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Editorial

What can you do in 60 seconds?

60 seconds is precious. Ask the athletes. At times, winning the gold just take fractions of a second. Ask the marathoner and he will confirm it. In basketball, with the opposite team ahead by one point, one minute seems like an eternity.

What would you do with your one minute? Or the things that you think should accomplish if you're given just one year? What would you do if you're told that you only have 50% chance of surviving beyond five years?

Heart Failure is a most dreaded disease. Data has it that only 50% of people with Heart Failure survives beyond 5 years. Despite modern medicine and despite organized standards of best practices, we fail to improve both the quantity of years of life and the quality of those years. Besides survival rate as an issue, patients spend most of their time inside the wards of the hospital, spending precious amounts of finances, opportunities and time.

But not all is lost, we are still at its tail, not giving up, hopefully catching up. This is the reason for this PHCJ special issue.

In this issue we described the profile of the Heart Failure patient. We needed predictors and parameters - and measurable, because we cannot successfully manage something if we cannot measure it. We measured likewise the adherence to the guidelines and its effects on outcomes. We measured the effects of various therapies on all variants of Heart Failure patients.

Hopefully these 18 papers on Heart Failure guide you and move you to an enhanced and aggressive fight against Heart Failure deaths and disability. It's all about our passion to improve patient outcomes and our commitment to add more life to their years.

Time is essential. It is a gift that hopefully an effective Heart Failure management can reward.

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Clinical Profile of Symptomatic Adults with Congestive Heart Failure Admitted at Philippine Heart Center

Joseph George G. Tamayo, MD; Jesus D. Jorge, MD

Background --- The aim of this paper is to provide Filipino cardiologists and non-cardiologists as well with an initial demographic profile based on descriptive statistics of patients diagnosed with congestive heart failure (CHF).

Methods --- Medical data were gathered using the National Heart Registry Form on admission and completed upon discharge. Descriptive statistics was performed on the demographic data.

Results --- A total of 708 patients were included in the study, 57.7% were men with a mean age of 58.78±16.59; 7l.2% are currently working, 60% had reached a college degree; and 79% have a BMI of less than < 25 kg/m^2. The most common symptom is orthopnea. Hypertension and diabetes comprised the 2 most common risk factors. Nearly a third of the population smokes. Patient presented with pulmonary congestion (75.5%) and bipedal edema (66.5%). CXR showed cardiomegaly in 97.7% and pulmonary congestion in 10.9%. Echocardiogram showed depressed EF in 65.8%. Etiology is CAD in 48.4%. Mortality rate is 11.3% and secondary to progression of CHF(46.8%) and arrhythmia (23%).

Conclusion --- Coronary Artery Disease is identified as the single most important cause of heart failure with high prevalence in the elderly population. The finding of CAD has treatment implications in addition to revascularization. CHF is based on non-specific clinical symptoms and signs in association with evidence of left ventricular systolic dysfunction. Our findings also showed that heart failure can occur in patients with preserved systolic function. Therapy is based on improving symptoms and survival. ***Phil Heart Center J 2016;21(2):1-5.***

Key Words: Congestive Heart Failure ■ Coronary Artery Disease ■ Revascularization ■ Symptomatic Congestive Heart Failure

Heart failure is a devastating disease characterized by frequent hospitalization, poor quality of life and increased mortality rate as high as 20%.[1] Despite decline of other cardiovascular diseases, the incident rate increases with more than 500,000 new cases of heart failure diagnosed annually in the United States alone.[2] This is due to the increase in aging population which are predisposed to heart failure.

Heart failure is predominantly a disease of the elderly. Approximately 6% to 10% of people older than 65 years old have heart failure.[3] The cost reaches billions of dollars annually.

Congestive heart failure has a great impact not only on the patient, health personnel and also to his family and society as well. The risk for developing heart failure is 1 in 5, both men and women[4] and affects approximately 1% of the population at any given time. Their life span averages 4-5 years on diagnosis.[5] Limited data are available regarding heart failure in our country and most of our information comes from the developed countries, where our management are based. In this paper, we report the partial result of the National Heart Failure Registry at the Philippine Heart Center from February 2003 to September 2004 in conjunction with its program manager.

The aim of this study is to provide Filipino cardiologists and non-cardiologists as well with an initial demographic profile based on descriptive statistics of patients diagnosed with congestive heart failure.

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METHODS

This is a retrospective study employing a descriptive design. There were a total of 708 patients with CHF admitted at PHC as defined by the Framingham Criteria and confirmed by ancillary diagnostic procedure. Medical data were gathered using the National Heart Registry Form on admission and completed upon discharge. Descriptive statistics was performed on the demographic data and the results are expressed as the mean ± SD, range or percentage.

RESULTS

A total of 708 patients diagnosed with CHF were included in this study. The basic demographic characteristic of patients with CHF are detailed in Table 1. Majority were men, have a mean age of 58.78±16.59, 71.2% are currently working; 60% had reached a college degree and more than 2/3, (79%) have a BMI of less than 25 kg/m^2.

Figure 1 shows symptoms of CHF. The most common symptom is orthopnea (59%) followed by exertional dyspnea (53%). Hypertension (38.8%) and DM (29.9%) comprises the two most common risk factors. Nearly a third of the population (28%) smokes as seen in Figure 2.

Patients presented with pulmonary congestion (75.5%), Nerve Vein Engorgement 48%), S3 (17.3%), murmurs (66%) and bipedal adema (66.5%). Table 2 details the signs of congestive heart failure.

Ancillary procedures results are shown in Table 3 and 4. Chest x-ray showed pulmonary congestion (10.91%) and cardiomegaly (97.7%). Table 4 showed echocardiographer's finding; half of the patients (51.5%) have LVEDD of more than 5 centimeters and most of them (65.8%) have depressed EF. IVRT is increased in 54.1% of patients, DT is normal in most patients 91.1 %, and have a reversed E/A ratio in 34.7%. mitral valve is noted to be abnormal in 62.1%.

Most common etiology is CAD (48.4) in almost half of the cases.*(Table 4)* Some of them underwent ACB (12.3%) and valve surgery (4%). *Table 5)*

Table 1. Basic Patient Demographics

Variables	Frequency	Proportion
Gender		
N	699	
Male	403	57.7%
Female	296	42.3%
Age		
Mean	58.78 ±16.59	
Occupation		
N	708	
Working	504	71.2%
Non-working	204	28.8%
BMI		
N	464	
<25	370	79.7%
>25	94	20.3%
Education		
N	433	
Elementary	40	9.3%
High School	133	30.7%
College	259	60%

Table 2. Signs of Heart Failure

Variables	Frequency	Proportion
Pulmonary Congestion		
N = 614		
Present	537	75.8%
Absent	77	14.2%
Neck vein engorgement		
N = 708		
Present	338	48%
Absent	370	52%
Apex beat		
N = 673		
Normal	283	42.1%
Displaced	390	57.9%
Cardiac Rhythm		
N = 689		
Regular	500	72.6%
Irregular	189	27.4%
SI		
N = 687		
Normal	301	43.8%
Loud	5	0.7%
Soft	316	46%
Variable	65	9.5%
S2		
N = 687		
Normal	428	63.1%
Loud	52	7.7%
Soft	198	29.2%
S3		
N = 619		
Appreciated	107	17.3%
Not appreciated	512	82.7%
S4		
N = 592		
Appreciated	42	7.1%
Not appreciated	550	92.9%
Murmurs		
N = 708		
Appreciated	242	34%
Not appreciated	466	66%
Abdomen		
N = 668		
Normal	565	84.5%
Ascites	79	11.8%
Hepatomegaly	24	3.7%
Bipedal edema		
N = 708		
Present	471	66.5%
Absent	237	33.5%

Table 3. Chest X-ray Findings

Variables	Frequency	Proportion
Pulmonary Congestion		
N = 623		
Present	68	10.9%
Absent	555	89.1%
Cardiomegaly		
N = 623		
Present	609	97.7%
Absent	14	2.3%

Table 4. 2D Echocardiographic Findings

Variables	Frequency	Proportion
LVEDD		
N = 535		
<5 cm.	240	49.9%
>5 cm.	295	55.1%
Ejection Fraction		
N = 495		
<55%	326	65.8%
>55%	169	35.2%
IVRT		
N = 342		
>63	31	9.1%
68-89	126	36.8%
>89	185	54.1%
DT		
N = 326		
<167	260	80%
167-231	36	11.1%
>231	30	8.9%
LA size		
N = 528		
<3.0	66	12.5%
>3.0	462	87.5%
E/A ratio		
N = 300		
Normal	149	49.7%
Increased	47	15.7%
Reversed	104	34.7%
Mitral Valve		
N = 515		
Normal	191	37.1%
Abnormal	320	62.1%
Prosthetic	4	0.8%
Aortic Valve		
N = 490		
Normal	293	59.8%
Abnormal	194	39.6%
Prosthetic	3	0.6%
Tricuspid Valve		
N = 508		
Normal	249	49%
Abnormal	259	51%
Pulmonary Valve		
N =479		
Normal	307	64%
Abnormal	172	36%

Table 5. Etiology of Heart Failure

Variables	Frequency	Proportion
N = 708		
IHD	343	48.4%
VHD	150	21.2%
CMP	68	9.6%
Congenital Heart Disease	25	3.5%
Arrhythmia	29	4.1%
Uncontrolled HPN	18	2.5%
Others	49	5.5%

Table 5. Intervention

Variables	Frequency	Proportion
N = 708		
Coronary Angiogram	166	2.3%
ACB	87	12.3%
±AB	23	3.2%
TCT	28	3.9%
Valve replacement	24	3.4%
Valve repair	4	0.6%
CHD repair	6	0.8%
Others	39	5.5%

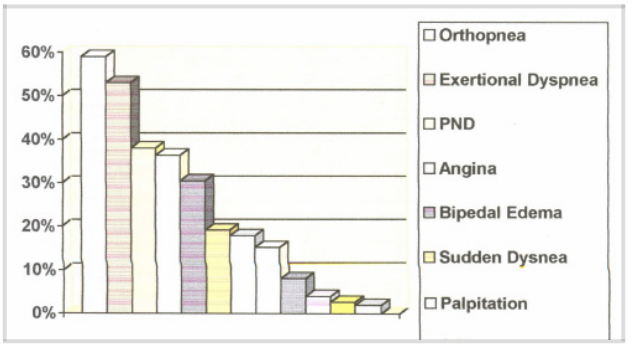

Figure 1. Symptomatic Evidence of Heart Failure

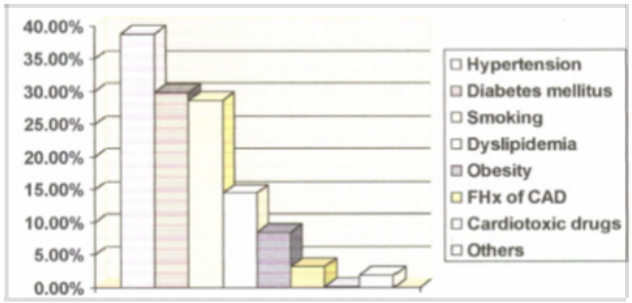

Figure 2. Risk factors of Heart Failure

Commonly given medications were diuretics, glycosides and ACE inhibitors. Followed by beta-blockers. *(Figure 3)*

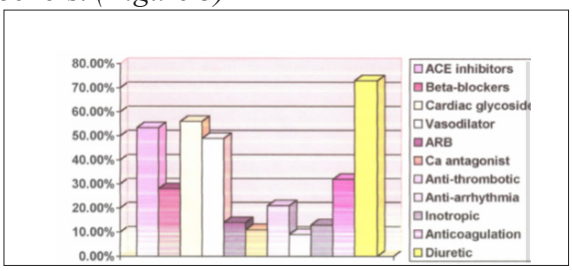

Figure 3. Medications received by heart failure patients

Most of the patients were discharged improved (82.7%). *(Figure 4)* The mortality rate was 11.3%, They died secondary to progression of CHF (46.8%) and arrhythmia (23%). *(Figure 5)*

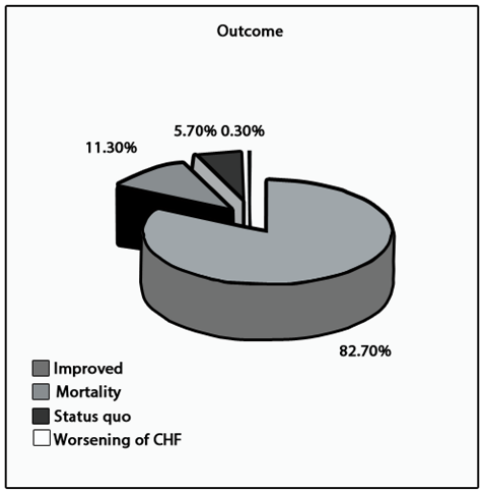

Figure 4. Outcomes of heart failure patients

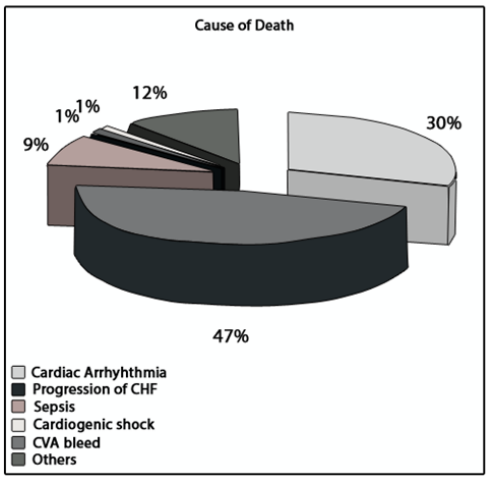

Figure 5. Causes of death among heart failure patients

DISCUSSION

Heart failure is defined as a pathophysiological state in which an abnormality of cardiac function is responsible for failure of the heart to pump blood at a rate commensurate with metabolic requirement, or to do so only from an elevated filling pressure.[6] Congestive heart failure is a clinical syndrome in which heart failure is accompanied by the symptoms and signs of pulmonary and/or peripheral congestion.[7]

In this study, though half of our population falls within the age of 40-70, which is considerably a wide range- a remaining 33.7% comprised only of those patients aging from 70 and above. Truly, that as one individual ages, the more you are predisposed to heart failure. These are related to changes in ventricular function. In addition, risk factors for heart failure are generally not treated aggressively in the elderly, yet elderly patients commonly take medications that can exacerbate the syndrome of heart failure. Coronary risk factors are common in males. Luckily, most of our patients are currently employed or are working. Our figures showed that an abnormal BMI does not correlate in having congestive heart failure since a large number of our patients had a normal BMI. Or abnormal BMI in this set of patients could be associated with wasting syndrome or cardiac cachexia characterized clinically by anorexia, malnutrition, muscle wasting, reduced bone mass and impaired performance in addition to a volume overloaded patients. Majority of the patients have volume overload as they presented with orthopnea, dyspnea, pulmonary congestion and bipedal edema. Although most them presented clinically with pulmonary congestion, radiologically most of them were not noted to have pulmonary congestion. There is a high prevalence of CAD as the etiology of our heart failure patients, and echocardiographic findings of systolic function predominates. A third of our population have a normal left ventricular systolic function with note of increased IVRT in 54.1 % and reversed E/A ratio in 34.7 % which are indices of diastolic dysfunction. Diastolic dysfunction is a major cause of heart failure in the elderly population.

Mitral valve was the one commonly affected, this is secondary to high incidence of RHD coupled with MVP in developing countries. Most of the drugs routinely used are prescribed on the basis of their ability to improve symptoms (diuretics, digitalis) or survival (ACE inhibitor and beta blockers). Angiography was done in 23% of our patients since almost half have CAD as the cause of their heart failure and clinical assessment without angiography underestimates the proportion of patients with coronary artery disease, and fails to identify those who may benefit from revascularization.

Revascularization procedures were done in 16.2% of our patients. Despite improvement in the symptoms of most of our patients, we noted an 11.3% mortality mostly secondary to progression of heart failure and arrhythmia.

CONCLUSION

Coronary Artery Disease is identified as the single most important cause of heart failure with high prevalence in the elderly population. The finding of CAD has treatment implications in addition to revascularization. CHF is based on non specific clinical symptoms and signs in association with evidence of left ventricular systolic dysfunction. Our findings also showed that heart failure can occur in patients with preserved systolic function. Therapy is based on improving symptoms and survival.

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Hospitalization of Heart Failure Patients in the Presence of a Normal Left Ventricular Ejection Fraction Based on ADHERE Registry

Darwin O. Misa, MD

Background --- Heart failure with normal left ventricular ejection fraction (LVEF) has not been studied extensively as heart failure with systolic dysfunction. This study aims to described patients hospitalized for heart failure with normal LVEF based on the ADHERE registry.

Methods --- This is a retrospective-descriptive study. Data from the Acute Decompensated Heart Failure National Registry (ADHERE) database of the Philippine Heart Center as of April 2006 served as the source of the clinical data.

Results --- In the ADHERE Registry, wherein 60 patients are included, 25 patients (42%) have EF ≥40%. These patients were treated with loop diuretic (52%), ACE inhibitors (96%), ARB (12%), Beta blocker (40%), Digoxin (44%) and ASA (36%).

Conclusion --- The ADHERE database clearly indicates that patients with normal ejection fraction is associated with almost one half of hospitalization for heart failure. Patients admitted with heart failure and normal ejection fraction are typically diabetic and non-smoker women. Clinical outcome was favorable for heart failure patients with normal LV ejection fraction. ***Phil Heart Center J 2016;21(2):6-8.***

Key Words: Congestive Heart Failure ■ Left Ventricular Ejection Fraction (LVEF) ■ ADHERE Registry

Congestive heart failure (CHF) is a major cause of death and disability. Mortality rates approach 20% per year inspite of current medical therapy, and nearly one million patients are hospitalized with CHF per year in the USA alone. Another two million are hospitalized annually with CHF as a secondary diagnosis.[1] The clinical characteristic of patients with CHF is variable. Several hospital-based reports have documented that a high proportion of patients with CHF have normal left ventricular (LV) systolic function,[2] and and 4 different epidemiological investigations further confirmed that nearly half of CHF subjects in the community have normal LV systolic function.[3] The cause of HF in these patients is thought to be related to LV diastolic dysfunction. Further stratification of CHF subjects into those with LV systolic dysfunction and those with predominantly LV diastolic dysfunction has been suggested because of the important therapeutic and prognostic differences between thse 2 subsets of CHF patients.[2] Heart failure with normal LV ejection fraction has not been studied as extensively as heart failure with systolic dysfunction. Data are lacking regarding management, clinical outcomes, and predictors of mortality for patients with heart failure and normal systolic function.

This study aims to describe the clinical features, management and outcome of patients hospitalized for acute decompensated heart failure with a normal left ventricular ejection fraction.

METHODS

This is a retrospective-descriptive study. Data from the Acute Decompensated Heart Failure National Registry (ADHERE) database of the Philippine Heart Center as of April 2006 served as the source of the clinical data. These data

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include demographic information, medical history, baseline clinical characteristics, initial evaluation, treatment received, procedures performed, hospital course and patient disposition. Patients hospitalized with a primary diagnosis of acute heart failure and found to have normal LV ejection fraction (>40%) were included in the study. A hospitalization was attributed to heart failure if there was evidence of clinical signs and symptoms of heart failure. Patients with a secondary diagnosis of heart failure were excluded.

Statistical Analysis. Data from the ADHERE database were used for retrospective analysis of clinical characteristics, treatments, and outcomes for patients with acute episode of heart failure in the presence of a normal systolic function based on the availability of LV ejection fraction assessment during hospitalization. Data were described as mean, standard deviation, frequency and percent distribution.

RESULTS

Left ventricular ejection fraction was qualitatively determined during hospitalization in 52 of 60 patients taken from ADHERE registry. In this population, 25 (42%) patients had >40% LV ejection fraction (*Table 1*).

Demographics and clinical characteristics of the patients are shown in Table 2. Most of the patients were women, diabetic, and has prior history of heart failure. A history of hypertension (52%) and coronary artery disease (36%) were also present. Only 28% of the population was smoker. Dyspnea (96%) and fatigue (96%) were the common symptoms (*Table 3*). Rales was noted in 84% of patient which was confirmed to have pulmonary congestion on chest x-ray (88%). In addition, peripheral edema and atrial fibrillation occurred more often while hemoglobin level was noted to be low. Most of the patients were maintained on loop diuretic (40%) and Digoxin (36%) while only 20% was given ACE inhibitor (*Table 4*). During hospitalization, the use of oral therapies for heart failure increased relative to the use before hospitalization, especially of ACE inhibitor (96%). The use of intravenous diuretic was high while inotropic was only used in 4% of the patients who presented with hypotension. (*Table 5*) Clinical outcomes during hospitalization (*Table 6*) showed 20% admission to ICU with average length of ICU stay of 7-8 days. Most of the patients were discharged improved and no mortality was noted.

Table 1. Number of Patients with Normal LV Ejection Fraction

LV Ejection Fraction	N=60
≥40%	25 (42%)
<40%	27 (45%)
Not determined	8 (13%)

Table 2. Demographic Characteristics and Medical History

LV Ejection Fraction	N=25
Women (%)	60
Hypertension (%)	48
CAD (%)	36
Diabetes (%)	56
Chronic Renal Insufficiency (%)	8
History of heart failure (%)	56
Prior myocardial infarction (%)	16
Smoking (%)	28

Table 3. Clinical Presentation

LV Ejection Fraction	N=25
Dyspnea (%)	96
Fatigue (%)	96
Rales (%)	84
Peripheral Edema (%)	52
Systolic BP	110 ± 22
Diastolic BP	70 ± 17
Heart rate	92 ± 28
Atrial Fibrillation (%)	32
Congestion on CXR (%)	88
LV Ejection Fraction	63 ± 8
Serum Hgb	126 ± 22
Serum crea	97.28 ± 55
Serum Na	139 ± 7

Table 4. Medications before hospitalization

Medications	N=25
loop diuretic (%)	40
spirinolactone (%)	16
ACE inhibitor (%)	20
ARB (%)	12
Nitrate (%)	16
Beta-blocker (%)	16
Digoxin (%)	36
Warfarin	8
Clopidogrel	8
Aspirin (%)	24
Statin (%)	8

Table 5. Medications during hospitalization

Medications	N=25
loop diuretic (%)	52
spirinolactone (%)	12
ACE inhibitor (%)	96
ARB (%)	12
Nitrate (%)	32
Beta-blocker (%)	40
Digoxin (%)	44
Warfarin (%)	12
Clopidogrel	20
Aspirin (%)	36
Statin (%)	4
IV diuretic (%)	80
Inotropics (%)	8

Table 6. Clinical Outcome during Hospitalization

Medications	
Admitted to ICU (%)	20
Length of ICU stay (Mean, days)	7.75
Asymptomatic at discharge (%)	72
Mortality (%)	0

CONCLUSION

The ADHERE database clearly indicates that patients with normal ejection fraction is associated with almost one half of hospitalizations for heart failure. Patients admitted with heart failure and normal ejection fraction are typically diabetic and non-smoker women. We also observed the similarity of presentation for patients with HF and either normal LVEF or systolic dysfunction. For the treatment, ACE inhibitor was noted to be under used before hospitalization while intravenous diuretic was used in the vast majority of admissions. Clinical outcome was favorable for heart failure patient with normal LV ejection fraction.

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Blood Pressure Study Among Mortality in Heart Failure Patients

Mary Jennifer V. Dimayuga-Mendoza, MD; Jesus Jorge, MD

Background --- Blood pressure, a readily available vital sign taken during hospital admission has been identified as a key factor in the development of heart failure. Separate relations of systolic blood pressure, diastolic blood pressure and pulse pressure were associated with mortality among heart failure patients seen upon admission of patients at the Emergency Room of our institution. The objective of this study is to determine the value of blood pressure as a predictor of mortality among patients with heart failure.

Method --- This is a cross-sectional study done at the Philippine Heart Center. Included in the study were patients with Class III Heart Failure seen at the Emergency Room of our institution from April to November 2006.

Results --- The mean SBP among survivors was 121 mmHg while the mean DBP was 77 mmHg and 48 mmHg for the mean pulse pressure. On the other hand, mean SBP for mortality was 109 mmHG, mean DBP 60 mmHg and mean pulse pressure was 30 mmHg.

Conclusion --- This study focused only on the BP and its components in association with mortality of heart failure patients in the hope to use blood pressure as a predictor of mortality. The study showed a direct relationship between age and mortality among heart failure patients as well as an association between mortality and both systolic and diastolic blood pressure. ***Phil Heart Center J 2016;21(2):9-12.***

Key Words: Blood Pressure ■ Heart Failure

Blood pressure, a readily available vital sign during hospital admission has been identified as a key factor in the development of heart failure. Separate relations systolic blood pressure, diastolic blood pressure and pulse pressure were correlated with mortality among heart failure patients seen upon admission of patients at the Emergency Room of our institution.

