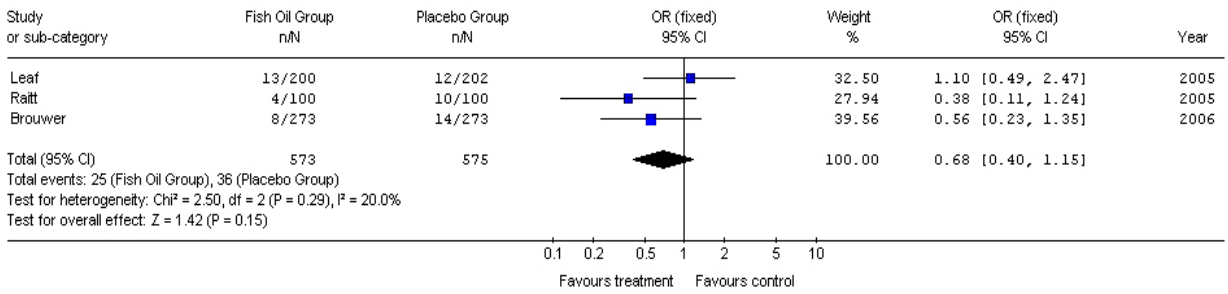

Figure 2. Forrest Plot of Hazard Ratios of Fish Oil Treatment for All-Cause Mortality.

The discordance between these three trials and those of previous studies may lie in the fact that experimental models used ischemic VF as an endpoint, and the cohort and clinical trials used sudden death as an end point. These studies used ICD therapy for VT or VF as the primary end point, and this may not be an ideal surrogate for the risk of sudden death. In addition, prior clinical studies were performed in patients with recent myocardial infarction and relatively well-preserved ventricular function, in whom ischemic VF might be the expected primary cause of sudden death. In contrast, the patients in our study were substantially different in that they had not had a recent myocardial infarction, had significantly reduced left ventricular function, and, perhaps, had a history of sustained ventricular arrhythmia. A hypothesis suggested by Leaf et al. suggests that fish oil may have its most profound anti-arrhythmic effects in the setting of acute ischemia and VF. Although the majority of patients in the study had coronary artery disease, they all had experienced episodes of sustained VT or VF outside of the setting of acute myocardial infarction. The mechanism of arrhythmia in such patients, is unlikely to be ischemic but, instead, was probably myocardial scar-based reentry (Leaf 2005).

Limitations

This meta-analysis is limited by the small number of studies and patients, including the large noncompliant rate.

Conclusion

This meta-analysis supports the evidence that a supplement containing long-chain n-3 fatty acids has anti-arrhythmic actions in humans and may reduce the risk of potentially life-threatening arrhythmias in those at risk.

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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 re-injection 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.

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Department of Education,
Training & Research

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Jerome blaya, MD (Basic ECG Course)
Jona maria mandap, MD (Adult BLS)
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(Heart Educational Advancement for Research And Training)
H.E.A.R.T. Foundation, Inc.

in coordination with

Philippine Heart Center
Department of Education Training and Research

Training Schedules for 2009

East Avenue Quezon City Philippines 1100
Trunkline: 925 - 2401 loc 3903
Telefax: 927 - 9956
Direct line: 441 - 1049
website: www.HEARTPHC.com
www.heartfoundation.multiply.com
E-mail Address: heartphc@yahoo.com

MARCH

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	Mar 10&17, 2009	P 800	Mar 4, 2009
ECG	Mar 11-13, 2009	P 3000	Mar 4, 2009
ACLS	Mar 24-26, 2009	P 3,600	Mar 4, 2009
PALS	Mar 18-20, 2009	P 2000	Mar 4, 2009

APRIL

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	April 13&17, 2009	P 800	April 1, 2009
ECG	April 14-16, 2009	P 3000	April 1, 2009
ACLS	April 28-30, 2009	P 3,600	April 1, 2009

MAY

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	May 12&13, 2009	P 800	May 6, 2009
ECG	May 19-21, 2009	P 3000	May 6, 2009
ACLS	May 26-28, 2009	P 3,600	May 6, 2009

JUNE

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	June 15&16, 2009	P 800	June 3, 2009
ECG	June 9-11, 2009	P 3000	June 3, 2009
ACLS	June 23-25, 2009	P 3,600	June 3, 2009
PALS	June 17-19, 2009	P 2000	June 8, 2009

JULY

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	July 6&13, 2009	P 800	July 1, 2009
ECG	July 7-9, 2009	P 3000	July 1, 2009
ACLS	July 14-16, 2009	P 3,600	July 1, 2009

AUGUST

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	Aug. 11&12, 2009	P 800	Aug. 5, 2009
ECG	Aug. 18-20, 2009	P 3000	Aug. 5, 2009
ACLS	Aug. 25-27, 2009	P 3,600	Aug. 5, 2009
Back to Basics	Aug. 10-11, 2009	P 2,000	Aug. 5, 2009