METHODS

This is a cross-sectional study aims to determine the value of blood pressure as a predictor of mortality among patients with heart failure; to determine the association of blood pressure with age; and the association of blood pressure with the cardiac cause of death.

Included were patients in Class III Heart Failure seen at the Emergency Room from April to November, 2006. Records of all patients who were listed in the heart failure registry from April to December 2006 were reviewed. All heart failure mortalities during this period were also included in the study. Blood pressure on admission at the ER as well as baseline characteristics namely age, sex, etiology of heart failure (coronary artery disease, valvular heart disease, congenital heart disease, etc.) and presence of co-morbid conditions are presented. The subjects were divided into two, namely: mortalities from heart failure (Group A) and those who were managed and discharged improved from pulmonary congestion (Group B). Both groups were further divided according to age: a. 19-39; b. 40-59; c. ≥60 to further determine the association of blood pressure with age. Blood pressure and its components were correlated between Groups A & B. Analysis of data was done using Fisher Exact Test to determine the significance of each co-morbidity in relation to death caused by heart failure. The *T* test was used to analyze the association of age with mortality caused by heart failure as well as the association of blood pressure and its components with age. To adjust

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the factors between subjects' age, univariate analysis of variance was used.

RESULTS

A total of 318 adult subjects age 19 and above were included in this retrospective study with mean age 56 ± 17 yrs The subjects were divided into mortality and survivors, 94 patients belonged to group A (mortality) and 224 belonged to Group B (survivors). The 5 causes of heart failure identified were CAD (72%), valvular heart diseases (23%), congenital heart disease (3%), cardiomyopathy (2%) and atrial myxoma (0.9%). Figure 1 shows the distribution of heart failure patients seen at our ER according to cause. One hundred thirty-three (42%) were females and 185 (58%) were males. The subjects were also divided according to age group and were classified as early adulthood, adulthood and elderly. Majority of the heart failure patients seen at the Emergency Room of our institution were elderly, aged 60 and above, Table 1 lists the number of patients per age group.

The co-morbidities of the subjects are shown in Table 2. Hypertensive cardiovascular disease (65%) is the most common co-morbidity followed by Diabetes (29%) and Dyslipidemia (18%). Other co-morbidities were cerebrovascular and Peripheral Vascular Disease, chronic obstructive pulmonary disease and chronic kidney disease.

The Mean SBP among Group B (survivors) was 121 mmHg while the mean DBP was 77 mmHg and the mean pulse pressure was 48 mmHg. While among Group A (mortality), the mean SBP was 109 mmHg, mean DBP was 60 mmHg and mean pulse pressure was 30 mmHg. In this study, the gender difference among the heart failure patients was not associated with mortality. This study has also shown a direct relationship of age to mortality among heart failure patients, with the most number of mortality (45%) in the elderly group while mortality in the adult age group and early adult age group were 35% and 20%. By using the Fisher Exact Test, the study showed that the presence of Hypertensive Cardiovascular Disease (0.014)

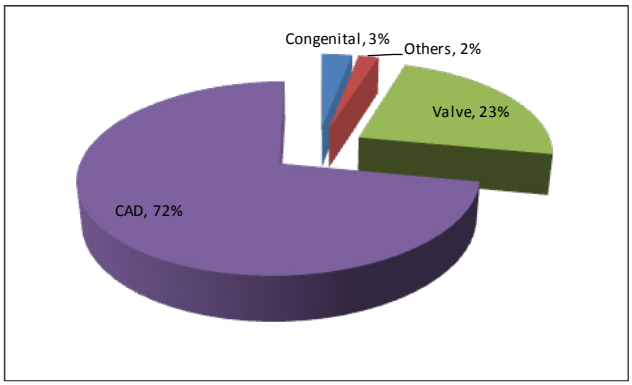

Figure 1. Distribution of Heart Failure Patients at PHC-ER According to its Cause

Table 1. Distribution of Heart Failure Patients at PHC-ER According to Age Group

Age Category	Age in years	Total
Early adulthood	19-39	63
Adulthood	40-59	110
Elderly	≥60	110

Table 2. Co-morbidities of Heart Failure Patients

	Mortalities n = 94	Survivors n=224	P value
HCVD	34	112	0.014
Dyslipidemia	2	39	NS
DM II	19	45	0.00
COPD	2	3	NS
CVD/PVD	3	4	NS
CKD	4	1	NS

HCVD - Hypertensive Cardiovascular Disease; DM II - Diabetes Mellitus Type II; COPD - Chronic Obstructive Pulmonary Disease; CKD - Chronic Kidney Disease

Table 3. Mean Blood Pressure of Mortalities and Survivior

	Mortalities n = 94	Survivors n=224
Mean SBP	121	109
Mean DBP	77	60
Mean Pulse Pressure	48	30

and Diabetes Mellitus (0.00) predisposes heart failure patients to death. Other co-morbidities such as COPD, CVD/PVD and CKD are not predisposing factors for mortality among heart failure patients in this study. While other studies found a strong association of SBP and PP with mortality among heart failure patients, this study showed that SBP and DBP as well as the age of an individual are the factors that are associated with mortality among heart failure patients. The lower the systolic and diastolic blood pressure, the greater the risk of mortality among these patients.

DISCUSSION

The signs and symptoms of heart failure are common reasons for ER consult at our institution. It is also one of the most common causes of mortality among patients admitted. There is an association with age and mortality among the subjects. There were 52 (55%) deaths in the elderly group (≥60 yrs) compared to 28% (26) in the adult age group and 12% (15) in the young adult group. This can be attributed to several age-related changes in the elderly such as increased arterial stiffness and changes in ventricular function.

Coronary artery disease being present in majority of the patients in both groups is mainly due to atherosclerosis which then increases arterial stiffness. This is initiated by presence of atherosclerotic plaques that triggers inflammatory mediators in the intima of the blood vessels which starts the endothelial damage causing the destruction of elastic fibers in the Tunica media and subsequent stiffness of the vessel wall which places a great burden to the heart as hypertension and heart failure. Coronary artery disease was identified as the major cause of heart failure in our study group. Dyslipidemia on the other hand is the most important and most potent risk factor for atherosclerosis in general and coronary heart disease, though it failed to show a direct association with mortality among our study group. Disorders of lipoprotein metabolism are mainly from too much exogenous intake and rarely from inborn metabolic defects. Diabetes Mellitus was was likewise found to be strongly associated with mortality among heart failure patients. Several pathophysiologic factors causing vascular disease among patients with diabetes. First, it alters the function of the vascular endothelium, smooth muscle cells and platelets promoting atheroma formation. Secondly, hyperglycemia, increased FFA and insulin resistance, all of these decrease the bioavailability of NO secreted by the vascular endothelium causing impaired vasodilator function of the endothelial cells promoting atherogenesis and arterial thrombosis which again leads to arterial stiffness and subsequent heart failure.

Previous studies have yielded different results regarding the effect of blood pressure on the general population and no study have investigated the association of a low blood pressure with mortality in this group of patients and yet most medications we give our heart failure patients lower blood pressure.

Review of Literature: The Framingham Heart Study is the largest trial among patients with heart failure. From this study, several studies were made examining long term associations of systolic, diastolic and pulse pressures with heart failure, and concluded that the systolic and diastolic blood pressures conferred the greatest risk for congestive heart failure. With these studies, the pulse pressure helped the authors identify hypertensive patients who are at high risk for developing heart failure and who are candidates for aggressive BP control with therapies that will improve arterial compliance. Despite these, there is still a big number of patients coming at our ER for symptoms of heart failure and the only thing a physician can do is to improve quality of life and prevent mortality among these individuals. Gheorghiade and Fonarow[3] also did a study on systolic blood pressure as a predictor of mortality in heart failure patients but included only those subjects with coronary artery disease. Several studies on predicting mortality among heart failure patients were done during the last 5 years. Fonarow et al. made a study in 2005 and used demographics, medical history, physical examination, laboratory examination and heart failure history as factors for risk stratification for in-hospital mortality in acutely decompensated heart failure

patients. They came up with 7 variables namely heart failure cause, heart rate, blood pressure, serum sodium, intraventricular conduction time, LVEF and peak oxygen consumption to stratify patients into low, medium and high risk. In our setting, other causes of heart failure namely congenital, valvular and other heart diseases namely cardiomyopathy and those due to malignancy were also included.

CONCLUSION

This study focuses only on the BP and its components in association with mortality of heart failure patients in the hope to use blood pressure as a predictor of mortality. It showed a direct relationship between age and mortality among heart failure patients as well as an association between mortality and both systolic and diastolic blood pressure but not the pulse pressure which was demonstrated by other authors in earlier studies. Our study group was also found to have coronary artery disease as the most common cause of heart failure followed by valvular heart disease. Hypertensive cardiovascular disease and diabetes mellitus were identified to play a big association with mortality among heart failure patients.

RECOMMENDATION

A study on the possible predictors of mortality among heart failure patients using readily available entities (laboratory data, LVEF) can be pursued in the future if adequate recording of all heart failure patients in a registry is done to predict in-hospital morbidity as well as mortality. A risk stratification model can be derived from these predictors which may be used as a guide in the management and prognosis of these individuals.

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The Association of QT Dispersion with the Development of Congestive Heart Failure in Post Acute Myocardial Infarction Patients at the Philippine Heart Center

Rowena Tianero-Rocha, MD; Sylvie Gunigundo, MD; Ma. Belen O. Carisma, MD

Background **---** QT dispersion may be influenced by the extent of myocardial damage after myocardial infarction. On the premise that this scarred myocardium is a risk factor for the development of heart failure, the measurement of QT dispersion then can in a way be used to predict if patients post infarction would eventually go into heart failure. This study was conducted to assess the association of QT dispersion with the development of congestive heart failure in patients one year after acute myocardial infarction at the Philippine Heart Center from January 1, 2011 to March 31, 2012.

Method **---** This is a prospective cohort study involving adult patients admitted for acute myocardial infarction (ST or Non-ST elevation) at the Philippine Heart Center from January 1, 2011 to March 31, 2012 presenting within a week of symptoms. QT dispersion were determined from their first electrocardiograms and correlated with the development of heart failure using the Framingham Criteria one year after the event.

Results **---** Eighty-nine patients were included in the study with a mean age of 56.30 ± 11.58 years. There was no association of QT dispersion with the development of heart failure one year after myocardial infarction. The different patient characteristics including comorbid conditions showed no significant association with the development of heart failure after one year. Low ejection fraction and prev ous history cerebrovascular disease significantly correlated with adverse outcomes post MI (p value = 0.015 &0.021 respectively).

Conclusion **---** Development of heart failure after one year was not associated with QT dispersion in post MI patient. A longer follow-up period is thus recommended to better assess the association of QTd with heart failure. ***Phil Heart Center J 2016;21(2):13-17.***

Key Words: QT Dispersion ■ Congestive Heart Failure ■ Acute Myocardial Infarction

Heart failure is a progressive disorder heralded by an index event that damages the cardiac muscles or disrupts the myocardium's ability to generate force preventing it from contracting adequately.[1] This index event may be acute in onset as in the setting of an acute coronary syndrome or gradual as in chronic pressure overload in chronic hypertension. Either way, the net effect is a progressive decline in the ability of the heart to pump blood.

Acute myocardial infarction is one of the more well studied causes of heart failure. A surveillance study in Eastern Finland using non-invasive data reported coronary artery disease as the etiology in 61% of cases of heart failure.[2] It has been said that the infarcted area is a region of variable homogeneity, hence, a substrate for arrhythmogenesis. This can be reflected in the 12 lead electrocardiogram as QT dispersion. Extent of myocardial damage after myocardial infarction may be reflected in the ECG as QT dispersion.[3] The QT interval in a 12 lead electrocardiogram (ECG), measured from the beginning of the QR complex up to the end of the T wave, represents ventricular repolarization. QT dispersion (maximum QT interval minus minimum QT interval) was originally proposed as an index of the spatial dispersion of ventricular recovery times.[4] It has been suggested that increased QT dispersion predicts the risk of ventricular arrhythmia early in the course of the acute myocardial infarction.[5] Regional electrical in homogeneity is the cornerstone for

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the development of reentrant ventricular tachyarrhythmia in these myocardial infarction patients. Homogeneity of the myocardium, which may be accompanied by increased or decreased dispersion of the ventricular recovery times and prolongation of repolarization, can be measured by QT dispersion.

Over the past 10 years, QT dispersion as a measure of cardiac electrical heterogeneity has been shown to be of prognostic value in many common medical conditions: Long QT Syndrome, Hypertrophic Obstructive Cardiomyopathy and Dilated Cardiomyopathy, to mention some. As an index of cardiac dysrhythmia, QT dispersion may be a prognostic guide in patients with AMI who eventually develop congestive heart failure. Christian Schneider et al. in his article mentioned that QT dispersion may be determined by the extent of viable and scarred myocardium post MI. QT dispersion of <70ms had a sensitivity of 85% and a specificity of 82% to predict viable myocardium in the infarct region.[6] Larger infarcts are thought to bring about larger amounts of fibrous tissue influencing the duration and homogeneity of repolarization. These larger infarcts are likewise accompanied by increased mechanical stretch or dilatation of the affected ventricle potentially increasing repolarization inhomogeneity; hence, leading to longer QT dispersion values.

We hypothesized that the presence of QT dispersion is associated with the development of congestive heart failure after myocardial infarction. Through this study, we aim to determine the QT dispersion of these patients as well as the incidence of congestive heart failure one year after the index myocardial infarction.

METHODS

This is a prospective cohort done at the Philippine Heart Center. Adult patients admitted for acute myocardial infarction (ST or Non-ST elevation) from January 1, 2011 to March 31, 2012 were screened for eligibility for the study. Inclusion criteria is as follows: patients above 18 years old admitted for acute myocardial infarction presenting within the first week of symptoms. The following were excluded from the study: patients previously diagnosed or with a history of cardiac dyssrhythmia from any cause, those with heart failure symptoms prior to the acute myocardial infarction and those on treatment for heart failure. Patients with pacemakers were also excluded from the study. Sample size computed was n= 87 at 95% confidence level, 20% relative error and assumed average rate of congestive heart failure of 23% at 28 days and 36% at 5 years, as presented in the paper of Incidence of Heart Failure after Myocardial Infarction: is it changing over time? By Jens P. Hellermann[8] from the American Journal of Epidemiology 2003. Those eligible were asked to sign a written consent for participation in the study. This study was approved by the Institutional Ethics Review Board (IERB).

Pertinent data were obtained from the patient's medical chart and interview of the subject or his accompanying relative/watcher. Manual reading of the ECG taken at the ER on the day of admission was done by an independent reader. QT dispersion, defined as the difference between the longest ard shortest QT interval in the 12 lead ECG were recorded. QT was measured from the start of the QRS complex up to the end of the T wave. If the T wave is followed by a U wave, the nadir of the T wave was taken as the endpoint of the QT interval. At least 8 leads with clear cut QT intervals were included. These patients were then evaluated for development of heart failure symptoms based on the Framingham criteria one year after the event. The subjects were notified by telephone call or text message to come in for check-up at the OPD/ doctor's clinic for evaluation. For patients who were unable to come due to financial constraints or transfer of residence to very far away places, only an interview was done. Association of QT dispersion with the development of congestive heart failure was carried out using Chi Square test. Variables with a p value ≤ 0.05 were considered significant and subjected to multivariate analysis.

RESULTS

A total of 89 myocardial infarction patients were included in the study. Of these, only 13 (15%) developed heart failure after one year,

11% among the men and 25% among the women. Smokers comprised 42% of the population. There were 66 patients (74 10) who were hypertensive, 24 (27%) diabetics and 12 (13%) dyslipidemic. Patient characteristics are summarized in Table 1.

Low ejection fraction, both M-Mode and Simpsons on admission, cerebrovascular disease, intake of calcium channel blockers and diuretics were associated with the development of congestive heart failure after one year of study.

Table 1. Characteristics of Subjects with Acute Myocardial Infarction Included in the study (PHC, 2013)

Charateristics	(+) Congestive Heart Failure n(%) N=13	(-) Congestive Heart Failure n(%) N=76	p-value
Age	56.69 ± 12.46	55.92 ± 10.703	0.815
Sex			
Male	7 (11)	58 (89)	0.104
Female	6 (25)	18 (75)	
Smoking	6 (16)	32 (84)	1.00
Medical History			
Hypertension	12 (18)	54 (82)	0.170
Diabetes Mellitus	6 (25)	18 (75)	0.104
Cerebrovascular	3 (60)	2 (40)	0.021
Disease	1 (8)	11 (92)	1.00
Chronic Kidney Disease	9 (12)	64 (88)	0.240
Dyslipidemia	13 (16)	66 (85)	0.347
Medications			0.001
Beta-blocker	6 (55)	5 (45)	0.008
ACE inhibitors	4 (57)	3 (43)	
CCB	13 (15)	76 (85)	
Diuretic	13 (15)	76 (85)	
Statins	13 (17)	65 (83)	0.356
Antiplatelet			
Nitrate			
LVEF	48.20 ± 11.08	61.20 ± 13.44	0.005
M-Mode	47.22 ± 15.16	58.35 ± 11.56	0.013
Simpsons	129.46 ± 36.75	119.29 ± 28.52	0.258
GRACE score	3 (14)	18 (86)	1.00
PCI	1 (25)	3 (75)	0.475
CABG	0	2 (100)	
Thrombolysis			

Table 2. Association of QT dispersion With the Development of CHF in Post MI Patients

	Congestive Heart Failure		p-value
	Present n (%) N=13	Absent n (%) N=76	
QT Dispersion			
0.05 ms	3 (9.7%)	28 (90.3%)	0.112
0.05-0.07 ms	0 (0%)	11 (100%)	
>0.07 ms	10 (21.30%)	37 (78.7%)	

DISCUSSION

QT dispersion in post myocardial infarction patients has no association with the development of congestive heart failure after one year. Although previous studies have reiterated the contention that QT dispersion is a marker for the risk of cardiac arrhythmia in patients with congestive heart failure or those post myocardial infarction, the premise is that there is already a pre-existing heart failure in these patients. In the present study, enrolled patients had no underlying heart failure prior to the event and the possibility that QT dispersion at this time could foretell the development of heart failure after one year is the main interest. Adjusting for factors that were found to be significantly associated with congestive heart failure, QT dispersion was found to be not statistically associated with congestive heart failure. Even at a QT dispersion of >70ms, there is still no relationship at all with the development of congestive heart failure after one year.

As has been proven in previous studies, low ejection fraction (48.12 ± 13.4 by M-Mode and 41.17 ± 9.9 by Simpson) was associated with the development of heart failure. Patients with history of cerebrovascular disease were also likely to end up with congestive heart failure after one year. Atherosclerosis is a diffuse progressive disease and concomitant cardiovascular and cerebrovascular affectation is not uncommon. The fact that these patients already had an atherosclerotic event puts them at a higher likelihood of other end organ involvement, in this case, the heart.

Diuretics which were given to some patients on admission also showed correlation with congestive heart failure. This perhaps was because, at the outset, these patients already had a substrate for such adverse event to set in. A higher Killip score has been shown to have worse outcomes compared to those with lower scores. As for the calcium channel blockers, these were mostly the second generation dihydropyridines such as amlodipine, given for concomitant hypertension. Although short acting dihydropyridines, like nifedipine, are contraindicated in the setting of acute myocardial infarction, no harm

has been shown with long-term treatment with the long-acting drugs (amlodipine and felodipine) in patients with documented left ventricular dysfunction and CAD. In addition, two recent trials documented the benefit of amlodipine in patients with hypertension and stable CAD.[1] This seemed incongruent with the findings of this present study, which warrant further investigation.

A study by Spargias et al.[5] has addressed the prognostic value of QT dispersion in a selected group of patients after acute myocardial infarction, all of them presenting with heart failure. They studied a relatively large registry of patients enrolled in the AIRE study, who were followed-up for a mean of 6 years. They chose a very early ECG recording (mean Day 1-5, median day 2), before randomization to the study drug, and they found that QT dispersion measurements were significantly increased in those patients who died (QT dispersion 92.0 vs, 82.7 ms). In addition, QT dispersion resulted in an independent predictor of all-cause mortality on multivariate analysis.[7] In the aforementioned study, as in the previous others, the QT dispersion leading to adverse outcomes occurred in a background of preexisting heart failure, which was an exclusion criteria in the present study. The changes occurring in QT dispersion following acute myocardial infarction are dynamic and therefore the timing of the QT dispersion measurement may be crucial when examining its prognostic value. In view of the effects of acute ischemia on QT dispersion, early recordings may contain additional information on residual ischemia. QT dispersion increases from the very first hours possibly is greatest around day 3 and then falls with lime in most cases.[5] In the present study, 12 lead ECG analyzed for QT dispersion were done on admission at the Emergency Room regardless of the time of onset of the index event as long as it fell within one week of symptoms. This deserves further investigation since this factor was not considered beforehand and may affect the measurement of QT dispersion.

While myocardial infarction provides the milieu for scarring and in homogeneity, which can supply the setting for the development of arrhythmia and sudden death, development of congestive heart failure does not necessarily follow. Cardiomyocyte necrosis and slippage, disturbed intercellular connections, altered ventricular geometry and dilatation, and reactive hypertrophy, are all part of the ventricular remodelling process after acute myocardial infarction. All these factors are liable to have an effect on the heterogeneity of ventricular repolarization and unfavorably influence QT dispersion.[5] This does not, however, necessarily equate with the development of heart failure. Advances in the management of coronary artery disease, such as angioplasty and coronary artery bypass grafting, has greatly alleviated the outcomes of these patients. A decline in the heart failure post MI has been attributed mostly to administration of reperfusion therapy within 24 hours of MI.[8] Indeed, the GRACE registry has reported that in this changing era of acute coronary syndromes, with increasing rates of primary PCI for STEMI and PCI after non-STEMI, and increasing use of evidence-based pharmacotherapies, rates of heart failure fell by 9% in those with a STEMI and by 6.9% in those with a non-STEMI.[9] Of those who underwent revascularization by PCI, CABG or thrombolysis, only 15% had adverse events after one year, the rest fared better.

In the AIREX study, the patient were followed-up for 6 years. Even the study of Hellerman[10] reevaluated post-MI patient s after 5 years. Perhaps, the one year follow-up set in this study was too short for obvious symptoms of heart failure to develop. Another issue is the determination of QT dispersion. Some ECGs had T waves whose terminations were difficult to determine. In these ECGs, a minimum of 8 leads with well delineated T waves were utilized. Although a blinded independent investigator assessed the QT interval and computed for the dispersion, newer ECG machines which provide QT dispersion readings would have been more objective, perchance, more accurate. After one year of study, some of the patients were unable to come for follow-up at the outpatient clinic, hence, only subjective complaints and any history of admission for heart failure symptoms were used to assess for the primary outcome.

CONCLUSION

QT dispersion in post myocardial infarction patients is not associated with the development of heart failure after one year.

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Echocardiographic Predictors of Future Heart Failure After Myocardial Infarction

Glenn A. Mana-ay, MD; Luis Raymond T. Go, MD

Background **---** Clinically significant heart failure is a common complication after acute myocardial infarction and remains a significant contributor to morbidity and an independent predictor of mortality. Two-dimensional echocardiography and doppler study offers a non-invasive and complete evaluation of the systolic and diastolic function of the heart especially in patients with acute myocardial infarction. Subsequent clinical heart failure occurred in 21% with Killip I acute MI in most studies with two thirds of the patients with clinical heart failure are due to combined systolic and diastolic dysfunction and the remaining one third is due primarily to diastolic dysfunction despite preserved LV function.This is a prospective study to answer the hypothesis of whether simple echocardiographic parameters can predict future heart failure in patients admitted with Killip I acute MI and if there is significant difference in echo parameters between those who presents with heart failure and those Killip I on presentation but subsequently developed heart failure.

Method **---** Patients who were admitted in Philippine Heart Center from January to September 2003 diagnosed of acute MI were evaluated. Baseline clinical and echocardiographic parameters were gathered within 36 hours of the onset of infarction. Excluded are those patients during initial physical examination or at the time of 2D echo doppler study if they have complications other than clinical heart failure, moderate to severe mitral regurgitation, technically unsatisfactory imaging of LV wall motion and absence of sinus rhythm. Patients were followed up until development of clinical heart failure or if symptoms suggesting heart failure were present or had any changes in their medications from discharge. Patients were divided into 3 groups: Group IA, those who did not developed heart failure; Group IB, those who developed subsequent heart failure and Group II, those who presents with clinical heart failure on admission.

Results **---** Total of 47 patients were admitted with acute myocardial infarction, 6 (13%) presented with clinical heart failure on admission, 41 (87%) had Killip I on admission and 19 (46%) developed subsequent heart failure, Follow-up duration after discharge was 1 to 7 months (mean 3.5 months). One patient died due to ventricular arrhythmia, 1 had reinfarction and 4 had recurrent chest pains despite absence of heart failure. Demographic characteristics showed older patients are more likely to developed subsequent heart failure (Mean age = 62 ± 8, P=0.002). Medications received did not differ in both groups. Statistically significant predictors for subsequent heart failure by univariate analysis were WMSI (P=0.0007), AIE velocity ratio (P=0.000002), A% (0.00005), DT (P=0.00001), IVRT (P=0.015), EF by M mode (P=0.005) and Simpson's (P=0.011) and DTI early diastolic velocity (P=0.019). Best cut-off values to predict subsequent heart failure were A/E velocity ratio ≥ 1.3 and A% ≥45 with each having sensitivity of 68%, specificity of 82% and predictive accuracy of 76%, WMSI ≥ 1.5 with sensitivity and specificity of 68% and predictive accuracy of 65%, DT ≥ 200 msec with sensitivity of 84%, specificity of 63% and predictive accuracy of 66%.There were significant difference in echocardiographic parameters between those who presents with heart failure and those Killip I on admission that subsequently developed heart failure.

Conclusion **---** Simple echocardiographic parameters can predict future heart failure in patients with Killip I acute MI. There were significant difference in echocardiographic parameters between those who presents with heart failure and those Killip I on admission that subsequently developed heart failure. ***Phil Heart Center J 2016;21(2):18-26.***

Key Words: WMSI Wall Motion Score Index ■ Myocardial Infarction

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Congestive Heart Failure is one of the most common cardiac problems in adults. In two thirds of the patients, the syndrome of congestive heart failure is due to the combination of systolic and diastolic dysfunction of the left ventricle (LV), and in the other one third, the primary cause of heart failure is diastolic dysfunction with preserved systolic function.

Based on radionuclide evaluation of peak filling rate, 38% of these patients who have intact systolic function (LV ejection fraction (EF) 62 ± 11%) were found to have significant abnormality in diastolic function as measured by peak filling rate. The disease states most frequently associated with CHF and intact systolic function were coronary artery disease and systemic hypertension.[1] The development of failure of the left side of the heart after myocardial infarction remains a significant contributor to morbidity and is associated with a worse prognosis than that which could be expected from the degree of systolic dysfunction alone.[2]

Because doppler echocardiography has been proposed as one possible way of assessing LV global diastolic function,[3] they prospectively evaluated whether parameters of LV filling could improve upon the two-dimensional echocardiographic assessment of wall motion to predict the development of heart failure after a myocardial infarction. Subsequent clinical heart failure occurred in 21% (10/48) with Killip I MI. The univariate predictors of heart failure were age, anterior infarction, early diastolic peak filling velocity (E = 0.42±0.12 m/sec), filling velocity with atrial systole (A= 0.65±0.11 m/sec), the ratio of these velocities (A/E ≥ 1.4), the percentage of filling with atrial systole (A%=52.2 ± 9.9) and the wall motion score index (WMSI). However, the only independent predictors of heart failure by use of multivariant stepwise logistic regression analysis were the WMSI and either the A/E ratio or the A%. The combine use of a measure of systolic function and the measures of relative contribution of atrial systole to ventricular filling were useful predictors in identifying patients likely to develop subsequent heart failure after MI. History of hypertension and previous MI both showed a trend toward greater prevalence in heart failure but neither was significant.[4]

Study using 16 segment wall motion analysis model demonstrated that most of the patients with Killips II-IV heart failure after acute MI had WMSI of 1.7 or higher but many patients with this score did not develop any complications. In addition to the WMSI, restrictive filling variables correlate with incidence of post infarct heart failure and LV filling pressures.[8]

Pulmonary capillary wedge pressure is one of the few measures of diastolic function that has been studied as a predictor of outcome, Henning et al, found that a pressure > 20 mmHg within the first 24 hours of admission conferred a more than fourfold increase in mortality within 30 days and more that two-fold increased mortality beyond 30 days.[6] The difference in pulmonary venous and mitral A durations correlated well with left ventricular end-diastolic pressure (LVEDP) and pulmonary venous reversal duration exceeding the duration of mitral A velocity curve provide high sensitivity (82%) and specificity (92%) for detection of LVEDP of 20 mmHg or greater.[7]

In a local study done in the Philippine Heart Center, echocardiograpic parameters that significantly correlated with signs and symptoms of heart failure were lateral (53%), posterior (62.5%) and anterior IVS (81%) locations of infarct, mean ejection fraction by M-mode (55.5 ±15.9%) and deceleration time (188.5 ±86 ms).[5] Mitral annular velocities determined by pulse wave doppler tissue imaging after first myocardial infarction showed lower velocities compared to healthy subjects (10.8±2.3 vs. 13.2±2.9 cm/s, p value of <0.01).[10] After MI patients may develop different degrees of diastolic dysfunction. With conventional doppler parameters, these changes may be detected by the development of abnormal LV relaxation, pseudonormalization or a restrictive pattern depending on the extent of myocardial changes. Therefore, conventional doppler parameters may fail to identify diastolic dysfunction after MI because of overlap of doppler findings. Since early diastolic mitral annular velocity measured by doppler tissue imaging (DTI) has been postulated to be independent of the filling pressure.[11] Thus, by using mitral annular peak velocity by DTI, it may

possible to assess early diastolic dysfunction after MI even in the presence of pseudonormalization of transmitral flow velocity or with elevated LV end-diastolic pressure. Quantification of myocardial velocity by DTI opens up a new possibility assessing future LV dysfunction in patients with MI.

Clinically significant heart failure is a common complication after acute MI and an independent predictor of mortality. Despite its frequency and several studies done attempting to identify predictors of it, no local study was done on the echocardiographic predictors for the development of heart failure after Killip I acute myocardial infarction.

The purpose of this study is to identify echocardiographic parameters that leads to future heart failure after acute MI. Many patients came in at the emergency room beyond the golden period of revascularization after acute MI and most of them were discharged after stabilization. Identifying the risk of future heart failure by echocardiography could make us aware of the need of aggressive treatment to prevent future heart failure either by medical means or revascularization depending on amount of salvageable myocardium.

METHODS

Patient Population. This is a prospective study of 47 patients admitted with acute MI. Doppler and two-dimensional echocardiography was done within 36 hours of the onset of the infarction. Myocardial infarction was defined as chest pain lasting longer than 30 minutes in association with both electrocardiographic changes and a typical serum enzyme pattern indicating myocardial necrosis. Patients were divided into Group I, those with no signs of heart failure (Killip I) and Group II, those who presents with heart failure on admission. Group I is further subgrouped into Group IA, if there were no signs of heart failure on follow-up and Group IB, if there were signs of heart failure on follow-up.

Included in the study were patients diagnosed to have acute ST and Non-ST MI on admission with typical history of chest pain, ECG changes and elevated or positive cardiac enzymes (CK-MB and/or troponin) and with sinus rhythm by ECG. While excluded in the study were patients having complications other than development of heart failure; moderate to severe mitral regurgitation at the time of doppler echocardiographic study; technically unsatisfactory imaging of left ventricular wall motion; and with absence of sinus rhythm at the time of initial study.

Follow-up. Patients were followed-up until the development of clinical heart failure. Clinical status was ascertained from the charts and by physical examination while admitted, by telephone contact and on follow-up check up after discharge if symptoms suggesting heart failure or had any changes in their medications since discharge. The duration was 1 month to 7 months (mean of 3.5 months).

Doppler and Two-Dimensional Echocardiography. The two-dimensional echocardiograms were obtained by the use of all available echocardiographic windows. The pulse doppler tracings of LV filling were obtained by use of either the apical two or four-chamber view with sample volume placed within 1-2 mm between mitral leaflet tips at their points of maximal excursion in diastole. In recording pulmonary venous flow, pulse doppler tracings are recorded in an apical four chamber view placing sample volume (2-4mm) within 1-2 cm into the right upper pulmonary vein with the guide of color flow doppler. All echocardiographic and doppler information will be recorded on video tape for later analysis.

Locations of infarct or ischemia were determined by noting areas of wall motion abnormality on the standard views of the parasternal long and short axis, and apical chamber views. Ejection fraction was evaluated from the standard apical two and four chamber views using Simpson's biplane disc method and by M-mode using the parasternal long and short axis views at the level of papillary muscle.

The LV regional wall motion analysis is based on grading the contractility of individual segments. The LV is divided into three levels (basal, mid and apical) and 16 segments. The

basal and mid levels are each subdivided into six segments and the apical level is subdivided into four segments. A numeric scoring system was adopted based on the contractility of individual segments (l-normal, 2-hypokinesia, 3-akinesia, 4- dyskinesia, 5-aneurysmal). The wall motion score index (WMSI) is derived by dividing the sum of wall motion scores by the number of visualized segments (normal=1).[9]

A/E ratio is the ratio of the peak velocity of filling with atrial systole and peak velocity of early diastolic filling. Percentage of LV filling contributed by atrial systole (A%) is estimated as the time velocity integral (TVI) of the A wave divided by the total TVI of mitral inflow x 100. Pulmonary venous-mitral A duration difference in milliseconds is determined by subtracting the duration of mitral A from the duration of pulmonary venous A by doppler recordings.[7]

Mitral annular velocity by doppler tissue imaging is performed by activating the DTI function in the echocardiographic machine. Images were be acquired by using a frequency of 2 to 4 MHZ. Early diastolic velocity (cm/sec) were recorded on the apical 4 chamber view with pulse doppler. A 3.5 mm sample volume was used with the DTI cursor placed on the lateral site of the mitral annulus.

Statistical Analysis. Data were presented as mean values ± standard deviation. Continuous variables were compared between groups by student unpaired *T* test. A univariate analysis was used to determine which of the clinical and two-dimensional echocardiographic variables significantly predicts future heart failure. Statistical significance was set at $P < 0.05$. A receiver-operating curve was made to set a cut off point on the values of the highly significant echo parameters to separate those who developed subsequent heart failure and those who did not after Killip I acute MI.

RESULTS

A total of 47 patients were diagnosed of acute MI at the emergency room. Only 6 (13%) presented with clinical heart failure (Group II) upon admission and 41(87%) had Killip I (Group on admission. The prevalence of future heart failure in Killip I acute MI in this study was 46%. One died with subsequent heart failure due to ventricular tachycardia after 1 month, 4 of the patients without signs of heart failure had recurrent chest pains and 1 of them had reinfarction. Demographic characteristics of the patients (*Table 1*) showed no significant difference between the three groups except the age on those who developed heart failure (Groups IB and II) which are older than those who did not (Group IA), P=0.002.

Univariate analysis of doppler and 2 dimensional echocardiographic variables (*Table II*) showed a highly significant difference in the WMSI (P=0.0007), A/E velocity ratio (P=0.000002), A% (P=0.00005), DT (P=0.0001) and IVRT (P=0.015) which values are higher in Group IB than IA. Other least variables which showed a statistically significant difference between two groups were ejection fraction by M mode (P=0.005) and Simpson's (P=0.0011) and diastolic doppler tissue velocities (P=0.019) which showed lower values in Group IB than IA. Comparing the echo parameters between Group IB and Group II, there were significant difference in the values with regards to EF by M mode, A/E velocity ratio, A%, DT and IVRT which are lower in Group II. (*Figs. 1-4*)

We selected the best 4 echocardiographic predictors of subsequent heart failure (Group IB) such as A/E velocity, A%, WMSI and DT and used a receiver-operating curve characteristics (*Figs. 5-8*) to determine which is the best cut-off value to predict subsequent heart failure. The best cut-off points to predict subsequent heart failure in the A/E velocity was ≥ 1.3 (*Fig. 5*) and in A% was ≥ 45 (*Fig. 2)*, each of them having sensitivity of 68%, specificity of 82% and predictive accuracy of 76%.

The best cut-off point to predict subsequent heart failure in WMSI was ≥ 1.5 (*Fig.7*) with sensitivity of 68%, specificity of 68% and predictive accuracy of 65%. The next is deceleration time with best cut-off point of ≥ 200 msec (*Fig. 8*) with sensitivity of 84%, specificity of 63% and predictive accuracy of 66%.

Table 1. Demographic Characteristics

Variables	Group IA (N=22)	Group II N=6	Group IB N=19	p value
Age	53 ± 9*	65.7 ± 12⁺	62 ± 8⁺	0.002*
Gender (%)				
Male	16 (73%)	75 (83%)	10 (53%)	0.251
Female	6 (27%)	1 (17%)	9 (47%)	
Systolic BP (mean)	130 ± 34	123 ± 33	142 ± 36	0.380
Heart rate (mean)	72 ± 12	89 ± 10	80 ± 19	0.060
History of Previous MI (%)	3 (13%)	3 (50%)	5 (11%)	0.163
History of HPN (%)	12 (54%)	2 (33%)	13 (68%)	0.295
ECG (%):				
Ant Infarct	7 (33%)	3 (50%)	10 (52%)	
ST elevation	15 (68%)	5 (83%)	12 (63%)	0.828
Q wave	13 (59%)	5 (83%)	9 (47%)	
Troponin T ng/ml (mean)	0.80 ± -0.8	-	0.83 ± -0.7	0.94
Medications (%)				
ACE inhibitor	20 (90%)	6 (100%)	19 (100%)	
ASA	21 (95%)	6 (100%)	19 (100%)	
ADP receptor	1 (5%)	3 (50%)	2 (10%)	NS
Nitrates	17 (77%)	5 (83%)	15 (78%)	
Beta-blocker	17 (77%)	3 (50%)	16 (84%)	
LMWH/Unfrac.	20 (90%)	6 (100%)	18 (95%)	

⁺ = no significant difference between these groups
* = significant
** = highly significant
NS = no significance

Table 2. Two-Dimensional Echocardiographic and Doppler Variables

Variables	Group IA (N=22)	Group II N=6	Group IB N=19	p value
Ejection Fraction (mean)	61 ± 12*	44 ± 15⁺	52 ± 9*	0.005*
M-mode Simpson's	53 ± 10*	42 ± 13⁺	43 ± 6⁺	0.011*
WMSI (mean)	1.4 ± 0.2*	1.9 ± 0.30⁺	1.7 ± 0.3⁺	0.0007*
A/E Velocity ratio (mean)	0.89 ± 0.4⁺	0.62 ± 0.2⁺	1.5 ± 0.4*	0.000002**
A%	34 ± 10⁺	32 ± 10⁺	48 ±8*	0.00005**
Deceleration time (mean)	190 ± 38*	142± 24*	233 ± 42*	0.00001**
IVRT (mean)	100 ± 27⁺	112 ± 62⁺	131 ± 25*	0.015*
Pulmonary Venous-Mitral A duration difference in MS (mean)	43 ± 30⁺	-	55 ± 42*	0.388

Figures 1-4: Comparison between Doppler Echocardiographic Parameters Group IB Group II

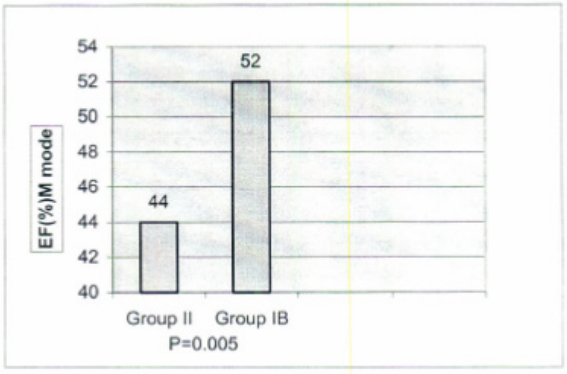

Fig. 1 Ejection Fraction

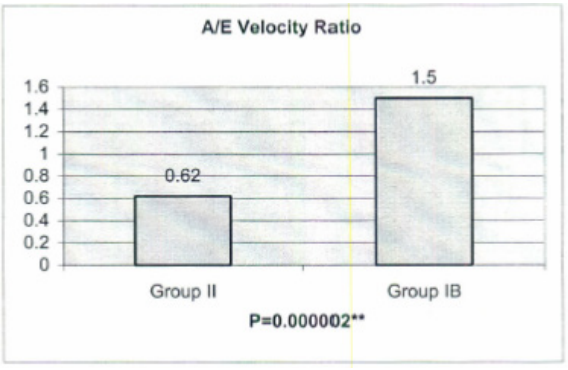

Fig. 2 A/E

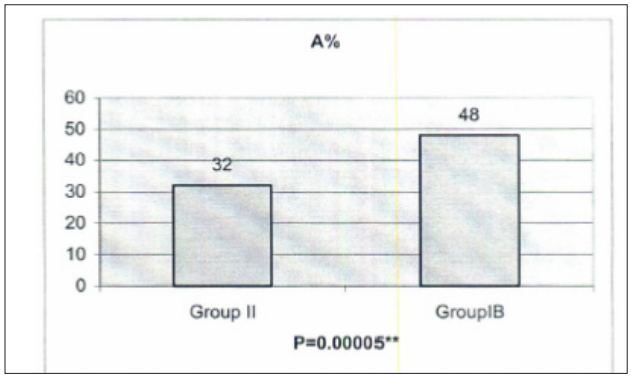

Fig. 3 A%

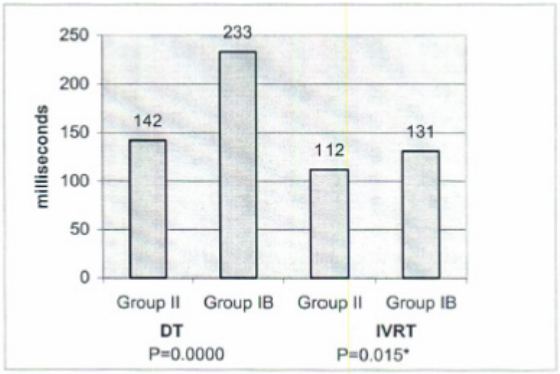

Fig. 4 DT and IVRT

Figures 5-8: ROC Curves of Different Echocardiographic Parameters

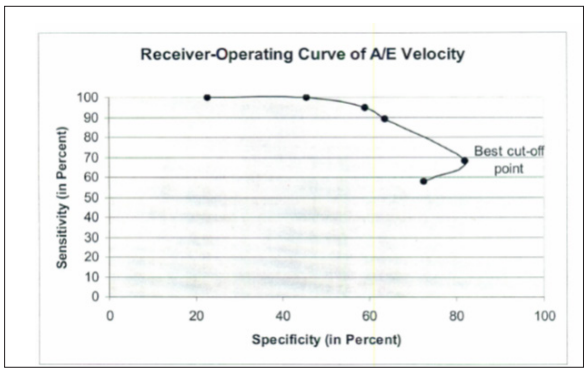

Fig. 5 A/E Velocity

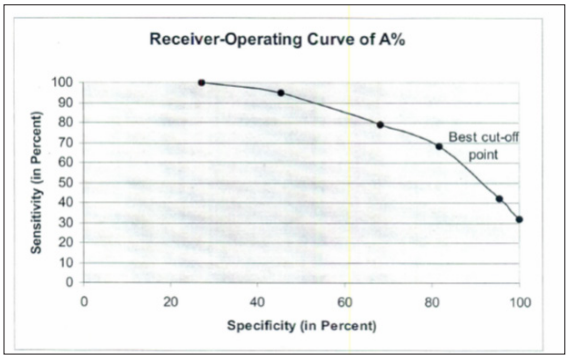

Fig. 6 A%

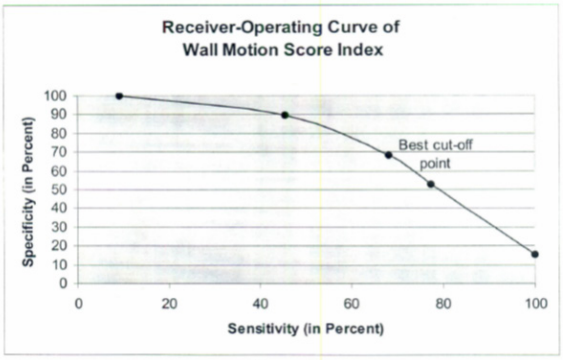

Fig. 7 Wall Motion Score Index

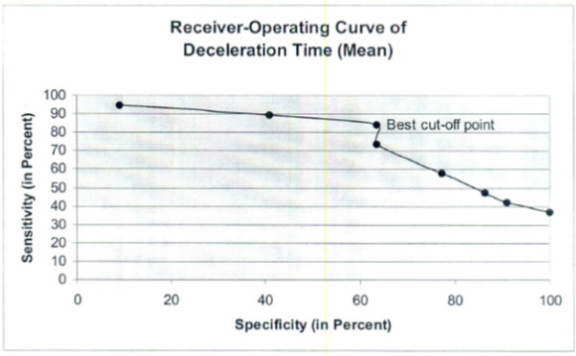

Fig. 8 Decelation Time

DISCUSSION

Clinical heart failure is a common complication after myocardial infarction. Despite its frequency, few studies have specifically attempted to identify its predictors even though heart failure is an independent predictor of mortality. This study has shown that echocardiographic measures of LV filling and assessment of LV wall motion were able to separate patients with high and low likelihood of heart failure after Killip I MI. The combination of systolic and diastolic measures provided better prediction of outcome than either parameter alone.

Echocardiographic Wall Motion Score Index as a predictor. Many studies established the clinical importance of echocardiographic wall motion score index in predicting both early and late complications from MI[1,2] with findings comparable to those of ejection fraction. Because of the ability to visualize myocardial thickening and endocardial excursion, it is able to differentiate motion caused by tethering effect and and can exclude hyperdynamic regions from the overall score and thereby avoid misinterpretation of a normal ventricle that woul be conveyed by using global ejection fraction. These factors may make echocardiographic assessment of wall motion a more sensitive method than global ejection fraction for detecting subtle changes in ventricular function.[13] Neither radionuclide nor contrast angiography are able to make this distinction.

A wall motion score index is also simple to derive because it does not require any special equipment and it does not require all segments in one imaging plane to be viewed simultaneously,

as is needed for determination of ejection fraction. Because an abnormal wall motion score index has predicted an increased mortality after MI and because heart failure is associated with an increased mortality, it is not surprising that the wall motion index appeared as a good predictor of heart failure in our study.

Significance of Doppler Echocardiographic measures of LV filling. Doppler transmitral velocity profile reflects the summed effects of many variables such as rate of ventricular pressure decay, preload and afterload conditions, myocardial viscoelastic properties and force of atrial contraction.[14] No single doppler measurements specifically reflects anyone of these factors, and similar patterns of ventricular filling can be observed in every different clinical settings. Nevertheless, it is important to prospectively determine if any of the patterns of transmitral inflow velocities can predict outcome in a specific clinical setting. Numerous studies have shown that a small peak E velocity with a prolonged deceleration and a large A velocity can be seen with acute myocardial ischemia, myocardial infarction and hypertensive heart disease.

Impaired muscle relaxation and dyssynchronous regional wall motion in early diastole[15] contribute to a slower rate of LV pressure decay and account for the reduced velocity and prolonged deceleration time for early diastolic filling in these conditions. This incomplete early diastolic ventricular filling results in higher atrial volume at the onset of atrial systole, therefore augmented ventricular filling occurs with atrial systole. However, this pattern of altered ventricular relaxation can also be produced or accentuated by a reduced preload.[14] This pattern of ventricular filling was predominant in our patients in whom heart failure later developed. It may be that these doppler measurements are markers for more significant residual coronary artery disease, although angiographic verification was not performed in most of our patients.

The opposite pattern of filling, with high peak E velocity, short deceleration time and low A velocity have been described in conditions where there is a high atrial pressure leading to rapid early diastolic inflow which is immediately curtailed by the limits imposed by the ventricle or pericardium. There is little or no inflow in the remainder diastolic phase. This pattern can be seen in constrictive pericarditis and in various heart failure states including restrictive cardiomyopathy.[16] This pattern was uncommon in the group of patients who subsequently developed heart failure in our study occurring in only 1(5%) in 19 patients. It is common (83%) in patients who presents with heart failure on admission. A normal appearing mitral inflow pattern can occur when an abnormal relaxation and a restrictive physiology are simultaneously present. This could occur during the transition from an abnormal relaxation pattern to a restrictive pattern as acute failure is actually developing which is seen in 2 (10%) of 19 patients who developed subsequent heart failure in our study.

Study Limitations. The small study population does not allow us to do multivariate regression analysis to reach statistical significant values to determine independent predictors of subsequent heart failure. Our study with regards to outcome may have been affected by variable therapeutic interventions since patients received thrombolytics/revascularization while others did not, although only a small group (14%) received either thrombolysis, Transcatheter therapy (TCT) or coronary artery bypass. No correlation with angiographic findings were done to compare severity of lesions and echocardiographic measures. Finally, because the type of heart failure that often develops in ischemic heart disease maybe episodic and related to transient ischemia or may be uniquely related to the ventricular remodeling that occurs as recovery progresses, the findings of our study should not be extended to other forms of valvular or non-valvular heart diseases leading to heart failure.