SEPTEMBER

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	Sept. 7&8, 2009	P 800	Sept. 2, 2009
ECG	Sept. 9-11, 2009	P 3000	Sept. 2, 2009
ACLS	Sept. 22-24, 2009	P 3,600	Sept. 2, 2009
PALS	Sept. 16-18, 2009	P 2000	Sept. 14, 2009

OCTOBER

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	Oct. 8-9, 2009	P 800	Oct. 1, 2009
ECG	Oct. 13-15, 2009	P 3000	Oct. 1, 2009
ACLS	Oct. 27-29, 2009	P 3,600	Oct. 1, 2009

NOVEMBER

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	Nov. 13,17,2009	P 800	Nov. 9, 2009
ECG	Nov. 18-20,2009	P 3000	Nov. 9, 2009
ACLS	Nov. 24-26,2009	P 3600	Nov. 9, 2009

DECEMBER

TRAINING	TRAINING DATE	FEE	REG. DATE
BLS	Dec. 7&8, 2009	P 800	Dec. 2, 2009
ECG	Dec. 9-11, 2009	P 3000	Dec. 2, 2009
ACLS	Dec. 14-16,2009	P 3,600	Dec. 2, 2009

Dates of activities are subject to change without prior notice.

REQUIREMENTS:

- Photocopy of PRC License / TOR
- 1x1 / 2x2 ID picture

F.P.A._08

BASIC LIFE SUPPORT

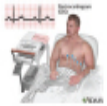
Designed for medical and paramedical hospital and clinical personnel, rescue and emergency response professionals, health care employees, and students of medical and allied medical fields using American Heart Association standards. Participants learn Adult Cardiopulmonary Resuscitation, Rescue Breathing, and Foreign Body Airway Obstruction Management through lecture-demonstration classes and skills exercises and testing. **A must for those who intend to take Advanced Cardiac Life Support training.**

Target Participants: *All Healthcare Providers*
Pre-requisite course: *None*
Total training time: *8 hours*
Training fee: *P800.00*
Validity: *1 year*

BASIC ECG COURSE

A workshop for nurses, caregivers, medical, and paramedical personnel to provide them with a basic understanding of Electrocardiography. Participants learn to take and interpret ECG tracings through lecture-demonstrations and hands-on exercises.

Target Participants: *Paramedical Healthcare Professionals*
Pre-requisite course: *None*
Total training time: *20 hours*
Training fee: *P3000.00*
Validity: *no expiration*



ADVANCED CARDIAC LIFE SUPPORT

Comprehensive and very challenging, the Advanced Cardiac Life Support (ACLS) training course incorporates all the theoretical and practical aspects of resuscitation. It includes lectures on BLS, ECG interpretation, and the pharmacologic administration of critical drugs.

The course also includes small group discussions on basic core cases in ACLS. Participants here tackle the prudent use of algorithms recommended by the American Heart Association (AHA), and American College of Cardiology (ACC) in each of the respective core cases. The course also boasts of skills and testing stations using state-of-the-art training aids where participants are taught intubation, defibrillation, and arrhythmia recognition.

ACLS is for medical and paramedical professionals with a working knowledge in BLS and ECG reading interested in furthering their knowledge with advanced resuscitation principles and techniques.

Target Participants: *Medical & Paramedical Healthcare Professionals*
Pre-requisite course: *BLS and Basic ECG*

Total training time: *20 hours*
Training fee: *P3600.00*
Validity: *2 years*

PEDIATRIC ADVANCED LIFE SUPPORT

Target Participants: Paramedical HealthCare Professionals
Pre-requisite course: *None*
Total training time *16 hours*
Training fee: *P2,000.00*

CARDIO—RENAL Nurse Training Program

A five-week Cardio – Renal Course designed to equip participants with the knowledge and skills necessary to provide dialysis treatment and efficient care to renal patients.

At the end of the course, participants should be able:

- To discuss the principles of Hemodialysis/Peritoneal Dialysis/CRRT;
- To operate hemodialysis machine/cycler/reprocessing machine and water system;
- To practice infection control in dialysis setting;
- To identify the renal patient needs based on a comprehensive assessment;
- To discuss the duties and responsibilities of a dialysis nurse; and;
- To formulate a nursing care plan based on the needs identified.

CARDIO— RENAL Nurse Training Program

Schedule	Registration Date
January 12, 2009 – February 13, 2009	Nov. 5, 2008
February 23, 2009 - March 27, 2009	Jan. 5, 2009
April 27, 2009 – May 29, 2009	Feb. 16, 2009
June 8, 2009 – July 10, 2009	April 6, 2009
July 27, 2009 – August 28, 2009	May 25, 2009
September 14, 2009 – October 16, 2009	July 13, 2009
November 2, 2009 – December 4, 2009	Aug. 13, 2009

Schedules are subject to change without prior notice.

Intended Participants *: Registered Nurses*
Number of Participants *: 25*
Fee *: Php 20,000.00*
(Inclusive of ECG, BLS, ACLS, 2 Scrub suits and 1 laboratory gown)

ON A FIRST COME, FIRST SERVED BASIS.
(Requires at least 25% down payment.)
COMPLETE requirements upon registration.