Clinical Applications. Subsequent heart failure occurred in 46% in our study group, much higher than other recent foreign studies[17] which was only 21%. This could due to limitations in aggressive treatment and early detection of acute myocardial infarction. This emphasizes the importance of the problem and the need for strategies to minimize this complication. Identification of patients at increase risk for the development of heart failure provides the potential of early intervention to modify outcome. If future

studies confirm our observations regarding the high probability of heart failure development when there are significant abnormalities of both systolic and diastolic function predicted by echocardiography, prospective trials of early therapeutic interventions can be focused on these patients. Our findings answered our hypothesis that there are echocardiographic parameters that can predict future heart failure in Killip I acute MI and there were significant difference especially in the doppler parameters of LV filling between those with Killip I acute MI that subsequently developed heart failure and those with acute MI presenting with clinical heart failure. The latter having restrictive LV filling doppler patterns with low A/E velocity ratio (0.6 ± 0.2 vs. 1.5±0.4), shortened DT (142 ±24 vs. 233 ± 42) and IVRT (112 ± 62 vs. 131 ± 25). Furthermore, combination of systolic dysfunction and abnormal LV filling existed in most of our patients (74%) in whom heart failure developed compared to either of the two alone. This emphasizes that both are likely to play an important role in the development of heart failure in ischemic heart disease.

CONCLUSION/RECOMMENDATIONS

We need to do additional prospective studies on these predictors of future heart failure after acute MI to be able to set adequate sample size for multivariate analysis to come up for independent predictors so that echocardiographic scoring could be done. We also suggest further follow-up on these patients for long term outcome such as all cause mortality, MI death and recurrent hospitalizations due to heart failure correlating it to echocardiographic parameters and therapeutic interventions and if possible with angiographic correlations.

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Association of Total Eosinophilic Count with the Development of Congestive Heart Failure in Patients with Acute Myocardial Infarction

Ivie Joyce U. Kong, MD; Frederick S. Gabriel, MD; James Ho, MD

Background **---** It has been seen that atherogenesis represents an inflammatory process in the addition to infiltration of lipids. There have been studies that showed that increased eosinophilic count is related to adverse cardiac events such as post infarction congestive heart failure. The objective of this study is to determine the asssociation of total eosinophilic count with the development of congestive heart failure in patients with acute myocardial infarction.

Method **---**This is a prospective cohort study conducted at Philippine Heart Center. Patients included in this study were those admitted for acute myocardial infarction with no signs of heart failure. Outcome measures include the development of congestive heart failure as described by clinical signs and symptoms within four days of admission.

Results **---** A total of 139 patient who fulfilled the WHO criteria for acute myocardial infarction were included in this study. In forty-three (30%) patients, congestive heart failure developed within the four days of admission. The total eosinophilic count was found not to be significant predictor in developing subsequent congestive heart failure.

Conclusion **---** Study showed no statistically significant association between total eosinophilic count in patients admitted for acute myocardial infarction and the development of congestive heart failure in the first four days of admission. However, our study showed age and diabetes mellitus can predict the risk for developing heart failure in post myocardial infarction patients. ***Phil Heart Center J 2016;21(2):27-30.***

Key Words: Acute Myocardial Infarction ■ Congestive Heart Failure ■ Eosinophilia

It has been seen that atherogenesis represents an inflammatory process in the addition to infiltration of lipids.[1] Studies showed that increased WBC count is related to adverse cardiac events such as post infarction congestive heart failure[2] and that atherogenesis represents an active inflammatory process rather than simply a passive injury with infiltration lipids. It also indicates that it is an important risk factor for cardiac events.

There are limited studies regarding the relation of leukocytes and the risk of cardiac events such as congestive heart failure and acute myocardial infarction. Barron and associates concluded that elevations in WBC count on admission are associated with reduced epicardial and myocardial blood flow, thromboresistance and higher incidence of new congestive heart failure.[3] A review by Madjidd et al[1] concluded that high leukocyte count is associated with increased coronary artery disease related mortality and morbidity in various clinical settings. In an article by Ogbugo et al. showed the thrombotic complication as a cardiovascular abnormality in patients with hypereosinophilia (HES).[4] The most characteristic cardiovascular abnormality in HES is endomyocardial fibrosis, initially described in 1936 by Loeffler, who called it "fibroplastic parietal endocarditis with blood eosinophilia." Clinical evidence of cardiac involvement signs and symptoms include heart failure and involved 38% of patients. There are several reports on the association of hypereosinophilia and the endomyocardial diseases.[5]

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However in one local study by Cruz et al. showed low eosinophil count was significantly associated with heart failure.[6]

With the results of the said studies, the examination of the absolute eosinophil count may serve as a simple, inexpensive, universally accepted marker to identify patients who are high risk for the development of congestive heart failure. The study would like to test the association between the absolute eosinophilic count on admission and the early development of post infarction congestive heart failure in these patients.

METHODS

The study was approved by the institutional review board and informed consent was obtained. This is a prospective cohort study done at the Philippine Heart Center from July 2014 to December 2015. Included in the study were patients from 19-80 years old and diagnosed with acute myocardial infarction according to pre-established WHO criteria specifically at least two of the following conditions had to be documented: a clinical history compatible with acute myocardial infarction Killip I with enzyme level elevation (Troponin I) or positive electrocardiographic findings.

Sample Size Calculation. The minimum sample size calculated was 138 based on the following parameters: alpha = 0.05, margin of error of 5% and with the prevalence of heart failure with eosinophilia at 10% based on the Eosinophil and Heart Disease in European Heart Journal.

Study Maneuver. Subjects with myocardial infarction was seen at the emergency room. The following data was obtained: age, sex, coronary risk profile (hypertension, diabetes mellitus, smoking history). Admitting CBC was taken along with admission troponin I and ECG. In hospital outcome for the development of heart failure after 4 days of hospitalization was determined. The Framingham criteria was used to determine the presence of heart failure. This includes the major criteria such as paroxysmal nocturnal dyspnea, neck vein engorgement, rales, cardiomegaly, pulmonary edema, S3 gallop, positive hepatojugular reflex. Minor criteria include ankle edema, night cough, dyspnea on exertion, pleural effusion, hepatomegaly, tachycardia. Chest x-ray was also obtained to determine signs of pulmonary congestion. Four days was chosen as cut-off because after this time, the development of heart failure may be influenced by therapeutic intervention and/or other post infarction complication and therefore may be less relevant as stated by Kyne L, et al.[7]

Statistical Analysis. Data was presented as mean and standard deviation for quantitative variables, frequency and percent distribution for the qualitative variables. Logistic regression analysis was used to determine the association of congestive heart failure with the total eosinophilic count and other predictor variables.

RESULTS

A total of 139 patients fulfilled the WHO criteria for the diagnosis of acute myocardial infarction and were included in this study. The study included were prodominently male (74%) with a mean age of 58 ± 11. Majority of the patients were hypertensive (71%) and more than half with history of smoking (56%). Majority of the patients were given Aspirin (99%), Clopidogrel (100%), Heparin (100%) and ACE inhibitors (79%). (*Table 1*)

Forty-three (30%) of patients developed congestive heart within the first four days of hospital admission. It was documented with clinical signs and symptoms compatible with the diagnosis of congestive heart failure. Of these eighteen (42%) had radiologic evidence of pulmonary congestion.

The baseline characteristics and risk factors were comparable on admission between the two graups. lncreasing age was seen to be an increased risk for development of acute heart failure along with the presence of diabetes mellitus. Total esinophilic count was not statistically significant in asasociation to the development of heart failure in post myocardial infarction patients. (*Table 3*)

Table 1. Baseline Characteristics in Acute Myocardial Infarction Cases.

Characteristics (n)	X ± SD or N (%)
Age	58 ± 11
Sex	
Male	103 (74%)
Female	36 (26%)
Hypertenstion	99 (71%)
Diabetes Mellitus	44 (32%)
Smoking history	79 (56%)
Ejection Fraction	54 ± 11
LVESD	3.51 ± 0.76
LVEDD	4.98 ± 0.61
LA size	3.56 ± 0.59
Therapeutic interventions	
ASA	138 (%)
Clopidogrel	139 (100%)
Heparin	139 (100%)
Nitrates	81 (58%)
Beta Blockers	99 (71%)
ACE inhibitors	110 (79%)
ARB	19 (14%)
Diuretics	43 (31%)
PTCA	92 (66%)
Thrombolysis	4 (2%)
Total Eosinophilic Count	0.22 ± 0.20

Table 2. Variables Associated with the Development of CHF in the First Four Days after MI

Characteristics (n)	CHF n = 43	No CHF n = 96	O d d s Ratio	P value
Age	61 ± 10.72	56 ± 11.17	1.03	0.035
Sex (Male)	29 (21%)	74 (53%)	0.62	0.23
Hypertension	32 (32%)	67 (62%)	1.03	0.58
Diabetes Mellitus	20 (46%)	24 (25%)	2.60	0.013
Smoking history	21 (48%)	58 (60%)	0.62	0.20
Trop I	8.78 ± 16.24	7.23 ± 13.16	1.0	0.55

Table 3. Association of Total Eosinophilic Count with Development of Congestive Heart Failure

Characteristics (n)	CHF n = 43	No CHF n = 96	O d d s Ratio	P value
Eosinophilic Count	0.20 ± 0.16	0.24 ± 0.21	0.38	0.35

DISCUSSION

Any level of eosinophilia was not associate with the early development of congestive heart failure in patients with AMI in contrast with the study of Loeffer. In 1963, Loffler first recognized the association of a distinct form of severe heart failure with the development of heart failure with marked eosinophilia.[8] In one study by Tores et al., low eosinophil count was reported to be significantly associated with the development of congestive heart failure in myocardial infarction patients.[6] A study by Bass noted that after an initial response to acute inflammation, there is rapid drop in the number of circulating eosinophils due to either destruction of eosinophils or peripheral sequestration of eosinophils in the inflammatory regions.[5]

Our study showed that patients's age can likely increase the risk of developing heart failure. Bershtein et a1,[9] noted that advanced age was seen in patients with heart failure in post MI patient. Thus, age can be a predictor for the development of heart failure.

Aside from patient's age, presence of diabetes mellitus likewise showed an increased risk for the development of heart failure. Several studies have showed the direct relationship of diabetes mellitus in heart failure. It also showed that patients with diabetes who developed heart failure appeared to have higher mortality especially if heart failure was caused by coronary artery disease.[10]

This study has some limitations. The measurement of complete blood count was done at only one point and it was not consistent in all patients. We can try to do serial determination to increase the sensitivity of the study. The strength of the study can further be strengthened if we can increase the time of follow-up to observed the development of heart failure.

CONCLUSION

Study showed no statistically significant association between total eosinophilic count in patients admitted for acute myocardial infarction and the development of congestive heart failure in the first four days of admission. However, our study showed age and diabetes mellitus can predict the risk for developing heart failure in post myocardial infarction patients.

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The Accuracy of Chest Radiograph in Diagnosing Left Ventricular Systolic Dysfunction Using 2D Echocardiography as the Reference Standard

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Background --- The chest radiograph is an affordable and accessible imaging modality that has been used in the past to evaluate the heart for the presence of disease but has taken a backseat in the recent years with the development of newer diagnostic techniques. Furthermore, most recent guidelines do not take a clear stand as to the position of the chest x-ray in patient management. Hence, the role of the chest radiograph in the diagnosis of left ventricular systolic dysfunction is now being investigated in this study.
Method --- The chest radiographs of 187 patients were independently evaluated by 3 radiologists who were not aware of each other's reading and the 2D echocardiography results. The diagnosis as to the presence of pulmonary congestion and left ventricular dilatation (LVD) was made from the consensus reading of the 3 radiologists. These results were then correlated with left ventricular systolic dysfunction by 2D echocardiography. The sensitivity and specificity results as well as the negative and positive predictive values, kappa and p- values of the chest x-ray findings for the diagnosis of left ventricular systolic dysfunction were determined.
Results --- Among the 33 subjects who had radiographic left ventricular dilatation and pulmonary congestion, only 3 of them actually had left ventricular systolic dysfunction on 2D echocardiography [Sn= 18.7, Sp= 52.6, PPV=3.6, NPV= 87.4, p value= 0.17). Of the 35 subjects with LV dilatation on chest x-rays, 7 had LV dysfunction by 2D echocardiography (SN=70.0, Sp=72.0, PPV=16.7, NPV=96.8, p- value= <0.01). On the other hand, only 3 patients with pulmonary congestion on chest radiograph were diagnosed to have LV dysfunction by 2D echocardiography (Sn= 50.0, Sp= 84.9, PPV= 15.8, NPV= 96.8, p- value= 0.02). Remarkably, 90 of the 93 patients who neither had left ventricular dilatation nor pulmonary congestion by chest radiographs were also negative for left ventricular dysfunction by 2D echocardiography.
Conclusion --- The chest x ray is a reliable modality for establishing the absence of left ventricular dysfunction. However, it is not a very good screening tool since the presence rf radiographic left ventricular dilatation and/or pulmonary congestion has low sensitivity in detecting LV systolic dysfunction. ***Phil Heart Center J 2016;21(2):31-36.***

Key Words: Ventricular Dysfunction ■ Left Ventricular Dilatation ■ Ejection Fraction ■ Pulmonary Congestion ■ Sensitivity ■ Specificity

Heart failure is the most frequent cause of hospitalization in the industrialized world and is a disabling, deadly and costly condition. Unlike coronary artery disease and stroke, the incidence of hospital admissions and deaths attributed to heart failure is increasing and has been predicted to continue.[1,2]

Clinically, some patients with advanced systolic dysfunction remain symptom-free of congestive heart failure (CHF). Thus, individuals may have systolic dysfunction but not managed as CHF.[3] It is vital to make an accurate diagnosis as ACE inhibitors and β-blockers can markedly improve morbidity and mortality. However, diagnosis of mild heart failure can be difficult as the clinical signs and symptoms of heart failure vary,[2,4] the most common underlying cardiac mechanisms responsible for CHF are left ventricular systolic dysfunction or diastolic dysfunction either alone or in combination.[5]

Careful assessment of cardiac function is essential in choosing the optimal management

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of patients with congestive heart failure.[1,4,6,7] The most common underlying cardiac mechanisms responsible for CHF are left ventricular systolic dysfunction or diastolic dysfunction either alone or in combination.[5] Left ventricular systolic dysfunction is a major cause of congestive heart failure, but a large number of these patients have normal left ventricular systolic function. This was confirmed by the study done by Redfield, et al[4] stating that as much as 40-50% of the individuals with CHF had normal ejection fraction. It is well known that patients may advance through an asymptomatic phase of left ventricular systolic dysfunction (ALVD) before developing evident heart failure. ALVD has been demonstrated in current studies to be as prevalent as overt CHF in the general population.[6]

Hoilund-Carlsen, et al[6] evaluated the chest radiographs according to the left ventricular chamber size and pulmonary vascular findings as criteria for diagnosing left ventricular systolic dysfunction. The previous finding was graded as normal (Grade I), possibly enlarged (Grade II) or enlarged (Grade III). The latter was likewise graded as no pulmonary congestion (Grade I), isolated flow shift to upper lobes (Grade II), interstitial edema (Grade III), and alveolar edema (Grade IV). They found out that as the left ventricular size became larger, then the more tendency for lower left ventricular ejection fraction. They also claimed that even though many of the patients had no signs of pulmonary congestion, there was a higher tendency for lower left ventricular ejection fraction as the degree of pulmonary congestion worsened.[6]

Many other studies have shown different chest x-ray findings of left ventricular systolic dysfunction like pulmonary vessel cephalization, interstitial lung edema, alveolar edema, pleural effusion, cardiomegaly, and cardiothoracic ratio >0.50. According to Fonseca et al[3] cardiac enlargement was the most helpful measurement, but this was only seen in about half of the patients with heart failure.[8]

A study by Fonseca et al[3] on 6300 adult subjects with suspected heart failure concluded that the chest x ray findings were not sufficient to reliably predict the presence of heart failure. Research findings of Hoilund-Carlsen et al[6] among 111 survivors of acute myocardial infarction also question the value of chest roentgenogram in the detection and grading of left ventricular systolic dysfunction. However, the study conducted by Knudsen et al[2] among 880 patients who presented in the emergency room with acute dyspnea revealed that chest radiographs were useful in the early diagnostic evaluation of heart failure.

Therefore, chest radiograph, which has taken a backseat in the recent years with the development of newer diagnostic techniques, is still an affordable, accessible and reliable imaging modality that can be used in the workup in patients with known or suspected cardiac failure. One reason for this could be that most recent guidelines do not take a clear stand as to the position of the chest x-ray in patient management.[6] On the other hand; echocardiography is considered the gold standard in evaluating the heart structures and for any abnormality such as heart failure, valvular heart problems, or ischemia.[5] A decreased left ventricular ejection fraction is definitive of left ventricular systolic dysfunction. It is difficult to diagnose mild heart failure in the community on the basis of clinical grounds alone.

The chest radiograph is a quick and inexpensive method for clinicians to assess cardiac status. Studies suggest that it is one of the most accurate tools for identifying both congestive heart failure and systolic dysfunction. Many experts recommend obtaining chest radiographs of symptomatic persons with possible heart failure. Some experts also recommend that asymptomatic persons receive screening chest radiographs to identify cardiac disease in specific settings.[9]

The study hypothesized that the chest x-ray can be used to detect left ventricular dysfunction among adults. Hence, this research aims to determine the accuracy of radiographic left ventricular dilatation and pulmonary congestion in the diagnosis of left ventricular systolic dysfunction.

METHODS

We conducted a prospective, cross-sectional study at the Radiological Sciences Division and Cardiology Department of the Philippine Heart Center, a tertiary referral specialized hospital, from January 2011 - August 2011. This study was approved by the Institutional Ethics Review Board and informed consent was obtained from each participant. We consecutively enrolled 187 adults referred for echocardiography at the Division of Noninvasive Cardiology. Excluded were subjects with contraindication for chest radiography. The chest radiographs taken in the postero-anterior and lateral views, should demonstrate the following: proper exposure and technique enabling measurement of the cardiac size and left ventricular chamber size; diaphragmatic level at least at the level of 9th posterior rib and the chest radiographs and 2D echo are taken within the same day or at most 24 hours apart.

Radiographic Data. The left ventricular chamber size was visually evaluated as either normal (negative) or enlarged (positive). The films were measured by taking the cardiothoracic (CT) ratio and looking for the presence of Hoffman-Rigler sign. The CT ratio was determined on teleradiograph by the ratio of the maximal transverse diameter of the cardiac silhouette ('heart diameter') to the distance between the internal margins of the ribs at the level of the right hemidiaphragm ('transverse thoracic diameter').[10] An adult chest normally had a CT ratio of 0.5 and a measurement greater than that value was considered enlarged or cardiomegaly. The Hoffman-Rigler sign was obtained in the lateral view by drawing a vertical line two centimeters above the diaphragm at the point where it intersected the IVC, and the distance between this line and the LV border was measured. A positive Hoffman-Rigler sign was a distance of more than 1.8 cm confirming LV enlargement.[11]

Pulmonary vascular congestion was established by the presence of pulmonary blood flow redistribution, equalization, cephalization, interstitial edema, or alveolar edema.

The chest radiograph films were independently read by 3 radiologists who were unaware of the clinical data and 2D echo result. A radiographic result was considered positive if the readings of all 3 radiologists were positive. If only 1 or 2 out of the 3 readings were positive then the result was considered negative. Inter-observer variability and agreement as to the readings of the three radiologists were likewise determined.

Echocardiographic Data. Left ventricular systolic function was evaluated by using the linear method for fractional shortening and calculated the ejection fraction using the M-mode and modified Simpson's methods. Left ventricular ejection fraction (LVEF) results in the official report were tabulated in comparison with the chest radiogram findings. LVEF results lower than 0.45 were regarded as positive for LV systolic dysfunction and those greater than the defined cut-off were negative.

The echocardiographic findings of the subjects were determined in the Philippine Heart Center Division of Noninvasive Cardiology and each was read by two echocardiologists then reviewed and cross-checked by the supervising echocardiology consultant. The average of the three readings was used as the final diagnosis.

Statistical Analysis. The sample size computed was $n \geq 144$ based on $\alpha = 0.05$, relative error of 10% and assumed accuracy of chest radiograph findings of 70% in predicting LV systolic dysfunction as presented in the study of Hoilund-Carlsen et a1.[6] The sensitivity, specificity, positive predictive value, and negative predictive value were determined to establish the accuracy of chest x-ray findings. Kappa test was used to compute for the significance and degree of agreement of chest x-ray findings with 2D echocardiography results in diagnosing LV systolic dysfunction.

Table 1 shows the demographic characteristics of patients included in this study. It can be noted that there was almost equal distribution of male (49.7%) and female subjects (50.3%). The mean age of the subjects was 48.7 (19-86 y/o). Many of them had valvular pathology (24%) and intervention (21%) as well as hypertension (19%)

and coronary artery disease (18%). Few patients took maintenance medications: diuretics (7.5%); βeta-blockers (1.1%); ACE inhibitors (4.8%); Digoxin (3.2%); and Amlodipine (6.4%)

Table 2 reports the accuracy of chest x-ray findings in determining LV systolic dysfunction. Among the 33 subjects who had radiographic left ventricular dilatation and pulmonary congestion, only 3 of them actually had left ventricular systolic dysfunction on 2D echocardiography. This table likewise shows that among the 93 patients who did not present with LVD or congestion on x-ray, 90 of them in reality had no left ventricular systolic dysfunction on 2D echocardiography. Seven patients had LV systolic dysfunction on 2D echocardiography among the 42 patients who only had left ventricular dilatation of x-ray. Lastly, only 3 patients had LV systolic dysfunction on 2D echocardiography among the 19 patients who had radiographic pulmonary congestion.

Table 1. Characteristics of patients in the study. (PHC, 2013)

Characteristics	Frequency n=187
Age (Mean ± SD)	48.7 ± 16.7
Male Gender	93 (49.7)
Co-morbidities	
Hypertension	35 (18.7)
Diabetes Mellitus	19 (10.2)
Valvular pathology	46 (24.6)
Congenital heart anomaly	21 (11.2)
Coronary artery disease	33 (17.6)
Cancer	3 (1.6)
Others (ex. intervention)	40 (21.4)
Medication	
Diuretics	14 (7.5)
B blockers	2 (1.1)
ACE inhibitors	9 (4.8)
Digoxin	6 (3.2)
Amlodipine	12 (6.4)

Table 2. Accuracy of Chest X-ray Findings in Determining LV Systolic Dysfunction by 2D Echocardiography (PHC, 2013)

CXR Findings	LV Dysfunction -	LV Dysfunction +	Sn¶	Sp**	PPV‡‡	NPV‡‡	Kappa	P Value
1*	30	3	18.7	52.6	3.6	87.4	0.08 ± 0.07	0.17
2⁺	35	7	70.0	72.0	16.7	96.8	0.17 ± 0.07	<0.01
3≠	16	3	50.0	84.9	15.8	96.8	0.17 ± 0.11	0.02
4§	90	3	3.6	12.6	3.23	13.8	NC	<0.01
Total	171	16						

Chest x-ray findings were labeled as follows: 1* Positive for both LV Dilatation and Pulmonary Congestion; 2⁺ Positive for LV dilatation but negative for Pulmonary congestion; 3‡ negative for LV dilatatic n but positive for Pulmonary congestion; 4§ negative for both LV Dilatation and Pulmonary congestion. Sn¶ Sensitivity Sp** Specificity PPV⁺⁺ Positive Predictive Value NPV‡‡ Negative Predictive Value

DISCUSSION

Among the subjects who exhibited both left ventricular dilatation and pulmonary congestion on chest radiograph, only three of them were diagnosed to have LV dysfunction by 2D echocardiography (Sn = 18.7, Sp = 52.6, PPV = 3.6, NPV= 87.4, p value = 0.17). Of the 35 chest x-rays demonstrating LV dilatation, seven had LV dysfunction by 2D echocardiography (Sn = 70.0, Sp= 72.0, PPV = 16.7, NPV = 96.8, p value = <0.01). On the other hand, only three patients with pulmonary congestion on chest radiograph were diagnosed to have LV dysfunction by 2D echocardiography (Sn = 50.0, Sp = 84.9, PPV = 15.8, NPV = 96.8, p value = 0.02). Remarkably, 90 patients (97%) who neither had LV dilatation nor pulmonary congestion by chest radiographs were also negative for LV dysfunction by 2D echocardiography. These results show that the presence of radiographic LV dilatation and/or pulmonary congestion has low sensitivity in predicting LV systolic dysfunction; hence, the chest radiograph is not a good screening tool. However, due to its high specificity and negative predictive value, the absence of radiographic LV dilatation and/or pulmorary congestion on x-ray makes it a very reliable confirmatory examination in determining the absence of LV systolic dysfunction.

In the study conducted by Fonseca et al. in 2004 among 6300 adult Portuguese subjects, they found out that radiographic variables had high specificity (79-99%) but modest sensitivity (1-54%) for the diagnosis of heart failure. The most sensitive chest radiographic abnormalities were cardiomegaly (54%) and cardiothoracic ratio >0.5 (43%).[3] Their findings in relation with ours just proved that radiographic LV dilatation can be considered a good determinant of LV dysfunction.

However, contradicting results were noted in the study of Hoilund-Carlsen, et al. in 2005 among 111 myocardial infarction survivors. Their study demonstrated a weak negative correlation between cardiothoracic ratio and LVEF (r = -0.18). Furthermore, they found that although radiographic congestion was a sign of reduced LVEF, its absence could not rule out a decrease in systolic LV function.[6] Thus, x-ray findings cannot substitute for quantitative and more direct measurement of LV function.

According to Mair et al, the best chest radiographic findings for diagnosing increased preload and reduced ejection fraction were redistribution and cardiomegaly, respectively.[8] However, neither finding alone could adequately exclude or confirm LV systolic dysfunction; our findings conforms well with it.

In the published work of Badgett et al[9] chest radiographs when used alone can only exclude or confirm systolic dysfunction in patients who come from populations with an extremely high or low prevalence of cardiac disease. In relation to this, our study has shown the strength of chest radiograph in predicting the absence of LV dysfunction, which we surmise to be better demonstrated in patients with low prevalence of cardiac disease.

Since this study was conducted in a tertiary referral center for cardiac disease, results may vary greatly if done in a general hospital or community setting. The radiographic parameter used in this study (i.e. pulmonary congestion) is a subjective finding, which is susceptible to variable interpretation especially in mild stages. Although, lots of studies including ours have proven low inter-observer variability in the interpretation of chest radiographs findings, particularly pulmonary congestion.

CONCLUSION

For institutions lacking sophisticated modalities such as 2D echocardiography, the chest x-ray may be utilized as a reliable modality for establishing the absence of left ventricular dysfunction due to its high specificity and negative predictive value. On the other hand, radiographic findings of left ventricular dilatation and/or pulmonary congestion are not very sensitive in detecting the presence of LV systolic dysfunction thus cannot be used as a dependable screening tool. The chest x-ray may not be a very dependable procedure for diagnosing LV systolic dysfunction; however, this may be strengthened if used in conjunction with other clinical findings as well as excellent physical examination and history taking.

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The Lung Function of Children with Hyperreactive Airway Disease and Chronic Congestive Heart Failure

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Background --- Airway hyperresponsiveness (AHR) has been closely associated with congenital heart disease and chronic congestive heart failure (CHF). However the relationship of both has not been fully explored. This study was made to differentiate patients with predominantly pulmonary or cardiac causes for AHR.
Method --- This is a cross-sectional study involved pediatric patients who have hyperreactive airways disease and chronic congestive heart failure. A baseline spirometry was done to each patient (pre-bronchodilator and the pre-diuretic spirometry). Each patient underwent two treatments: treatment A: bronchodilator first then diuretic, and treatment B: diuretic first then bronchodilator. At each treatment, a spirometry was done. The decision to which treatment each patient will undergo, was made randomly.
Results --- There were 28 predominantly male patients in the study with a mean age of 11 years old. Cough, breathlessness and wheezing were the common symptoms with 32% of subjects having a family history of atopy. Results show reduced values of FVC as well as FEV_1 and $FEF_{25-75\%}$, indicative of a restrictive ventilatory defect with concomitant obstructive airways disease. $FEV_{25-75\%}$, suggestive of small airways disease also show a mean % change of ≥35% in bronchodilator studies. Post bronchodilator study shows reversibility. Response was largely observed in the postbronchodilator study.
Conclusion --- This study showed that in the bronchodilator treatments, significant spirometric parameter observed was the reduced FVC, suggestive a restrictive ventilatory defect and FEV_1 indicating also a concomitant obstructive airways. $FEV_{25-75\%}$ also showed reduced values with a significant response (>35%) and reversibility noted postbronchodilator study. Post diuresis study show no significant improvement in the spirometric values. ***Phil Heart Center J 2016;21(2):37-45.***

Key Words: Lung Function ■ Hyperreactive Airway ■ Congestive Heart Failure

Asthma is a distinct clinical condition which may or may not be associated with other disorders. While manifestation of asthma may at times be similar to that of other illnesses such bronchiolitis, a diagnosis of asthma can be made in the absence or presence of other illnesses with significant certainty in almost all situations, which is a pre-requisite for appropriate management. Clinically, it is characterized by airway hyperresponsiveness (AHR) presenting as widespread narrowing of the airway which results from a variety of stimuli like allergens, exercise, physical factors and irritant gases. It is also characterized by intermittent episodes of a constellation of symptoms in-between asymptomatic intervals.[1]

Airway hyperresponsiveness, the characteristic functional abnormality of asthma, results in airway narrowing in a patient with asthma in response to a stimulus that would be innocuous in a normal person.[2] In turn, this airway narrowing leads to variable airflow limitation and intermittent symptoms. Airway hyperesponsiveness is linked to both inflammation and repair of the airways and is partially reversible with therapy.[2] It has been observed in a study of Busse[3] that the persistent component of airway hyperesponsiveness (AHR) represents structural changes in the airway, whereas the variable feature relates to inflammatory events. The structural changes of the airway that contribute

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to AHR include those of remodeling and smooth muscle hypertrophy.

The diagnosis of asthma is usually based on the presence of characteristic symptoms. However, measurements of lung function and particularly the demonstration of reversibility of lung function abnormalities, greatly enhance diagnostic confidence. This is because patients with asthma frequently have poor recognition of their symptoms and poor perception of symptom severity, especially if their asthma is long-standing. Measurement of lung function provides as assessment of the severity of airflow limitation, its reversibility and its variability and provides confirmation of the diagnosis of asthma. Although measurement of lung function do not correlate strongly with symptoms or other measures of disease control in either adults or children, these measures provide complementary information about different aspects of asthma control.[2] Spirometry is the recommended methods measuring airflow limitation and reversibility to establish a diagnosis of asthma. Various methods are available to assess airflow limitation, but two methods have gained widespread acceptance for use in patients over 5 years of age. These are particularly the measurement of forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC), and peak expiratory flow (PEF) measurement.[2]

Wheezing is a common respiratory symptom that is commonly associated with hyperreactive airway disease secondary to any critical narrowing of the distal airways. It is a prominent sign of asthma and originates from oscillations of airways at many sites in the chest.[4]

It can also be present in patients with congenital heart disease especially when accompanied with congestion (cardiac wheeze). Congenital cardiovascular anomalies are believed to occur concomitantly with hyperreactive airway disease. Although the prevalence of asthma and/or airway hyperresponsiveness (AHR) in children with CHD is not well explored, some authors have suggested that asthma or AHR is more common in children with CHD than in the general population. Tsubata and co-workers[5] reported that 6 out of 10 of their patients with congestive heart failure (CHF) secondary to CHD had AHR elicited by histamine challenge, while Ackerman et al[6] identified an extremely strong association between a particular CHD (pulmonary atresia with VSD) and persistent AHR. Small airway obstruction has been a presenting sign of a group of infants with ventricular septal defects and left-to-right shunts. In addition, some children with interstitial edema as a result of left atrial obstruction (e.g., cor triatriatum) have also presented with a history of recurrent asthmatic attacks.[4] Overall, there is a paucity of literature, particularly from developing countries, concerning the co-existence of airway disease including asthma and AHR, with CHD.

Diuresis of healthy subjects results in increased lung volumes and flows suggesting that even in health, pulmonary function is influenced by the water content of the lung.[7] The protective effect of furosemide in asthma according to Lockhart et al, are poorly understood and is multifactorial. It was not due to a direct effect on airway smooth muscle but is by inhibition of the release of paracrine mediators evoked by physiologic stimuli.[8] A study done by Pison et al to adult patients with chronic left heart failure and on bronchial hyperresponsivenss to inhaled methacholine and after increasing diuretic therapy, significant airway obstruction was observed during acute decompensation manifested by a $PC_{20} \leq$ 16mg/ml (concentration of methacholine causing a 20% fall in FEV_1) with improvement of mean vital capacity and FEV, after diuretic therapy.[9]

It is the aim of this study to investigate the pulmonary physiology of hyperreactive airway disease and chronic congestive heart failure in those pediatric patients with congenital and acquired heart disease. This would then be an initial step in the differentiation of patients with predominantly pulmonary or cardiac causes for airway hyperresponsiveness. Therefore, once these patients are identified, a management plan will be efficiently applied to them. The maneuver done in the study in identifying these type of patients will also be useful for diagnosis in subsequent patients seen in the outpatient.

This study was done to determine the pulmonary physiology of children with hyperreactive airway disease and congestive heart failure; to determine the pulmonary physiology through

lung function using spirometric values (FVC, FEV_1, FEV_1/FVC and FEF_{25-75}) of children with hyperreactive airway disease and congestive heart failure; and to differentiate patients with congestive heart failure alone and those with concomitant hyperreactive airway disease through changes in spirometry values (FVC, FEV_1, FEV_1, FVC and FEF_{25-75}).

METHODS

This study is done at the Philippine Heart Center from September 2012 to March 2013. Included in the study were all pediatric patients aged 7-18 years old with chronic congestive heart failure, presenting as tachypnea, poor weight gain, frequent respiratory infection in congenital and acquired heart disease; patients who present with wheezing and/or other associated symptoms associated with airway hyperresponsiveness referred at the pediatric pulmonary outpatient department or admitted patients for pulmonary evaluation. Excluded in the study were patients with heart failure in Class III-IV; patients on mechanical ventilation and with acute exacerbation or with other co-morbidities such as pneumonia; patients who are dehydrated, with contraindication to beta 2 antagonist, diuretics or those with uncorrected hypokalemia; patients who may have hypercyanotic spells such as those with TOF and those with with uncontrolled arrhythmias.

Sample Size. Based on the 2011 census of hyperreactive airways of patients with congenital heart disease at the outpatient department in the pediatric pulmonology section, which is 52 out of 1,099 patients or 4.75%, the computed sample size is n=37 at 95% CI, 80% power, from an assumed mean percentage change in FEV_1 of -7.917 ± 7.115 and FEV_1/FVC of 2.75 ± 9.46 as computed from the data presented in the study made by Pison et al.[9]

Study Maneuver. All patients with congenital heart disease who present with wheezing or other associated symptoms of airway hyperresponsiveness referred to the pediatric pulmonary section for evaluation or inpatients for pre-evaluation were identified. Patients with airway hyperresponsiveness were considered as having symptoms of cough, wheeze and/or chest tightness, breathlessness or gurgly chest and any of the associated symptoms: association during exercise, with nocturnal occurrence, episodic/ seasonal occurrence, family history of atopy and other triggers. After approval from the Philippine Heart Center-IERB, consents were given and explained. Parents and patients aged 18 years old, were asked to sign the informed consent form and the participants aged 7-17 years old were asked to give their assent.

A baseline spirometry was done to each patient and this was labeled as the prebronchodilator and the pre-diuretic spirometry. Each patient was made to undergo two treatments: **Treatment A:** bronchodilator first then diuretic, and **Treatment B:** diuretic first then bronchodilator. At each treatment a spirometry was done. The decision to which treatment each patient will undergo, was made randomly.

The patients were given bronchodilator then the responses (post-bronchodilator spirometry were tabulated (FEV_1, FEV_1/FVC, FEF 25-75%). If the change in FEV_1 and FVC is more than or equal to 15% (≥15%) and in FEF 25-75%, a value of ≤35%, patients was classified as having a positive response to the bronchodilator. Otherwise, values <15% for FVC and FEV_1 and <35% for FEF 25-75% were considered a negative response.

The patients who underwent diuretic challenge either had an initial dose of diuretic in a patient without diuretic therapy before or the usual or increased diuretic dose for those patients already maintained on diuretics. This was done at the discretion of the attending physician. The investigator in this study did not take part in the initial treatment or the adjustment of the diuretic dose, but the dose received by the patient was noted. Six hours after intake of diuretic or when the patient had already a notable urine output, a spirometry was done (post-diuresis spirometry). A positive response to diuretic response was a change of ≥15% in the spirometry values (FVC, FEV_1 and FEV_1/FVC) from the baseline and negative response was a value <15%. In FEF 25-75%, a change of ≥35%was considered a positive response and a value of <35% was considered a

negative response.

Prior to all scheduled spirometry, patients with controller or reliever medications (bronchodilator) were asked to withheld these medications 12-24 hours prior to procedure. Those who are unable to withheld these medications were re-evaluated for eligibility on the next scheduled visit.

All spirometry (baseline or pre and post bronchodilator and diuresis) were tabulated including differences between initial and post treatment spirometry.

Statistical Analysis. Data on demographic characteristics and signs and symptoms of patients were presented as mean ± standard deviation, frequency and percent distribution. In the comparison of the spirometry values the pre- and post bronchodilator and post diuresis, the *T*-test and Pearson correlation for was used.

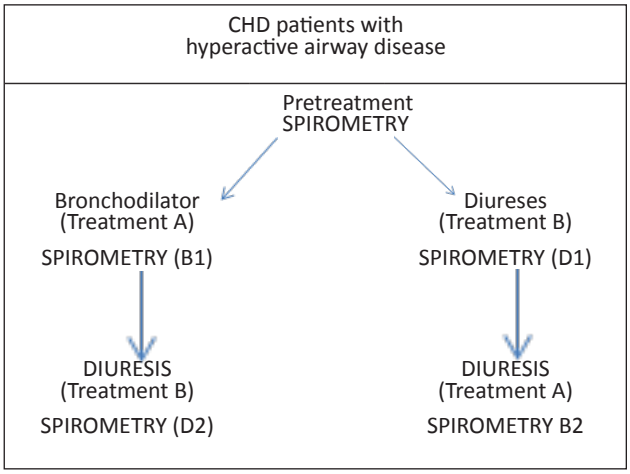

Figure 1. Flow chart of the spirometric maneuver and sequence of study treatments on every subjects

RESULTS

Table 1 shows that among the 28 patients, the mean age was 11 years and majority were males (64%). However, five patients who were eligible were unable to perform the forced expiratory maneuver. The common type of congenital heart disease were those with VSD and PDA. Clinical symptoms included mostly cough and breathlessness. Most patients had seasonal or episodic occurrence, however only 32% had a family history of atopy. Medications presently given to these patients were their main-

Table 1. Clinical and demographic characteristics of pediatric CHD patients

Variables	Frequency/Mean/ STD Deviation n=28
DEMOGRAPHICS	
Age	10.86 ±3.25
Weight	30.80 ±13.50
Height	1.37±0.20
BMI	15.80±3.50
Sex - Female Male	10 (36%) 18 (64%)
TYPE OF CARDIAC LESION	
Congenital Heart Disease	
ASD	1 (4%)
VSD	13 (46%)
PDA	5 (18%)
VSD & PDA	1 (4%)
AVSD	1 (4%)
TOF	2 (7%)
DTGA & PDA	1 (4%)
Ebstein Anomaly, ASD	1 (4%)
TVA	1 (5%)
Acquired Heart Disease (RHD)	
Valvular Disease	2 (7%)
DISPOSITIONS	
Preoperative	17 (61%)
Postoperative	11 (39%)
CLINICAL SYMPTOMS	
Cough	25 (89%)
Wheeze	13 (46%)
Breathlessness	18 (64%)
Chest tightness	-
ASSOCIATED SYMPTOMS	
Exercise	-
Nocturnal occurrence	-
Episodic/Seasonal occurence	14 (50%)
Family history of atopy	9 (32%)
Recognizable triggers	-
MEDICATIONS	
Bronchodilators	26 (93%)
Antileukotriene/anti-inflammatory	4 (14%)
Diuretics	14 (50%)
Heart Failure medication	1 (4%)
Inoptropes	15 (54%)
Antihypertensives	8 (29%)
PAH medications	3 (11%)
Antiarrhythmia	1 (4%)

tenance bronchodilators, inotropes (digoxin), diuretics (furosemide) and antihypertensive/ preloader (captopril). Three patients were maintained on a pulmonary vasodilator (sildenafil).

Table 2 shows the mean spirometric values in each patient where bronchodilator was given as first treatment. It showed values below the normal range (<80%) for FVC, FEV_1 and $FEF_{25-75\%}$ thus suggestive of a restrictive ventilatory defect with obstructive airways disease.

Mean percentage change reach the significant value of >35% in FEF_{25-75} which also showed statistical significance. It also showed reversibility in postbronchodilator study. Pre- and postbronchodilator values for FEV_1 and FEV_1/FVC were statistically significant however mean % change did not reach >15%.

Table 3 shows the mean spirometric results of patients in which diuretic was given as first treatment. All values were also below the normal range of 80% and mean change for all values did not reach at > 15%.

Table 2. Sprirometry results with bronchodilator (BI) as first treatment

SPIROMETRY RESULTS	Pre-bronchodilator n=21	Post-bronchodilator n=21	Mean Difference	% Change	p-value
FVC	1.80 ± 0.83 (79.25% ± 17.26)	1.81 ± 0.83 (78.57 ± 17.54%)	0.009 (0.68)	1.003	0.743 (0.740)
FEV_1	1.48 ±0.59 (71.68% ± 18.33%)	1.58 ± 0.68 (76.79 ± 17.76%)	-0.11 (-5.11)	6.711	0.009 (0.001)
FEV_1/FVC	83.68 ± 9.37	88.57 ± 7.75	-4.89	6.422	0.000
FEF_{25-75}	1.61 ± 0.62 (68.93 ± 27.75%)	2.12 ± 0.84 (88.57 ± 34.09%)	-0.51 (-19.64)	34.58	0.000

Table 3. Spirometry results with diuretic (DI) as first treatment

SPIROMETRY RESULTS	Pre-diuresis n=21	Post-diuresis n=21	Mean Difference	% Change	p-value
FVC	1.80 ± 0.83 (79.25% ± 17.26)	1.84 ± 0.87 (78.89 ± 19.91%)	-0.006 (0.36)	-0.117	0.769 (0.730)
FEV_1	1.48 ±0.59 (71.68% ± 18.33%)	1.48 ± 0.60 (73.68 ± 20.85%)	0.005 (-0.57)	0.048	0.853 (0.642)
FEV_1/FVC	83.68 ± 9.37	84.29 ± 10.61	-0.607	0.673	0.449
FEF_{25-75}	1.61 ± 0.62 (68.93 ± 27.75%)	1.77 ± 0.84 (75.36 ± 35.0%)	-0.16 (-6.43)	11.38	0.128 (0.095)

Table 4. Spirometry results with bronchodilator (B2) as second treatment

SPIROMETRY RESULTS	Pre-diuresis n=21	Post-diuresis n=21	Mean Difference	% Change	p-value
FVC	1.80 ± 0.83 (79.25% ± 17.26)	1.82 ± 0.85 (78.89 ± 19.91%)	-0.018 (0.36)	1.38	0.43 (0.79)
FEV_1	1.48 ±0.59 (71.68% ± 18.33%)	1.59 ± 0.69 (77.71 ± 18.54%)	0.113 (-4.6)	7.33	0.009 (0.004)
FEV_1/FVC	83.68 ± 9.37	88.86 ± 7.14	-5.18	6.81	.000
FEF_{25-75}	1.61 ± 0.62 (68.93 ± 27.75%)	2.15 ± 0.90 (86.82 ± 39.41%)	-0.54 (-17.9)	35.27	0.000 (0.004)

Table 5. Sprirometry results with diuretic (D2) as second treatment

SPIROMETRY RESULTS	Pre-diuresis n=21	Post-diuresis n=21	Mean Difference	% Change	p-value
FVC	1.80 ± 0.83 (79.25% ± 17.26)	1.82 ± 0.82 (78.5 ± 18%)	-0.002 (0.71)	1.03	0.465 (0.693)
FEV_1	1.48 ±0.59 (71.68% ± 18.33%)	1.57 ± 0.70 (75.96 ± 17.8%)	-0.10 (-2.86)	6.21	0.038 (0.114)
FEV_1/FVC	83.68 ± 9.37	87.86 ± 7.74	-4.18	5.56	0.001
FEF_{25-75}	1.61 ± 0.62 (68.93 ± 27.75%)	2.01 ± 0.78 (85.61 ± 34.32%)	-0.40 (16.7)	27.90	0.000

Table 4 shows the mean spirometry values of patients in which bronchodilator was given as second treatment. These values are observed to be below the normal range of 80% with a significant % change of >35% noted in $FEF_{25-75\%.}$ This value was also statistically significant as well. In the postbronchodilator study, spirometric values also show reversibility. FEV, and FEV,/FVC values are noted to be statistically significant, although a >15% mean change was not observed.

Table 5 shows the mean spirometric values of patients in which the diuretic was given as second treatment. All values showed a decrease with no significant % change even in $FEF_{25-75\%,}$ even if significant values in FEV_1/FVC, and FEV_1 were statistically significant.

In summary, comparing the mean % changes of all spirometric values, there is a >35% mean change in $FEF_{25-75\%}$, in the bronchodilator study both as an initial and second treatment.

Comparing the percent change of all spirometric values measured between patients who underwent corrective or palliative surgeries or not, no difference in the p-values were observed. Using the Pearson correlation, the percent change in FVC was also observed to be significant in the fluid balance values in the treatment group where diuretic was given as a second treatment (r=0.42).

Table 6. Comparison of the mean difference of the spirometric values with bronchodilator (B 1) as initial and diuretic (D 1) treatment

SPIROMETRY	% change	p-value
FVC	1.04 ± 10.38	0.593
FEV_1	6.67 ± 12.61	0.008
FEV_1/FVC	5.75 ± 9.26	0.002
FEF_{25-75}	2.32 ± 26 .24	0.000

Table 7. Comparison of the mean difference of the spirometric values with bronchodilator (B2) and diuretic as second treatment (D2)

SPIROMETRY	% change	p-value
FVC	0.35 ± 9.65	0.845
FEV_1	1.11± 9.31	0.524
FEV_1/FVC	1.24 ± 5.36	0.222
FEF_{25-75}	7.37 ± 31.30	0.215

Table 8. Comparison of the % change of the spirometric values with bronchodilator (B 1) as initial and second treatment (B2)

SPIROMETRY	% change	p-value
FVC	-0.45 ± 8.49	0.776
FEV_1	-0.61 ± 9.47	0.731
FEV_1/FVC	-0.38 ± 5.29	0.699
FEF_{25-75}	-0.69 ± 24.94	0.882

Table 9. Comparison of the % change of the spirometric values with diuretic (Dl) as initial and second treatment (D2)

SPIROMETRY	% change	p-value
FVC	-l.15 ± 10.37	0.557
FEV_1	-6.17 ± 13.20	0.018
FEV_1/FVC	-4.89 ± 9.11	0.007
FEF_{25-75}	-l.65 ± 43.31	0.049

In Table 6-9, using the *T* test to compare the percent change between the different treatments, statistically significant % change values were observed in FEV_1, FEV_1/FVC and $FEF_{25-75\%}$ in both treatments where bronchodilator and diuretic was given as initial treatments. However when comparing the mean % change in each treatment (*Table 2 and 3*), only spirometric values in the treatment with bronchodilator as initial treatment had values which showed a significant % change in $FEF_{25-75\%}$.

DISCUSSION

The results of this study generally show reduced values of FVC as well as FEV_1. This values indicate a restrictive ventilatory defect with concomitant obstructive airways disease. $FEF_{25.75\%}$, which generally suggests small airways also show a mean % change of >15% in the bronchodilator studies. Post-bronchodilator study shows positive response.

Several studies in the past had dealt with the lung function of children with congenital heart diseases. The study of Linde, Siegel, Martelle and Simmons showed that there was a significant reductions in the vital capacity (VC) and maximal ventilatory volume (MVV) and increased values for the functional residual capacity (FRC) and residual volume (RV). In contrast, those patients with severe pulmonary hypertension were noted to have decreased FRC and RV.[10] It was also shown that compliance was therefore reduced in children with large left-to-right shunt and/or pulmonary hypertension. Furthermore, these were supported by studies cited, like that of Wilson and Edwards where in they showed that reduced vital capacity was also observed in children with rheumatic heart disease.[11] The study of Binger further elucidates that increased residual volumes were noted when patients suffer from cardiac decompensation.[12] Another study by Gamalero and Segagni,[13] also observed that cyanotic patients with right-to-left shunts had the greatest reduction of vital capacity (VC) and MVV with less reduction in those children with left-to-right shunts.