Requirements:

1. PRC License (photocopy)
2. Resume
3. RENAP Membership (photocopy)
4. 2 1x1 pictures

PEDIATRIC CARDIOLOGY (BACK TO BASICS)

Providing a state of the art diagnosis and management of children with Heart Disease through continued research and education for all health providers

Through the years we have accepted residents in different hospitals to rotate in our institution for 2-3 months exposure in our subspecialty, However, not all institutions can send their residents for training. Because of this, we were to inspired to create and offer you our 3-day extensive and well rounded approach to pediatric cardiology entitled ***Pediatric Cardiology: Back to Basics***.

This course is open to all Pediatricians, Pediatric Residents, Family Physician and General Practitioners who are in direct care to our children with heart disease.

The course include:

- Simplified approach to the diagnosis and management of congenital as well as acquired heart disease.
- Reading and interpretation of 15-lead electrocardiogram and Chest Xray
- Exposure to basic 2D echocardiogram and Cardiac Catheterization.
- Streamlined approach to Cardiac Emergencies
- Hands-on examination and Diagnosis of cardiac patients during the workshop.

We are offering the course to a maximum of 30 participants for a better interaction between you and the faculty.

Pre-requisite course: *None*
Total Training time: *24 Hours*
Training Fee: *P2,000.00*

REQUIREMENTS:

- Photocopy of PRC License / TOR
- 1x1 / 2x2 ID picture

First Come, First Served Basis.
No reservations.

Dress Code: Smart Casual

CLAIMING OF ID's and CERTIFICATES

Tuesdays & Thursdays, 1:00–5:00 PM
9th floor HEART Foundation, Inc. Office

Renal Nurses Association of the Philippines

Calendar of Activities 2009	
Date	**Title of Event**
Jan. 25, 2009 8:00—12:00pm	Predictors of Vascular Access Selection RENAP Accreditation Exam
Feb. 22, 2009 8:00—12:00pm	Art, Science and Spirit of Negotiation and Collaboration RENAP Accreditation Exam
March 29, 2009 8:00—12:00pm	Diabetes Management in Renal Patient RENAP Accreditation Exam
July 26, 2009 8:00—12:00pm	ACCESS ASSESSMENT - Getting Back to Basics RENAP Accreditation Exam
Aug. 30, 2009 8:00—12:00pm	Update on Diabetes: Improving and Achieving Glycemic Control RENAP Accreditation Exam
Sept. 27, 2009 8:00—12:00pm	Anger Management in Dialysis Setting RENAP Accreditation Exam
Nov. 29, 2009 8:00—12:00pm	RENAP ANNUAL CONVENTION RENAP Accreditation Exam

FOR INQUIRIES FOR RENAP CALL/LOOK FOR:
Ms. Raquel Z. Tejada, RN, CRNS
Mark Anthony Panergo
4A Hospital Bldg. Philippine Heart Center
925 - 2401 local 2474

HEART EDUCATIONAL ADVANCEMENT RESEARCH TRAINING (H.E.A.R.T.) FOUNDATION INC.

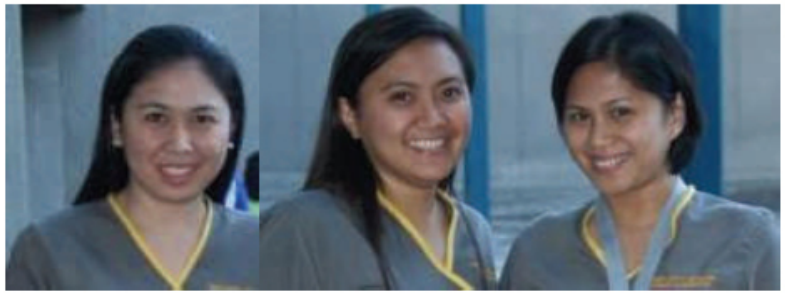
PHILIPPINE HEART CENTER

In partnership with UNIVERSAL WORKER

NCLEX

(National Council Licensure Examination)

REVIEW PROGRAM



Three-month review program

Comprehensive Review Program

Flexible Review Schedule **(Monday to Sunday)**

High Caliber Lecturers *(RN and USRN)*

High end facilities

Easy Terms of Payment

Free assistance *(how to apply for NCLEX exam)*

IELTS

(International English Language Testing System)

English Proficiency Course

*** IELTS-UNLIMITED ***

Best Instructors

Small class size, *(maximum of 15 students per batch)*

Supervised drills and training

Traffic Light System

Conducive learning environment
(air-conditioned rooms, high end facilities)

For inquiries:

Grace Sanguyo /Lloyda Javellana, R.N./ Marion Palencia

Office address: 9th flr. Roofdeck H.E.A.R.T. Foundation Office, Philippine Heart Center

Tel Nos. (02) 441-1049; (02) 925-2401 loc. 3903 **Telefax:02) 927-9956** **website: www.HEARTPHC.com**