These findings are in consonance with the results seen in Tables 2-5, in which the forced vital capacity (FVC) indicative of a restrictive ventilatory defect was noted to be decreased (<80%). Majority of the patients had left-to-right shunts (VSD and PDA). As mentioned in cited studies, the impairment of ventilatory function in left-to-right shunts were probably due to decreased pulmonary elasticity as well as decreased effective respiratory muscle strength. Furthermore, vital capacity decreased in disease and debilitation. Recurrent infection, poor general growth, poor development and enlarged hearts in small thoracic cages might reduce functional lung tissue in congenital heart disease. These children may also have limited opportunity to develop ventilatory function through exercise. For those with pulmonary hypertension, reduction in vital capacity (VC) and total lung capacity suggests that progressive medial hypertrophy and intimal proliferation of pulmonary vessels might decrease lung distensibility.[10] In our study in children with pulmonary arterial hypertension (PAH), there were noted differences in their spirometric values as compared with those who have normal and less severe PAH. However since this was not the main objective of this study, this was not done but would have been worthwhile study to be done.

In humans, the increase in airway resistance that occurs when there are small amounts of interstitial edema arises largely from a vagally mediated reflex. Once interstitial edema worsens, the peribronchiolar cuffs of fluid would be expected to lead to increased closing volume and airway resistance.[4] In a paper presented by Gehlbach et al[7], another mechanism for airflow obstruction in the setting of pulmonary congestion and edema is reflex bronchoconstriction

brought by the elevation of pulmonary or bronchial vascular pressure. Other potential causes of airway narrowing include the geometric decrease in airway size from reduced lung volume, obstruction from intraluminal edema fluid and bronchial mucosal swelling. As further cited by Gehlbach et a1[7], the studies of Cabanes et al[14] and Rolla G. et al[15], found increase in bronchial responsiveness to methacholine in patients with left ventricular dysfunction or mitral valve disease.[14] Contrary to earlier reasoning, there is no evidence that engorged bronchovascular bundles directly compress small airways. The study done by Rolla G. et al[16], found that ipratropium bromide produced bronchodilation in acute exacerbations of chronic CHF.

Previously mentioned, the study of Pison and coworkers was done to assess bronchial hyperresponsiveness to inhaled methacholine in adult subjects with chronic left heart failure during an exacerbation and after intensive diuretic therapy. Findings revealed evidence of airway obstruction with a significant reduction in FEV_1 and FEV_1/FVC in 6 of 8 subjects. However, there was no significant relationship between these spirometric parameters and concentration of methacholine causing a 20% fall in FEV_1 (PC20). Two subjects were noted to have improvement in FEV_1 after a 5-15 day intensive diuretic therapy.[9] In a related study done by Gertz, Hedenstierna and Wester in adult COPD patients in which spirometric recordings reveal stable but severe obstruction of the airways and enlarged residual volume were observed in hypervolemic and polycythemic patients with intensified diuretic (Furosemide, 120 to 250 mg/day) given for 2 weeks to 2 months. However the emphasis of this study was more on the improvement of blood volume, hematocrit reading and central hemodynamics assessed through cardiac catheterization.[17] These studies differs from the present study because our findings show that there is a restrictive ventilatory defect with concomitant obstructive airway defect, response to bronchodilator treatment show significant response and reversibility. Diuretic treatment did not show response probably because the diuretic therapy was not given in a longer duration (>2 weeks to 2 months) and doses were not increased >3 times the usual usual dose. The relationship of an elevated pulmonary blood flow and capillary pressure on lung responsiveness was investigated in the study of Petak and co-workers.[18] However this specific research was done in animals (rats) and responses of the above parameters were observed in lung perfusion study of isolated rat lungs. The results of this study demonstrate the development of bronchial hyperresponsiveness with acutely increasing pulmonary blood flow (Qp) in association with high capillary pressure (Pc). These changes was attributed to the increased tension of the pulmonary microvasculature, leading to an enhanced stiffness and dissipation of the parenchyma via mechanical attachment and the possible loss of lung volume with filled pressured capillaries.[18]

CONCLUSION/ RECOMMENDATIONS

The results of this present study show that in the bronchodilator treatments, significant spirometric parameter observed was the reduced FVC, suggestive a restrictive ventilatory defect and FEV_1 indicating also a concomitant obstructive airways. $FEF_{25-75\%}$ also showed reduced values with a significant response and reversibility noted post-bronchodilator study. The following recommendations are therefore suggested:

1. Diuretic therapy should be increase in dose and duration (2 weeks-2 months)
2. Comparison between the responses to bronchodilator and diuretic therapy in children with cyanotic and acyanotic heart disease
3. Study carried in a longer period of time to further acquire an adequate number of participants
4. Patients with results showing significant responses to bronchodilator (mean change >15%) should be maintained on inhaled bronchodilators. These patients should also be encouraged to join asthma education programs conducted quarterly by the section of Pediatric Pulmonology.

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Validity of the Paragas Risk Scoring System in the Assessment of Cardiac Function Among Children With Chronic Heart Failure Due to Rheumatic Valvular Heart Disease

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Background --- Congestive heart failure is one of the most common causes of morbidity and mortality among pediatric patients with chronic rheumatic valvular heart disease. It is therefore the objective of this study to validate the outcome of the Paragas' Risk Scoring System in predicting mortality among pediatric patients with chronic heart failure due to chronic rheumatic valvular heat disease.

Method --- This cohort study included 30 patients with chronic rheumatic valvular heart disease (mitral regurgitation [MR], aortic regurgitation [AR], tricuspid regurgitation [TR], or a combination). Patients were admitted due to chronic heart disease, in NYHA Functional Class II- IV that necessitated Pediatric ICU admission, from January 1, 2005 to September 31, 2005. Upon admission, patients were scored using the 4-variable Paragas' Risk Scoring System. The variables were analysed using the Statistical Packages for Social Sciences (SPSS) version 10.0 for Windows. Frequency tables were used to describe the relationship of each score with the patient. The Chi-square tests were used to determine the association between each score and the outcome. The Mann-Whitney test was used to determine relationship between the four parameters used for scoring and the outcome.

Results --- Total of 30 subjects were included in the study. Most of the patients have an LV ejection fraction of more than 50%, and those with less than 45% all died (p=0.042). Almost all patients that were intubated also have significant mortality (p=0.000). All patients that died does respond to any inotropic support (p=0.000) the presence of hyperkalemia does not seem to affect outcome (p=.156).

Conclusion --- The 4-variable Paragas' Risk Scoring System is a good predictor of outcome and mortality among pediatric patients with chronic heart failure secondary to chronic valvular rheumatic heart disease. ***Phil Heart Center J 2016;21(2):46-51.***

Key Words: 4-variable Paragas' Risk Scoring System ■ Chronic Heart Failure ■ Chronic Congestive Heart Failure ■ Mitral Regurgitation ■ Aortic Regurgitation ■ Tricuspid Regurgitation

Congestive heart failure is probably the most important cardiovascular condition that is still increasing in incidence and prevalence. Its assessment and prognosis is often difficult due to a lack of objective and easily obtainable parameters that accurately reflect disease status especially among children. Rheumatic heart diseases continue unabated, causing heart failure among young individuats in most of the developing countries. It comprises the single largest subset of admissions in pediatric cardiology and accounts for the largest mortality.

Hemodynamic evaluation is helpful for optimization of treatment, monitoring clinical outcomes, and overall prognostication of heart failure patients, but historically could only be attained via costly invasive procedures that carry substantial risks. In the era of widespread concern about quality of care and use of limited health care resources, methods to assess success of medical management and the risk of cardiac surgery are of increasing importance. In this country however, because of various reasons ranging from limited resources from both the

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health care provider and the patient's family, inability of access to good health care, as well as cultural beliefs, majority of these patients with this type of cardiac diseases are admitted in decompensated state. The ability to predict the outcome in this subgroup of patients is advantageous because primarily, it guides decision-making on whether to do surgery or not on a particular high-risk patient. It also provides a means to assess measures designed to improve outcome among high-risk group of patients. In addition, it allows realistic assessment of possible outcome of the medical management among this subgroup of patients.

This study was formulated to address the above concerns. It is hoped that upon completion, and with the subsequent information generated, a realistic assessment of the quality of care given to pediatric patients with chronic heart failure due rheumatic valvular heart diseases can be done and that measures to improve care can be recommended.

In 1998, South African Medical Group developed a guideline based on the published literature, which aims to properly diagnose and managed patients with chronic heart failure. The recommendation is to identify symptoms of heart failure together with an attempt at identifying an etiology and precipitating factors underlying the syndrome. Clinical examination is emphasized, including identifying the three tenets of the clinical diagnosis of CHF (syndrome, etiology, precipitating factors). The chest x-ray, ECG (resting, effort), selected blood tests are recommended as a routine in the diagnosis of CHF.[1]

In 1995, Doughty et al. showed that the most common cause of chronic heart failure is chronic rheumatic heart disease.[2] In 2002 at Philippine Heart Center, Paragas developed a two scoring system that would predict risk of mortality among patients with chronic heart failure due to rheumatic valvular disease. The first is the 13-variable risk index where it uses the NYHA functional class, LV ejection function, LV fractional shortening, and degree of pulmonary hypertension if any, the arterial blood gas and presence or absence of associated problems like renal failure, seizure, intubated, inotrope response, absolute neutrophil count, hyperkalemia, and hypoalbuminemia. In this scoring, an increasing total corresponded with higher probability of mortality. The observed significant cut-off value that was developed was 16-18, with a predictive value of positive test of 100%, predictive value of negative test of 73%, 31% sensitivity and 100% specificity. The second scoring system consisted of 4-variable risk scoring system including intubation or ventilatory support, non-responder to inotropic supports, LV ejection fraction, and hyperkalemia. The total risks score for mortality in an ICU setting if from zero to 10. The higher the score, the greater the probability of mortality cut-off score of seven was noted to be a significant predictor and have a predictive value of positive test of 100%, predictive value of a negative test of 7 %, 39% sensitivity, and 100% specificity.[3] The response to inotropes is on of the important factors in determining mortality among patients. Bagirova et al. in 2000 showed that hemodynamic parameters and exercise intolerance improved after capoten and atenolol treatment in patients with mitral valve or aortic valve defects with chronic cardiac failure.[4]

Another study done in Mexico in 2002 by Cossio et al, identified risk factor for heart failure among patients with rheumatic valvular heart diseases. In their study, the end-systolic dimensions, and volumes, left atrial area combined with ejection fraction, in their clinical evaluations were able to predict surgery mortality.[5]

METHODS

This is a cohort study. Subjects were from ages 19 years and below with rheumatic valvular heart disease and was admitted within the period of study (January 2005 - September 2005). All pediatric patients (age 19 years and below) with rheumatic valvular heart disease (mitral regurgitation or aortic regurgitation or a combination) in NYHA functional class II - IV admitted at the Philippine Heart Center, that necessitated pediatric intensive care unit (PICU) admission from January 2005 to September 2005 were enrolled in the study. Excluded in the study were: patients admitted to the PICU with valvular heart disease other than rheumatic in etiology (e.g. mitral valve prolapse, connective tissue disorder);

patients with rheumatic valvular involvement other than mitral regurgitation and/or aortic regurgitation (e.g. mitral stenosis, aortic stenosis); patients with acute mitral regurgitation, and/or acute aortic regurgitation; patients with rheumatic heart disease whose valvular regurgitation is less than one year; patients with chronic rheumatic valvular heart disease in NYHA functional class I -II admitted for elective surgery, either valvular replacement or valvular repair; and patients with chronic rheumatic valvular disease who necessitated ICU admission but whose medical condition is unrelated to cardiac disease.

Upon admission, patients will be scored using the Paragas' 4-variable scoring system. The following parameters will be used: 1. use of mechanical ventilatory support; 2. response to inotropes, which is defined as nonimprovement in the cardiac function with persistence of signs and symptoms and poor ejection fraction; 3. left ventricular ejection fraction, and; 4. presence of hyperkalemia. For each patient, the cut-off score will be seven, a score of more than seven indicates poor survival.

Data Analysis: Required sample size was determined using power analysis of established ICG data from other reports. Logistic regression analysis using Statistical Packages for Social Sciences (SPSS) version 10.0 for Windows was used to determine associations between the four parameters used for scoring. Frequency tables were used to describe the relationship of each score among patient. The chi-square tests were used to determine the association between each score and the outcome. The Mann-Whiney test was used to determine relationship between the four parameters and survival.

RESULTS

A total of 35 cases were enrolled in the study, however five patients were excluded because two patients underwent mitral valve replacement and the other three had pericardial effusion. Table 2 shows the characteristics of the study population. Demographic profiles of all subjects showed a mean age of 13.53 years old (SD ± - 3.67) ranging from 4 to 18 years old. More than half of the cases were male at 73.3% (22 cases) and only 26.7% were female. Most of these patients were admitted at the charity pediatric ICU (80%) and 20% were admitted at the pay pediatric ICU. Half of the cases (57%) admitted were labeled as active or having recurrence of rheumatic activity as the cause of congestive heart failure. In addition, most of these patient that were labeled as active had poor compliance to monthly secondary prophylactic injection.

More than half of the cases were in New York Heart Association (NYHA) functional class IV (57%), and had been having valvular regurgitation (mitral, aortic or a combination) with the mean of 5 years (range 1 - 12 years).

Table 3 summarizes the scores of the patient using the four parameters for risk. Among these patients, 53% (16) were intubated upon admission. Most of the cases that were included in the study have good response to inotropes (70%) and only 30% did not respond. More than half of the patients (83%) were noted to have good ejection fraction of more than 50%, 13% (4) have ejection fraction of 45-50%, and 3% (1) have LV ejection fraction of less than 45%. Only 20% (6) of these patients were noted to have hyperkalemia.

Table 4 shows the summary of the total scores of the patients. Majority of the patient (87%) have a total score of 7 and below, and most of them scored zero (46.7%). There were only 4 (13%) patients that scored more than 7.

Among the 30 cases studied, ther were 11 (36.7%) mortalities. Table 5 shows the percentage of survival in relation to the different parameters used in the Paragas' Risk Scoring System. There was no significant difference between the two sex groups (p value 0.770). Most of the patients with LV ejection fraction of more than 50% survival (p value of 0.042). There was no significant difference in the presence of hyperkalemia among those who survive and died (p value 0.156). All patients that died were intubated (p value of 0.000) and most of the patient that died were also non-responder to inotropes and statistically significant with p value of 0.000.

Most of the mortalities came from the older age group, between 12 to 18 years of age, with a p value of 0.000.

Figure 1 showed the overall distribution of patients admitted with chronic valvular rheumatic heart disease using the Paragas' Risk Scoring System.

Table 1. Paragas' four-variable scoring parameters

Variable		Risk Score
Intubated	yes	3
	no	0
Response to inotropes	yes	0
	no	4
LV Ejection Fraction	Less than 45%	2
	45-50%	1
	More than 50%	0
Hyperkalemia	yes	1
	no	0

Table 2. Summary of the demographic profile of patients with chronic valvular heart disease (n=30)

Age, years (range, mean ± SD)	4.0-18.0, **13.53**. ± 3.67		
Sex	Male	22	73.3%
	Female	8	26.7%
Category	Pay	6	20%
	Charity/Service	24	80%
Compliance to secondary prophylaxis	yes	19	63%
	No	11	37%
Active RF/RHD	Yes	17	57%
	No	13	43%
Years with chronic rheumatic valvular reguration (range, mean ± SD		1.0-14.0, **4.5**. ± 2.915	
NYHA Functional Class	III	13	43%
	IV	17	57%

Table 3. Summary of the demographic profile of patients with chronic valvular heart disease (n=30)

		Frequency	Percent
Intubated	Yes	14	46.7%
	No	16	53.3%
Responses to inotropes	Yes	9	30%
	No	21	70%
LV Ejection Fraction	Less than 45%	1	3.3%
	45-50%	4	13.3%
	more than 50%	25	83.3%
Hypokalemia	Yes	6	20%
	No	24	80%

Table 4. Summary of the total scores of patients with chronic rheumatic valvular heart disease using the Paragas' Risk Scoring System (n=30)

Score	Frequency	Percent
0	14	46.7%
1	2	6.7%
3	3	10.0%
4	1	3.3%
6	1	3.3%
7	5	16.7%
8	2	6.7%
9	2	6.7%

Table 5. Summary of statistical analyses (Chi-Square Test) of the different parameters in relation to the survival of the patients (n=30)

	SURVIVE		P Value
	YES	NO	
SEX			
Male	16	6	0.770
Female	3	5	
LV Ejection Fraction			
>50%	19	6	0.042
45-50%	0	4	
<45%	0	1	
Hyperkalemia			
	2	4	0.156
	17	7	
Intubated			
	3	11	0.000
	16		
Response to Inotropes			
	19	2	0.000
	0	9	

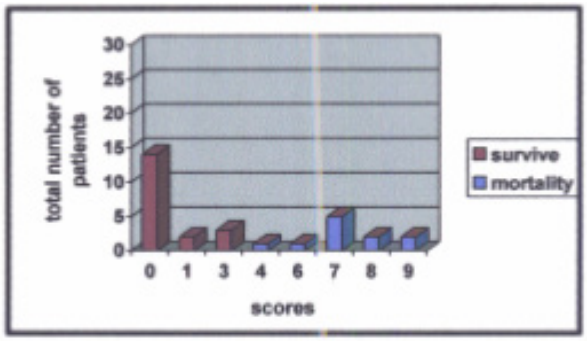

Figure 1. Distribution of subjects using the Paragas' Risk Scoring System

DISCUSSION

Rheumatic Fever (RF), a non-infectious delayed complication of streptococcal sore throat due to group B-hemolytic streptococcus (GABHS), is an enigmatic disease that has ravaged the humankind since the industrial revolution. Rheumatic heart disease (RHD) is the collective term relating to the structural and functional changes as a result of RF. Although the disease has been largely controlled in the industrialized nations, which were devastated by it in the early and middle part of this century, it continues to surface intermittently even in the most developed countries. It is still a major problem in the developing world. Given the inexplicable nature of the rise and fall, RF/RHD constitutes a major challenge to health care providers.[6] RF and the threat of residual heart disease make it imperative that we recognized and manage acute episodes of the disease effectively. The valvular lesion of rheumatic heart disease and ultimate heart failure due to its hemodynamic consequences causes the high mortality rate in rheumatic fever.

Chronic mitral regurgitation maybe the result of a slowly progressing valvular heart disease. The lesion usually becomes apparent within a few days or at most, few weeks after the onset of a rheumatic attack. Chronic mitral valvular insufficiency is the most common type of rheumatic heart disease in childhood. Prompt recognition and management of this valvular lesion prevents further involvement of other parts of the heart and the progression into intractable heart failure.

All of the patients included in the study have the chronic mitral regurgitation for more than 6 months. Almost half of the patients have involvement of other valves like aortic insufficiency and tricuspid regurgitation.

Most of the patients that were admitted belong to the older age group and were immediately intubated. The most common cause of congestive heart failure was recurrence of the disease. Sexual characteristics do not seem to affect the four different parameters and the outcome. Among the four parameters used in the assessment of cardiac function for chronic rheumatic valvular heart disease, the variable that gives significant result is the response to inotropes, the LV ejection fraction, and mechanical ventilatory support. Failure to respond to inotropic supports is secondary to the long-standing ventricular dysfunction, myocardial/ mechanical failure, or cardiomyopathy.

In order to have adequate cardiac output, a left ventricular ejection fraction of more than 50% is needed. In the Paragas' Risk Scoring System, an LV ejection fraction of 50-60% or more should be considered to have a normal LV function and should be considered high risk in the context of mitral regurgitation. The result of our validation study showed that those with LV ejection fraction of less than 45% have poor survival. Patients with good LV ejection fraction (more than 50%) have significant survival.

Another parameter used in the Paragas' Risk Scoring System is the presence of hyperkalemia. It is defined as having serum potassium levels of more than 4.5mmol/L. Almost half of the patients that were admitted have normal serum potassium level. Our study show no significant effect of this parameter on the outcome.

Like in other studies done, most of the patients are intubated and necessitated ventilatory support. lronically, although it is one of the appropriate management, intubations were likewise found to be a strong independent predictor of mortality. This could be because patients with all these manifestations are already severely decompensated. The inability to wean from the mechanical ventilator once intubated because of the minimal cardiac reserve, poor nutrition and and almost always the development of nosocomial pneumonia results to poor outcome.

The ability to predict outcome using the Paragas's Risk Scoring System in the assessment of patients with chronic heart failure secondary to chronic rheumatic valvular heart disease provides a means to improve outcome among high risk group patients. It allows realistic assessment of possible outcome of the medical management among this subgroup of patients with chronic rheumatic heart disease.

CONCLUSION

The 4-variable Paragas' Risk Scoring System used in the assessment of mortality among pediatric patients with chronic heart failure secondary to chronic rheumatic valvular heart disease was validated. The need for ventilatory support, response to inotropes and LV ejection action of less than 45% were all good predictors of mortality.

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The Association Between Serum Sodium and In-Hospital Mortality of Congestive Heart Failure Patients Admitted in Philippine Heart Center

Ronald P. Galicio, MD; Jesus D. Jorge, MD

Background **---** Hyponatremia has been identified as a risk factor for increased mortality and morbidity in patients with congestive heart failure (CHF). It has been shown to prognosticate patients with mild-to-moderate chronic heart failure in the outpatient as well as to predict length of hospitalization and mortality of the admitted patients.

Method **---** This is a concurrent cohort study which was conducted from January to October, 2007 and successively enrolled patients admitted in Philippine Heart Center who met the set criteria.

Results **---** Thirteen of the 104 subjects (12.5%) had hyponatremia (serum Na <130 mmol/L) on admission, whereas 8 patients out of 104 (7.7%) died. The difference between the mean serum Na level of those who died and those who survived was not statistically significant. The mortality between the hyponatremic and normonatremic groups did not also differ. Likewise, the association between serum Na on admission and the length of hospitalization did not reach statistical significance.

Conclusion **---** This study didn't show a clinically significant use of serum sodium determination on admission in terms of predicting outcome and length of hospital stay. ***Phil Heart Center J 2016;21(2):52-55.***

Key Words: Congestive Heart Failure ■ Serum Sodium ■ Hyponatremia

Hyponatremia has been identified as a risk factor for increased mortality and morbidity in patients with congestive heart failure (CHF).[1,2] It has been shown to prognosticate patients with mild-to-moderate chronic heart failure in the outpatient as well as to predict length of hospitalization and mortality of the admitted patients.[3-5] Low cardiac output and blood pressure associated with CHF triggers a compensatory response of the body that activates several neurohormonal systems designed to preserve arterial blood volume and pressure.[1,6] Hyponatremia in patients with CHF is primarily caused by increased activity of arginine vasopressin (AVP). AVP increases free-water reabsorption in the renal collecting ducts, increasing blood volume and diluting plasma sodium (Na) concentrations.[1,2,5-8] In most of our local settings where there is a scarcity of sophisticated laboratory examinations to prognosticate CHF patients, making use of the simple and commonly available laboratory work-ups, such as serum Na, could somehow predict the outcome of this group of patients.

The objective of this study is to determine the relationship of serum Na level on admission and the outcome in CHF NYHA Class Ill-IV patients; to determine the relation of serum Na level and in-hospital mortality of CHF NYHA Class III-IV patients; to determine the percentage of CHF NYHA Class III-IV patients admitted with hyponatremia; and to determine and compare the length of hospitalization of hyponatremic and normonatremic CHF NYHA Class III-IV patients.

METHODS

This is a concurrent cohort study which was conducted from January to October, 2007 and successively enrolled patients admitted in

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Philippine Heart Center who met the following criteria: *Inclusion Criteria*. Patients 18 years old and above on admission and those who presented on admission as CHF by Framingham criteria NYHA Class III-IV.[9] *Exclusion Criteria.* Patients with decompensated liver disease on admission; those who had renal co-morbidities such as nephrotic syndrome or end-stage renal disease on admission; those patients who had severe mitral stenosis (MS) with a MVA of ≤ l cm^2, and/or severe aortic stenosis (AS) with an AVA of ≤0.75cm^2 necessitating urgent interventional or surgical procedure on admission; those patients who did not have baseline serum sodium on admission; and those patients whose baseline serum sodium on admission was done in other laboratories using different methods.

Target population was set at ≥104 at α=0.05 and β=0.20 to allow significant relationship based on 40% and 69% death among patients with serum Na of >l35 mEqs/L and ≤135 mEqs/L respectively in the study of Panciroli C et al.[10] Serum Na results on admission determined in the Philippine Heart Center pathology laboratory using Vitros Chemistry Ion Selective Electrode (lSE), direct method, dry chemistry by Johnson & Johnson (NV:130-144 mmol/L) were collected, along with the patients' baseline characteristics. The outcome of these patients was followed-up, including the length of hospitalization. Chi-square and independent *T*-test were employed to determine the association of different factors with mortality. A p value of ≤0.05 was considered significant.

RESULTS

There were 104 patients included in the study with a mean age of 50 years old, 55 males and 49 females, and with ischemic and rheumatic heart diseases comprising the majority of the population. Table 1 summarizes the baseline characteristics and the etiologic distribution of the subjects.

Thirteen of the 104 subjects (12.5%) had hyponatremia (serum Na <130 mmol/L) on admission, whereas 8 patients out of 104 (7.7%) died (*Table 2*). The difference between the mean serum Na level of those who died and those who survived was not statistically significant, likewise the mortality between the hyponatremic and normonatremic groups did not also differ (*Table 3*). The association between serum Na on admission and the length of hospitalization did not also reach statistical significance (*Tables 4*).

Table 1. Baseline Characteristics of the Patient

Charateristics	n	Mean	SD
Age	104	50	15.72
Systolic BP (mmHg)	102	110	23.69
Diastolic BP (mmHg)	99	70	15.42
Cardiac rate per min	102	94	19.64
Respiratory rate per min	101	25	4.06
Serum (mmol/L)			
Sodium (Na)	104	135	5.87
Potassium (K)	102	4.18	0.76
Magnesium (Mg)	53	0.8	0.17
Calcium (Ca)	52	2.12	0.16
Creatinine	79	0.14	0.07
		No.	%
Gender			
Male	104	55	52.9
Female	104	49	47.1
Hypertension	104	7	6.7
Diabetes Mellitus	104	10	9.6
Nephropathy	104	2	1.9
Community Acquired Pneumonia	104	2	1.9
Urinary Tract Infection	104	1	1
Cerebrovascular disease	104	2	1.9
Buerger's disease	104	4	3.8
Etiology of Heart Failure			
Ischemic	104	40	38
Rheumatic	104	35	34
DCMP	104	15	14
Congenital	104	10	10
Miscellaneous	104	4	4

Table 2. Distribution of Patients Who Died According to Etiology (n=104)

Etiology	No.	%
Ischemic	4	3.8
Rheumatic	3	2.9
Congenital	1	1
TOTAL	8	7.7

Table 3. Association of Mean Serum Sodium Level with Mortality

Etiology	Mortality				p value
	(+)		(-)		
	Mean	SD	Mean	SD	
Serum Na (mmol/L)	132	5.98	135	5.80	0.007 NS
	No.	%	No.	%	
<130	1	12.5	12	12.5	
≥130	7	87.5	84	87.5	
	8	100	96	100	1.000 NS

SD - standard deviation ±, NS - not significant

Table 4. Association of Mean Serum Sodium Level with the Length of Hospital Stay

	Hospital Stay (days)		p value
	Mean	SD	
Sodium level mmol/L)			0.283 NS
<130	6.58	7.38	
≥130	4.42	6.38	

SD - standard deviation ±, NS - not significant

DISCUSSION

Our study failed to show an association between serum Na level on admission and mortality of patients in congestive heart failure NYHA class III-IV, and hence did not confirm the previous reports of some international literatures.[3-4] We were also able to determine that the percentage of hyponatremic NYHA class III-IV patients, based on our laboratory's normal value, who were enrolled was low. The length of hospital stay was not also influenced significantly by the serum Na level on admission. Taking into account the pathophysiology of congestive heart failure, these findings may suggest some variability in serum Na handling among groups of patients. This, however somewhat conforms with the findings of Fonarow et al. in their study involving a large number of patients.[11] They identified that among the laboratory parameters on admission, elevated serum creatinine and blood urea nitrogen (BUN) were among the best predictors of mortality in this group of patients. Furthermore, elevated serum creatinine was also identified as one of the independent predictors of mortality by Bouvy ML et al.[12] and Siirila- Waris K et al.[13] Indeed, we established in this study that elevated serum creatinine and potassium were significantly associated with in-hospital mortality.

CONCLUSION

This study did not show a clinically significant utility of serum sodium determination on admission in terms of predicting outcome and length of hospital stay in patients admitted with CHF NYHA class III-IV.

LIMITATION AND RECOMMENDATION

We cannot discount the fact that different etiologies of heart failure may differ in the progression of symptoms. Furthermore, the category of these patients, either private or service, may somehow influence their length of stay in the hospital. We therefore recommend further study focusing on a single etiology and category of this subset of patients.

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Quality of Life of Congestive Heart Failure Patients at the Philippine Heart Center

Gerald C. Vilela, MD; Ramoncito B. Tria, MD

Patients' perception concerning the effects of disease and its therapy on their lives have become increasingly important for the assessment of their quality of life (QOL). Congestive heart failure (CHF) is one of the disorders that have great impact not only on the patient, but also on his family and the society as well. The purpose of the study was to validate a QOL Scale for CHF patients in terms of the physical wellness, treatment related, emotional, functional, socio-economic, and cognitive dimensions. Item analysis was done to determine the reliability and validity of the scale. Item total correlation and Cronbach's coefficient alpha was calculated to determine internal consistency. The construct validity of the scale was also established. Interpretation of the scores made use of the following scoring system: high = 5.2-7; moderate = 3.1-5.1; low = < 3.0. This study has shown that the QOL scale is a valid means of assessing the QOL of Filipinos CHF patients. CHF patients have a moderate level of overall QOL (mean score = showed no correlation with NYHA FC and EF.
Phil Heart Center J 2016;21(2):56-64.

Key Words: Congestive Heart Failure ■ Quality of Life ■ NYHA Functional Class

Patients' perception concerning the effects of the disease and its therapy on their lives have become increasingly important for the assessment of their quality of life, especially those having chronic disorders. Congestive heart failure (CHF) is one of the disorders that has a great impact not only on the patient, but also on his family and the society as well. Heart failure is a principal complication or the final common pathway of virtually all forms of heart disease. Braunwald in 1997 defined heart failure as a pathophysiological state in which an abnormality in cardiac function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirement of the metabolizing tissue and/or to be able to do so only from an elevated filling pressure.[1] Heart failure is an increasingly common patient problem and is a potentially debilitating disorder that affects a significant number of patients. At any given time, heart failure affects approximately 1% of the population. The age adjusted death rate has doubled over the past decade. Patients live an average of 4-5 years, and nearly all suffer from fatigue and breathlessness which limits exercise capacity and produces a poor quality of life (QOL).[2] The incidence is rising because of increase in the aging population which is predisposed to heart failure. Also, better management and improved survival following acute myocardial infarction have created a large population of patients who may succumb to heart failure.

Patients with CHF are known not only for exceptionally high mortality rate, but also for having the highest reported hospital readmission rate for all patient groups.[3] Chronic heart failure is the model for chronically ill, symptomatic patients, often elderly, receiving multiple drugs, with dietary and activity restriction, whose ambulatory care is punctuated by hospitalization for acute exacerbation. In CHF, there is such a poor long term survival that in some instances, prolongation of survival may be less important than the improved quality of remaining life.

The level of everyday physical activity in patients with CHF may be an important reflection of their quality of life, in fact it may be more relevant to the patient's quality of life than the measurement of their exercise capacity.[5] Patients

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with major cardiac disease often experience severe fatigue which results in a significant reduction of everyday activities often leading to reduced emotional well-being and disruption of family relationships. Hawthorne in 1994 showed that heart failure patients experience significant mood disruption that appears to be more than that reported by other cardiac patients.[9] Successful treatment whether medical or surgical, will be readily appreciated by the patient as directly contributory to improved quality of life. The clinical observation of a population of patients with heart failure suggested that some patients adapt to this disease more effectively than others. This difference in response appeared to be more related to psychological variables, including a positive orientation, than to variation in the severity of the disease.[7] Findings suggest that patients who are more hopeful maintain their involvement in life regardless of physical limitation imposed by their heart failure.[1]

Efforts to quantitate the severity of clinical incapacity in heart failure have taken new forms. NYHA classification has been widely used as a guide to the severity of the syndrome, but still represents the physicians subjective interpretation of the patients' report of exercise limitation. Furthermore, the classification provides little discrimination among the mild to severe heart failure that represent the bulk of the patients seeking medical care.[2] NYHA is often insensitive to clinically significant changes in the patients status within classes.[5]

The difficulties that are experienced in measuring the QOL stem back from the lack of an adequate definition, as quality of life manifest itself differently to different people at different times and in different forms of various diseases. Several determinants influence selection of a measurement technique to assess the overall quality of life or its components. Use of a battery measures, or multidimensional indices with separate subscales for each dimension, rather than one aggregate measure, may be more prudent. A review of quality of life ascertainment in treatment trials of heart failure emphasized the inability of the currently available validated test instruments to capture the range of features that require evaluation and to be responsive to the magnitude of changes that are anticipated. It is also the purpose of the study to refine the definition of the quality of life and improve methods of study on quality of life in order to contribute to a better understanding of this complex concept in heart failure patients. To improve a patient's quality of life would be to narrow the gap between the patient's hopes and expectations and what actually happens. Translating it to the patient's own words, an improved quality of life means functional independence, productivity, return to renumerative work, and increased level of satisfaction. Importantly, interference by therapy with any aspect of quality of life is likely to adversely affect compliance and thereby limit long-term outcome advantages. Also, patients with CHF need considerable education to enable them to provide the effective self-care for their chronic illness.

The aims of this study therefore are: 1.) to validate the QOL Scale for CHF patients at the Philippine Heart Center (PHC); 2.) to describe the nature and extent of the functional and psychosocial problems of the CHF patients; 3.) to determine if there are significant differences in the perceived QOL of CHF patients in terms of age, gender, level of education, civil status, functional classification (NYHA FC), etiology of heart failure, and their ejection fraction.

METHODS

This is a validation study of a quality of life measurement scale to be used in congestive heart failure patients. It is also a prospective study that intends to define and analyze the quality of life of Filipino CHF patients at the Philippine Heart Center.

Study Population. The sampling frame was derived from patients consulting at the PHC - OPD and admitted at the wards and intensive care unit (ICU) with the presumptive clinical evidence of CHF as defined by the Framingham Criteria and are confirmed by ancillary diagnostic procedures. The study population consisted of 113 patients presenting for consultation and/or treatment from January 1999 to August 31, 1999.

Study Maneuvers. This study was done in two phases. **I. Validation Phase**: Establishing the reliability and validity of the CHF - QOL Scale. The questionnaire was self-administered during this period after a brief, standardized instruction. The scale was answered by the respondents within 15 to 20 minutes. The questionnaire was scored by summing the responses to each question.

Item analysis was done to determine the reliability and validity of the scale. Quantitative methods of establishing reliability were used. Frequency endorsement rates and measures of internal consistency were computed. As measures of internal consistency, item-total correlation and Cronbach's Coefficient Alpha were calculated. Items with endorsement rate of 0.20 to 0.80 and item-total correlation of not > 0.20 were considered good items. A Cronbach's alpha of not <0.60 for each subtest was considered acceptable.

The construct validity of the scale was also established. The scale was said to have construct validity if the data derived from the scale jibe with the existing theories or clinical expectations. The following hypotheses were tested: 1) Lower NYHA FC (good functional capacity) exhibit a better QOL than patients with a higher functional classification (poor functional capacity); 2) QOL is not correlated with left ventricular ejection fraction; 3) Perceived QOL does not vary with the cause of CHF. **II. Descriptive Phase**: All 113 patients who were included in the validation phase were also included in this phase in order to assess the quality of life of CHF patients.

Inclusion Criteria. 1. age 20-80 years old. 2. All CHF patients of whatever etiology receiving appropriate medications for the last 3 months. *Exclusion Criteria.* 1. less than 20 and greater than 80 years old. 2. all primary pericardial diseases. 3. patients with the following concomitant disorders: a. neurologic disorders (e.g CVA) b. pulmonary diseases (e.g. COPD, CRLD, or bronchiectasis) c. hepatic disorders as evidenced by elevated liver enzyme of ≥ to 3x the upper limit of normal. d. renal disorder as suggested by kidney ultrasound and severe anemia + persistent reversal of Ca/P04 ratio. e. carcinoma.

Methods of Analysis. The research data were analyzed using both qualitative and quantitiative methods. Reliability analysis using item-total correlations and Cronbach's coefficient alpha was calculated. Frequency endorsement rates were also used for item analysis. With an assumption of an interval measurement for the scale values, the *T*-test and the one way ANOVA with unequal samples were utilized to compare the overall QOL scores and the domain-specific scores of two groups and more than two groups, respectively. Interpretation of scores in this study made use of the following scoring system as shown on the table below:

Table 1. CHF-QOL Scale Scoring System

Domain	Low	Mod	High
Overall QOL	<3.1	3.1-5.0	>5.0
Physical Wellness	<3.1	3.1-5.0	>5.0
Treatment Related	<3.1	3.1-5.0	>5.0
Functional	<3.1	3.1-5.0	>5.0
Emotional	<3.1	3.1-5.0	>5.0
Socio-economic	<3.1	3.1-5.0	>5.0
Sexual	<3.1	3.1-5.0	>5.0
Cognitive ability	<3.1	3.1-5.0	>5.0

RESULTS

Scale Development. The data for the scale development were based on the responses of 113 Filipino CHF patients consulting PHC-OPD or admitted at the wards or ICU. Table 1 shows the socio-demographic distribution of the respondents. The data revealed that 42% of the study population were females and 58% were males. Their ages ranged from 20 to 73 years old and the majority belongs to the 39-59 years age range. About 59% were married while 34% were single. Fifty-four percent were high school graduates, 27% obtained elementary education and only 19% had college degree. Majority of the respondents were skilled workers (38%) prior to the onset of the illness, while majority were unemployed (86%) at the onset of their disease.

Table 2. Socio-Demographic Distribution of Respondents

Variables	Frequency	%
Gender		
Male	65	58
Female	48	42
Age: (20-76 y/o)		
<39	42	37
39-59	55	49
>59	15	14
Status:		
Single	38	34
Married	67	59
Separated	6	5
Widow	2	2
Category:		
Private	41	36
Charity	72	64
Education:		
Elementary	31	27
High School	61	54
College	21	19
Previous occupation:		
Professional	9	8
Skilled worker	43	38
Business	22	19
None	39	35
Present occupation:		
Professional	0	0
Skilled worker	9	8
Business	7	6
None	97	86

Table 3. Distribution of Respondents by NYHA FC with their Average Ejection Fraction

NYHA	Frequency	%	Ejection Fraction (%) p = 0.065
I	19	17	59.3
II	59	52	55.7
III	28	25	43.2
IV	7	6	34.7

Table 4. Distribution of Respondents According to Etiology of CHF

Etiology	Frequency	%
Ischemic Heart Disease	32	28
Hypertensive Heart Disease	21	19
Rheumatic Heart Disease	43	38
Dilated Cardiomyopathy	11	10
Congenital Heart Disease	6	5

Table 5. Level of Internal Consistency

Subtest	Number of Items	Item - Total *r*	Alpha
Physical Wellness	7	0.35 - 0.80	0.85
Treatment related	3	0.37 - 0.80	0.68
Emotional	7	0.35 - 0.80	0.86
Functional	3	0.31 - 0.79	0.60
Socio-economic	4	0.25 - 0.75	0.63
Sexual	2	0.56	0.72
Cognitive	4	0.52 - 0.80	0.81

Majority of the sample population belongs to the CHF FC II (52%) while only 7 patients belong to the CHF FC IV (6%) (*Table 3*). The most common etiology of CHF in this study was Rheumatic Heart Disease (n = 43; 38%) (*Table 4*).

Reliability. The internal consistency of the scale was established using item-total correlations and Cronbach's Coefficient Alpha. The item analysis showed acceptable levels of internal consistency as shown below (*Table 5*). Based on these measures, the final scale consists of 7 subtests and a total of 30 items.

Validity. The exploratory phase confirmed the content validity of the items in each subtest. Items were contextualized on the basis of the perceptions and actual experiences of CHF patients, their relatives, clinicians, and psychiatrists. Construct validity was established by comparing the results with existing theories and clinical/social expectations. The following hypotheses and their results are presented in the tables below.

1. *Patients with good functional capacity exhibit a better QOL than those with poor functional capacity*. Table 6 shows that patients with NYHA FC I and II obtained a higher mean scores (higher QOL) than patients with NYHA FC III and IV. This finding confirms the research hypothesis. Therefore, functional aptness measured in terms of NYHA FC affects the quality of life of CHF patients.

Table 6. Dimension Specific and Overall QOL of Patients According to NYHA

NYHA FC	Physical	Treatment Related	Emotional	Socio-Economic	Functional	Sexual	Cognitive	Overall
I (n = 19)	5.1	4.5	5.3	5.1	4.91	3.51	5.9	5.1
II (n = 59)	4.7	3.4	4.6	4.71	4.25	3.32	4.97	4.56
III (n = 28)	3.9	3.1	4.1	4.2	3.9	3.29	3.96	3.93
IV (n = 7)	2.9	3.0	3.2	3.41	3.10	3.2	3.17	3.19
p value	0.012	0.020	0.014	0.013	0.01	0.051	0.03	0.023

2. *QOL is not correlated with left ventricular ejection fraction*. This study showed that ejection fraction has no association with the perceived quality of life as shown in Table 7. This is in concordance with prior studies which also confirms the research hypothesis. Sexual dimension was scored as low by all of the respondents but is statistically insignificant.

Table 7. Dimension Specific and Overall QOL of Patients According to EF

Ejection Fraction (%)	Physical	Treatment Related	Emotional	Socio-Economic	Functional	Sexual	Cognitive	Overall
<35 (n = 26)	4.21	3.6	4.29	4.05	3.91	2.9	4.73	4.15
35-49 (n = 53)	4.19	3.72	4.25	4.34	4.06	2.7	4.65	4.21
>50 (n = 34)	4.23	3.51	4.31	4.21	3.86	2.8	4.89	4.17
p value	0.07	0.071	0.31	0.18	0.09	0.08	0.06	0.59

3. *Perceived QOL does not vary with the etiology of CHF.* Table 8 shows the different etiologies of CHF with their corresponding QOL score. It shows that patients with Rheumatic Heart Disease have the lowest QOL score as compared to the other subsets of patients. This however disproved the research hypothesis. Sexual dimension was again scored as low by all of the population but is not statistically significant.

Table 8. Dimension Specific and Overall QOL of Patients According to Etiology of CHF

Etiology	Physical	Treatment Related	Emotional	Socio-Economic	Functional	Sexual	Cognitive	Overall
Ishemic Heart Disease (n=32)	4.91	4.01	5.1	4.71	4.65	2.4	4.3	4.71
Hypertensive Heart Disease (n=21)	5.1	4.98	4.31	4.31	3.98	2.9	4.1	4.91
Rheumatic Heart Disease (n=43)	2.98	3.0	2.81	2.71	2.9	2.2	3.0	2.7
Dilated Cardiomyopathy (n=11)	3.5	3.9	4.1	3.1	3.0	2.3	3.1	3.2
Congenital Heart Disease (n=6)	4.33	4.1	4.21	3.9	4.1	2.6	4.21	3.8
p value	0.021	0.015	0.03	0.03	0.01	0.065	0.02	0.031

The results showed that there are no significant differences in the QOL of patients classified by age. All age groups had a QOL score of moderate with a p value of 0.794 (*Table 9*).

This study also showed that gender has no association with QOL. Both the male and female population exhibited a moderate QOL score, however the sexual aspect was scored as poor (p value = 0.051). (*Table 10)*

Table 9. Dimension Specific and Overall QOL of Patients According to Age Group

Age	Physical	Treatment Related	Emotional	Socio-Economic	Functional	Sexual	Cognitive	Overall
<39 (n = 42)	4.12	3.94	4.59	4.48	4.32	2.71	4.86	4.27
39-59 (n = 55)	4.30	4.22	4.29	4.49	4.29	2.58	5.00	4.39
>50 (n = 16)	4.17	3.48	4.32	4.72	4.32	2.5	4.95	4.33
p value	0.05	0.08	0.07	0.08	0.054	0.63	0.071	0.18

Table 10. Dimension Specific and Overall QOL of Patients According to Sex

Sex	Physical	Treatment Related	Emotional	Socio-Economic	Functional	Sexual	Cognitive	Overall
Male (n = 65)	4.17	4.18	4.3	4.24	4.19	2.71	4.9	4.56
Female (n = 48)	4.3	4.51	4.81	4.71	4.6	3.0	4.7	4.79
p value	0.054	0.06	0.06	0.049	0.08	0.051	0.09	0.087

Data from the study also showed that civil status has no association with QOL score. All patients exhibited a moderate score with a p value of 0.057; again the sexual aspect was scored as low (*Table 11*).

Education as well has no correlation with the perceived QOL. The study population showed a QOL score of moderate (*Table 12*).

Overall, the quality of life of CHF patient-respondents was moderate. Sexual dimension was perceived as low quality of life by the population. Table 13 indicates the overall and dimension specific QOL of Filipino CHF patients at the PHC.

Table 11. Dimension Specific and Overall QOL of Patients According to Status

Status	Physical	Treatment Related	Emotional	Socio-Economic	Functional	Sexual	Cognitive	Overall
Single (n = 38)	4.21	4.3	4.14	4.18	4.2	2.7	4.1	4.16
Married (n = 67)	4.10	4.10	4.20	4.30	4.70	2.90	4.30	4.28
Separated (n = 6)	4.01	3.9	4.8	4.6	3.9	3.0	4.7	3.91
Widow (n = 2)	4.0	3.7	4.6	4.9	3.81	2.9	4.5	4.10
p value	0.056	0.053	0.08	0.07	0.06	0.09	0.06	0.057

Table 12. Dimension Specific and Overall QOL of Patients According to Education

Education	Physical	Treatment Related	Emotional	Socio-Economic	Functional	Sexual	Cognitive	Overall
Elementary (n = 31)	4.3	4.5	4.3	4.5	4.2	2.5	4.7	4.3
High School (n = 61)	4.1	3.9	4.6	4.5	4.5	2.6	5.1	4.3
College (n = 21)	4.7	4.2	4.9	4.8	4.5	2.3	4.9	4.6
p value	0.09	0.08	0.052	0.06	0.06	0.06	0.054	0.051

Table 13. Mean Scores and Interpretation of the Overall and Dimension Specific QOL

Domain	Mean	SD	Interpretation
Physical Wellness	4.32	0.81	Moderate
Treatment related	4.10	1.12	Moderate
Emotional	4.51	0.93	Moderate
Socio-Economic	4.62	0.86	Moderate
Functional	4.29	1.20	Moderate
Sexual	2.62	1.15	Low
Cognitive	4.81	1.00	Moderate
Overall	4.20	0.74	Moderate

DISCUSSION

The CHF questionnaire was developed to systemically and comprehensively assess the patients' perceptions of the effects of heart failure, and its treatment on his or her daily life. The scale incorporated a relatively comprehensive set of quality of life outcome measures in patients with congestive heart failure. Results indicated that internal consistency was adequate for all measures. One limitation of the study is the small number of items in the sexual dimension (2 items). Because of this, any result in this aspect may be inconclusive.

In many trials, the assessment of functional capacity has been limited to the NYHA classification. According to Smith et al. the NYHA Functional Classification is a subjective assessment made by the physician with poor discriminatory potential and it does not necessarily provide information about the patient's ability to carry out normal life activities.[6] However, this study showed that NYHA FC has a direct correlation with the perceived quality of life of congestive heart failure patients. Qualitatively, patients in NYHA FC I to IV exhibited a moderate score of QOL. However, quantitative assessment showed that patients in a lower functional classification has a a higher score as compared with those in a higher classification with a p value of 0.023. The lower the functional capacity (good functional capacity) the better is the quality of life. However, the small sample size of patients in NYHA FC IV (n=7) would be considered as a limitation. Thus, the patients' ability to do his/her activities affects so much their quality of life. No significant differences were found in the cognitive status of all groups.

In accordance with previous studies, there was little association between the quality of life measures and left ventricular ejection fraction. There is a poor correlation among hemodynamic features (i.e. ejection fraction and exercise capacity) and QOL attributes. Although this well established measure of severity of the disease is a poor predictor of patient functional status, a truncated range of ejection fraction is often used in this assessments. The reasons for the poor

correlaton between all these measures of functional capacity / quality of life and the severity of cardiac dysfunction as measured by the ejection fraction remain unclear. Some potential reasons are obvious: 1) ventricular function, particularly systolic function at rest, may not be predictive of ventricular function during activity. 2) systolic function disregards mitral insufficiency and provides no insight into diastolic dysfunction that may be an important factor in exercise disability. 3) the right ventricle may play an independently important role in supporting activity. 4) factors other function. 5) factors other than blood flow may influence skeletal muscle function during activity. 6) neurohormonal function may influence exercise/activity hemodynamics.

Weber et al. have suggested that the interaction between the right and left ventricles plays an important role in the left ventricular failure. With right ventricular overload, the intraventricular septum may bulge into the left ventricle and alter the geometry and distensibility of the left ventricle, impeding the preload recruitment necessary to augment stroke volume during activity. In 25 patients with chronic left ventricular failure, Baker et al. found that the right ventricular ejection fraction correlated much better with exercise performance than the left ventricular ejection fraction. Left ventricular diastolic function could influence exercise performance by altering the relations between ventricular feeling pressure and volume. Decreased compliance of the left ventricle might restrict the augmentation of ventricular filling during activity, limiting an increase in stroke volume or elevating ventricular diastolic and pulmonary venous pressures during exercise and leading to pulmonary congestion.[3]

Patients with chronic heart failure have been found to have an altered skeletal muscle metabolism and impaired skeletal muscle blood flow. It has also been shown that an early shift to anaerobic metabolism during exercise is associated with abnormal exercise performance in patients with heart failure.[3,12] There is activation of the sympathetic nervous system in patients with chronic congestive heart failure, and plasma norepinephrine levels are elevated in patients with left ventricular dysfunction who do not have symptoms of heart failure.

In summary, this analysis provides further evidence that the symptoms, impairment in lifestyle, exercise capacity, neurohormonal stimulation, and cardiac function in heart failure are variably and only weakly interrelated.

Five etiologies of CHF were recognized in this study. Table 8 displays the scores of specific etiologies of CHF. Qualitatively, the overall and dimension specific QOL score was moderate for all groups except for patients with RHD.

Aside from the NYHA Functional Classification, the overall QOL can be affected by several other variables. However, in the study the effects of age, gender, civil status, and level of education on QOL are not at all significant. Clinical observation of a population of patients with CHF suggested that some patients adapt to their disease more effectively than others. These differences in responses appeared to be more related to psychosocial variables, including a positive future orientation, than to variation and severity of the disease.[13] Findings suggest that patients who are more hopeful maintain their involvement in life regardless of physical limitation imposed by their heart failure.[13]

This study has shown that Filipino CHF patients at the PHC have a moderate quality of life. As shown in the study by Ramiro et al., culture has played a major role in the development of the QOL of the respondents.[10] Another significant factor that has contributed to a moderate quality of life among these respondents is a very good family support which is a characteristic of Filipino culture. Also, spiritual affluence has led the patients to a strong sense of hope. This spiritual richness and his often fatalistic and deterministic attitudes toward life have given substance to the physical pain.[10] That is, Filipinos have a tendency to find meaning in their sufferings.

CONCLUSION

The goal of treatment for most patients with chronic disease is not cure, but improvement in function as a result of a decrease in symptoms

or severity of the illness or limitation of disease progression. Thus, evaluation of new therapies for chronic cardiovascular disease should not be limited to biomedical measures. Evaluation should include dimensions of socio-economical status, functions in daily life, productivity, performance of social roles, intellectual capability, emotional stability, and life satisfaction. This study is an effort to establish quality of life as an important indicator of the health status of Filipino CHF patients. The scale was developed and validated to describe the quality of life of CHF patients according to disease status and some sociodemographic characteristics. It is a disease specific instrument that is applicable to all CHF patients of whatever etiology. However, the limitations cited above should be resolved and since the samples were taken only from PHC in which the majority of the patients belong to the low to moderate socio-economic class, this scale is only validated for the aforementioned population. Also, as it was meant to be a disease specific instrument for CHF patients, testing its sensitivity and specificity to the effects of other types of diseases must first be established before adopting the instrument to evaluate patients suffering from diseases other than CHF.

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Adherence to the 2009 ACC/AHA Guidelines for the Management of Chronic Congestive Heart Failure in Adults and its Impact on Patient's Outcome: the Philippine Heart Center experience

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Background --- The physicians' management of congestive heart failure has been known to be varied. This prospective cohort clinical Study aimed to determine the adherence of physicians to the 2009 ACC/AHA practice guidelines in the management of chronic congestive heart failure (CHF) in the Philippine Heart Center (PHC) and its impact on patients' outcome.

Methods --- This study included 62 eligible patients diagnosed with CHF Stages C and D, admitted at PHC from June 1, 2010 to June 30, 2011. Patient who presented with acute pulmonary edema, recent myocardial infarction (1 month), cardiogenic shock, or planned surgery in the next 6 months and those who have no contact numbers were excluded. Baseline characteristics were obtained through patient interview, through phone call and review of medical records. An adherence indicator was developed using a two-step procedure on the basis of the five pharmacological classes of drugs used in treatment of CHF. The same algorithm used in the MAHLER study was used to determine whether a physician is adherent or non-adherent to the guidelines for each medication. Patients were then followed up for the occurrence of death either through phone, review of medical records and through his attending physician during the index hospitalization and 6 months after discharge.

Result --- The baseline characteristics did not differ significantly. Thirty-five were males and 26 were females. Most of the subjects were hypertensive (n=28) and has diabetes mellitus (n=ll). Almost half of the subjects (48%) had smoking history. Forty-four subjects (72%) had ejection fraction less than 40%. The medications that were often prescribed were beta-blockers (79%), diuretics (72%), cardiac glycosides (77%) and spironolactone (79%). Most of the subjects belong to the NYHA Class II (71%) and Class III (29%). The three most common underlying causes of chronic heart failure were rheumatic heart disease (25%), ischemic cardiomyopathy (20%) and dilated cardiomyopathy (11%). Most of tbe subjects were in sinus rhythm (77%). The adherence to guide lines did not differ significantly between those who survived or not. Out of the 61 subjects, 2 (3.3%) died because of stroke and heart failure.

Conclusion --- There is no significant difference between the outcome of patients with congestive heart failure who are treated according to the 2009 updated ACCF/AHA Guidelines for the diagnosis and management of heart failure and those who were treated otherwise (p-value 1.000). However, this study is limited by an incomplete sample size. ***Phil Heart Center J 2016;21(2):65-68.***

Key Words: Congestive Heart Failure ■ ACC/AHA Guidelines

Congestive Heart Failure is an increasingly important health problem and continues to be a significant cause of mortality and morbidity even in the developed countries. The overall prevalence of heart failure in the adult population in developed countries is 2%.[1] Its prevalence rises with age following an exponential pattern, affecting 6-10% of people over the age of 65. Coronary artery disease, hypertension, and diabetes mellitus are the major etiologic risk factors.[1]

The physicians' management of congestive heart failure has been known to be varied. Although many studies and recommendations have been made, several factors influence the

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physicians' prescribing habits. It may include cost effectiveness of therapy, anecdotal experiences as well as social and moral issues. The definitive decision about individual patient care must be made by the healthcare provider depending on the patient's presentation.[2]

Generally acceptable approaches on specific diseases are recommended by the ACC/AHA to aid healthcare providers in the diagnosis, management, and prevention of such conditions. This is an effort to define practices that commonly meet the needs of most patients in most of the disease conditions.[2]

In the attempt to answer the emerging challenges in the diagnosis and management of chronic congestive heart failure, the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) Task Force on Practice Guidelines has produced a "focused update".[2] This is to incorporate to the guidelines, certain recommendations affected by the developing information or opinion.[2] This recommendation has been used by different training institutions in the Philippines including the Philippine Heart Center. There was also no local study done to associate physicians' adherence to the guideline and patients' outcome. Thus, this study was formulated to look into the outcome of patients managed adherent to the guideline as compared to those who were managed otherwise.

The objective of this study is to determine the adherence of physicians to the guidelines in the management of chronic congestive heart failure in the Philippine Heart Center and its impact on patients' outcome.

METHODS

This is a prospective cohort study done at the wards of Philippine Heart Center, a tertiary hospital located in East Avenue, Quezon City. Recruitment period was between June 1, 2010 to June 30, 2011. Follow-up period is from September 1, 2010 to December 31, 2011. Included were those diagnosed with CHF on the basis of the presence of signs and symptoms suggestive of CHF Stages C and D, admitted at Philippine Heart Center (PHC) from June 1, 2010 to June 30, 2011 and with contact numbers.

Excluded were those presenting with acute pulmonary edema, recent myocardial infarction (1 month), cardiogenic shock, or planned surgery in the next 6 months.

Eligible patients were included and informed consent was obtained. Baseline characteristics such as age, gender, co-morbidities and risk factors were obtained through patient interview, through phone call and review of medical records. The patients were classified as to their CHF stage classification according to the ACC/AHA guidelines for the diagnosis and management of heart failure.

Adherence of physician to guidelines was computed using the method adapted from the MAHLER Survey.[3] The MAHLER survey is a multi-center, observational study on the medical management and cost of CHF in six European countries (France, Germany, Italy, The Netherlands, Spain, UK). An adherence indicator was developed using a two-step procedure on the basis of the five pharmacological classes of drugs used in treatment of CHF.[4] The same algorithm used to determine whether a patient is adherent or non-adherent to the guidelines for each medication was used in this study.

In the MAHLER study,[3] for each of the five therapeutic classes of interest, a class adherence indicator is computed. It is defined as the proportion of patients whose physicians prescribed according to the guidelines. The same formula was used in this study.

Patients were followed up for the occurrence of death either through patient interview by phone, review of medical records and through his attending physician. Follow-up was done during the index hospitalization and 6th month from discharge.

Sample size: Sample size computed was $n \geq 160$ at 15% relative error, 95% confidence level and adherence rate of 3% as observed by Komajda et al. in the MAHLER survey.[4]

Statistical method. Chi-square test of association was used to test if there is a relationship between treatment adhering to guidelines and the outcome of patients with chronic congestive heart failure.

RESULTS

There were 61 eligible patients who were included in this study. The baseline characteristics did not differ significantly between the patients who were managed according to the guidelines and those who were managed other wise. (*Table 1*) Thirty-five were males and 26 were females. Most of the subjects were hypertensive (n=28) and has diabetes mellitus (n=11). Almost half of the subjects (48%) had smoking history. Forty-four subjects (72%) had ejection fraction less than 40%. The medications that were often prescribed were beta-blockers (79%), diuretics (72%), cardiac glycosides (77%) and spironolactone (79%). Most of the subjects belong to the NYHA Class II (71%) and Class III (29%). The three most common underlying causes of chronic heart failure were rheumatic heart disease (25%), ischemic cardiomyopathy (20%) and dilated cardiomyopathy (11%). Most of the subjects were in sinus rhythm (77%). The adherence to guidelines did not differ significantly between those who have outcomes or not. Out of the 61 subjects, 2 (3.3%) died because of stroke and heart failure.

Table 1. Baseline Characteristics of Patients with Chronic Congestive Heart Failure Stages C and D at the Philippine Heart Center. (PHC 2012)

Characteristics	Mortality (n=2)	Survivor (n=59	p-value
Male Female	2 (100%)	33 (56%)	0.503
Hypertension	-	28 (47%)	1.000
Diabetes Mellitus	-	10 (17%)	1.000
with previous Stroke/TIA	1 (50%)	4 (7%)	0.158
with previous Coronary Bypass	-	1 (1.7%)	1.000
with previous PTCA	-	1 (1.7%)	1.000
with previous Valve Replacement	-	1 (1.7%)	1.000
Smoking history	1 (50%)	28 (47%)	1.000
≤40%	1 (50%)	43 (73%)	1.000
Beta-blocker	-	48 (8%)	0.409
Diuretics	1 (50%)	43 (73%)	1.000
Cardiac glycoside	1 (50%)	46 (78%)	1.000
Spirinolactone	1 (50%)	47 (80%)	1.000
Nitrates	-	33 (56%)	0.207
Statin	-	14 (24%)	1.000
Anticoagulant	-	19 (32%)	1.000
Antiplatelet	-	18 (31%)	0.503
I	-	-	-
II	1 (50%)	42 (71%)	0.507
III	1 (50%)	17 (29%)	0.508
IV	-	-	-
HCVD	-	1 (1.7%)	1.000
DCMP	1 (50%)	10 (17%)	0.331
Ischemic	-	20 (34%)	1.000
Valvular Rheumatic	1 (50%)	24 (41%)	1.000
Non-rheumatic	-	4 (7%)	1.000
Sinus	2 (100%)	45 (76%)	1.000
Atrial Fibrillation	-	19 (32%)	1.000

Table 2. Patients Eligible for CHF Treatment versus Those Who Actually Received the Treatment (PHC 2012)

Treatment	Number of Patients Eligible for Treatment to be Enforced	Number of Patients Actually Receiving Treatment
ACE- inhibitors/ Angiotensin II receptor antagonist	54	47
Beta-blocker	51	54
Diuretics	59	47
Cardiac glycoside	55	48
Spirinolactone	41	33

Table 3. Consequences of Adherence to Heart Failure Guidelines on the Rate of Mortality (PHC 2012)

Outcome	Good Adherence (n)	Poor Adherence (n)	p value
In-hospital mortality	0	0	
Mortality	2	0	1.000

DISCUSSION

The subjects enrolled in this study are Filipino patients who were treated medically for chronic heart failure despite the need for surgery in some of them. Those patients who were already ready for surgery in the next 6 months were excluded in this study. This is the true scenario in the Philippine setting. We, Filipino physicians, would be likely treating chronic heart failure patients more medically in lieu of the expensive surgical management.

The MAHLER survey,[3] a multi-center, observational study on the impact on outcome of the implementation of European guidelines for the treatment of chronic heart failure (CHF), showed that adherence of physicians to treatment guidelines is a strong predictor of fewer cardiovascular hospitalizations in actual practice. This local study did not show this association. Taking a closer look at the two subjects who died, both of them belonged to Stage D of chronic heart failure and both were treated according to the guidelines. Their death can be probably attributed to the severity of the heart failure, that despite adherence to guidelines they have a high likelihood to die.

Limitation of the study. This study did not look into the immediate cause of mortality of those subjects who died. Both were managed according to the guidelines but still, died. Their individual cause of death is from stroke and from a probable arrhythmia, respectively. The study did not consider other contributory factors to their deaths. Also, this study was done in one institution, with patients managed by almost the same set of physicians. The same study including other hospitals is then recommended.

CONCLUSION

The outcome of patients with chronic congestive heart failure at Philippine Heart Center is good, with an observed mortality of 3.3%. This study demonstrated that the physicians in the Philippine Heart Center is adherent to the 2009 updated ACCF/AHA guidelines for the diagnosis and management of heart failure. In the treatment of this population of mild/moderate/severe chronic heart failure patients, there is no significant difference between the outcome of patients who are treated according to the said guidelines and those who were treated otherwise.

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Effect of Nicorandil 10-20 mg on Coronary Events and Left Ventricular Ejection Fraction of Patients with Compensated Congestive Heart Failure

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Background --- Studies have shown that the arterial and venous vasodilation and the nitrate - like property of nicorandil has benefit with regard to hemodynamic parameters and improvement of clinical outcome. There has been no published data on effect of nicorandil on left ventricular ejection fraction.

Method --- The study evaluated the effect of Nicorandil 10-20 mg on coronary events and ejection fraction of patient with compensated congestive heart failure in Philippine Heart Center. The study group are patients with compensated congestive heart failure (CHF), that is patients with left ventricular ejection fraction equal to or less than 40%. Nicorandil (10-20 mg BID) was given for 6 months in addition to their standard medication for CHF (digitalis, diuretics and dilators) and repeat 2D echo was taken on the 24th week to evaluate whether change in ejection fraction occured. The primary composite endpoints are coronary heart disease death, non-fatal myocardial infarction, or unplanned hospital admission for cardiac chestpain.

Results --- An increase in ejection fraction was noted both in 10 mg and 20 mg doses of nicorandil but improvement on clinical outcome was not shown maybe due to insufficient statistical power.

Conclusion --- Nicorandil would be a reasonable add on medication for patients with compensated congestive heart failure particularly in those who have left ventricular ejection fraction of 40% and below. The study is limited by its sample size, hence, insufficient statistical power. Further study using a larger population is recommended to be able to show if there is improvement on clinical outcome. ***Phil Heart Center J 2016;21(2):69-74.***

Key Words: Congestive Heart Failure ■ Left Ventricular Ejection Fraction ■ Nicorandil

The drug Nicorandil, a known antianginal, is believed to have its cardioprotective properties by its ability to perform the ischemic preconditioning phenomenon by opening potassium ATP channels, which is responsible for decreasing the subsequent effects of ischemia after an ischemic event by action potential preservation of mitochondrial integrity. At present, there is no available published molecular characterization regarding this, hence, the "mitochondrial potassium ATP" channels theory remains a possibility only, but the on going pharmacological evidence suggest their presence and nicorandil is thought to exert its preconditioning effect through the activation of this channels.[1] The nitrate-like properties of Nicorandil is by stimulating cyclic GMP formation and activation of potassium channels resulting in both arterial and and venous vasodilatation.[2,3,4] Nicorandil has been established as a monotherapeutic antianginal medication and was proven to be beneficial when added to optimal antianginal therapy as seen on clinical outcomes of high-risk patients with stable angina. The twice daily oral nicorandil dosing is a useful alternative or additional medication to other anti-anginal drugs.[5] Recently, the benefit with regards to hemodynamic effects of a single oral administration or intravenous injection of nicorandil have been reported in patients with congestive heart failure as seen in the study done by Tsutamoto et al.[6] The result of the study "Comparison of hemodynamic effects and plasma cyclic guanosine monophosphate of nicorandil and nitroglycerin in patients with congestive heart failure" done by Tsutamoto et al. showed a significant

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lowering of the mean blood pressure and pulmonary capillary wedge pressure (PCWP) from baseline values taken prior to infusion among patients under nicorandil group compared with those who are under the nitroglycerin group. The said study was designed to evaluate if the cardioprotective properties of nicorandil has an effect on coronary events and ejection fraction of patients with compensated CHF and depressed ejection fraction. In the study "Impact of Nicorandil in Angina" or the IONA study, Nicorandil showed a significant improvement in outcome due to reduction in major coronary events.[1] In another study by Kiowski et al. conducted in offices of general practitioner and internist in Switzerland, the use of Nicorandil showed to be highly effective when given alone or in combination with other anti-ischemic drugs.[7]

The objective of this study is to evaluate the effect of nicorandil on coronary events and ejection fraction in patients with compensated CHF in Philippine Heart Center and also to determine and compare ejection fraction of patients with compensated CHF on OPD patients with or without nicorandil treatment; to determine and compare rate of coronary events in patients with compensated heart failure with or without nicorandil treatment.

METHODS

This is a randomized-double blind, controlled trial. Study were conducted from August 2009 to December 2010 at the Philippine Heart Center.

Sample size and basis for the calculation. Included in the study were patients with chronic stable CHF; with left ventricular ejection fraction of ±40%. Excluded were patients with acute heart failure; concomitant use of sulphonylurea; patients with recent MI (within 4 weeks); decompensated CHF; patients with idiosyncratic hypersensitivity reaction to nicorandil, nicotinamide and nicotinic acid; with hypotension; has primary valve pathology and with primary congenital heart disease.

At alpha=.05, beta=.20 and assumed effect size of 0.67 $n \geq 37$/group. The assumption was based on the paper of Hughes, L et al. "Stable Angina Pectoris." Since there are no studies on ejection fraction, the computation of sample size was based on the exercise time of placebo group of 7.06 minutes and 9.77 minutes with nicorandil 20 mg with variability of response ±4 minutes.

RESULTS

Fifty-five patients were enrolled from Philippine Heart Center Out Patient Department between November 2009 and June 2010 with the final study visit in December 2010. Out of the 55 study patients that were included in this study, 20 patients are randomly assigned under nicorandil 10 mg group (Group A), 18 patients in nicorandil 20 mg group (Group B) and 17 patients in placebo group (Group C). Fifty patients had follow-up check-up and only 46 patients had official repeat 2D echocardiography after 6 months of taking nicorandil or placebo, depending on their group assignment. Out of the 46 patients who had official repeat 2D echocardiography, 16 patients belongs to nicorandil 10 mg group, 14 patients under nicorandil 20 mg group and 16 patients under placebo group. The baseline characteristics of the study ejection fraction are shown in Table 2 and the distribution of the major clinical outcome are presented in Table 3.

Table 1 showed that the mean age of patients under nicorandil 10 mg group is 54.95 (SD 13.26), 56.94 (SD 9.13) under nicorandil 20 mg group and 55.0 (SD 8.64) for the placebo group. No statistical significance was noted between the group (p value of 0.815). Among the 55 patients, 41 were male and 14 were female. The 10 mg group has 14 male and 6 female, 15 male and 3 female for the 20 mg group and also predominantly male (12 patients) and 5 female for the placebo group (p value 0.580). All of the patients included in this study are under New York Heart Association classification (NYHA) II. None had any prior surgery. Eleven patients have coronary artery disease (CAD), 4 belongs to 10 mg group, 5 in the 10 mg and 2 placebo group (p value 0.496). Eight patients have diabetes mellitus (DM), 5 of them are from the placebo group (0.097). Only 2 patients were recorded to have chronic kidney disease (CKD), 1 each for nicorandil 20 mg and placebo group (p value 0.552).

Five patients are hypertensive, 2 each for the treatment group and 1 under placebo group (p value 0.862). Placebo group has the most patient who are using angiotensin receptor blocker (ARB), having a total of 6 patients and the treatment group have 1 each (p value 0.781) while angiotensin converting enzyme inhibitor (ACE) is used by the 14 patients under 20 mg group, 13 and 9 patients for 10 mg and placebo group, respectively (p value 0.303). Only 1 patient is taking calcium channel blocker and this patient belongs to placebo group. Fifteen patients from the nicorandil 10 mg group, 12 from the 20 mg group and 14 patients from the placebo group were using diuretics (p value 0.566). Lanoxin was used more frequently by patients under the 10 mg group (17 patients), 12 and 15 patients for the 20 mg and placebo group, respectively, with a p value of 0.219. Ten, thirteen and eight patients under nicorandil 10 mg, 20 mg and placebo group, respectively, were using beta blocker (p value 0.251). Four patients under 10 mg, 8 patients under 20 mg and 5 patients under placebo group, were taking nitrates (p value 0.262) while 16 patients under 10 mg, 14 patients under 20 mg and 11 patients under placebo group, were taking aspirin (p value 0.527). On the other hand, 15 patients under 10 mg, 14 patients under 20 mg and 13 patients under placebo group, were taking statin (p value 0.918). Warfarin is being used by 3 patients for each treatment group and 5 patients under placebo group (p value 0.502) while 3 patients are using clopidogrel under the 10 mg and placebo group and 4 patients for the 20 mg group (p value 0.845). Two patients taking trimetazidine belongs to the 20 mg group and 1 patients each for the other groups (p value 0.743). Only 2 patients are using insulin, 1 each for the 20 mg and placebo group (p value 0.552). Eight patients are using metformin for their diabetes mellitus, none from the 10 mg group, 3 and 5 patients from 20 mg and placebo group, respectively. The use of metformin is statistically significant having a p value of 0.039.

Table 2 showed that using the M mode method for acquiring the ejection fraction (EF), the nicorandil 10 mg group has a mean baseline of 28.35 with standard deviation (SD of 7.91), while the 20 mg group has a mean baseline EF of 30.17 (SD of 9.45). On the other hand, the placebo group has a mean baseline EF of 31.88 (SD of 8.10). The p value of the mean baseline EF of the 3 groups is not statistically significant (0.457). After 24 weeks, the repeat 2 dimensional echocardiography (2DE) showed increased mean EF for the 3 groups, the nicorandil 10 mg group has a mean of 38.56 (SD of 10.15), the 20 mg group has a mean EF of 37.57 (SD of 11.24) and the placebo group has a mean EF of 35.56 (SD of 12.86). The p value of the mean EF after 24 weeks within the 3 groups is not statistically significant (0.755). However, the mean EF paired difference using the M mode between baseline and at 24 weeks showed statistical significance with a p value of 0.000 under the nicorandil 10 mg group, a p value of 0.028 in nicorandil 20 mg baseline and a statistically not significant p value of 0.444 for the placebo group. The mean baseline EF using Simpson's method is 29.15 (SD 5.18), 31.17 (SD 7.09) for the 20 mg group and 29.24 (SD 7.60) for the placebo group, with a not significant p value of 0.587. After 24 weeks, the nicorandil 10 mg group has a patients are listed in Table 1, the assessment of hemodynamic parameters or chance in mean of 38.69 (SD of 11.65), the 20 mg group has a mean EF of 32.79 (SD of 8.65) and the placebo group has a mean EF of 36.69 (SD of 11.55). Again, the p value of the mean EF after 24 weeks within the 3 groups is not statistically significant (p value 0.329). However, the mean EF paired difference using

Simpson's method at baseline and at 24 weeks showed statistical significance with a p value of 0.007 under the nicorandil 10 mg group and a statistically not significant p value of 0.374 and 0.066 for 20 mg and the placebo group, respectively.

Table 3 showed that there is 1 reported death in this study, the reported case belongs to nicorandil 20 mg group, the patient initially complained of chestpain and difficulty of breathing. He was brought to a local hospital, the patient expired with coronary artery disease as a cause of death. Another patient from the placebo group reported hospital admission due to chestpain, he was discharged with maintenance medications. None of the patient in this study had nonfatal myocardial infarction. Nine patients had headache during the first 2 weeks of the medications, 4 each for the treatment group and 1 in the

placebo group with a not significant p value 0.366. Two patients reported muscle pains, with 1 patient each belonging to nicorandil 20 mg and placebo group (p value 0.552). One patient had palpitations and this patient belongs to placebo group. Six patients stopped taking the medications and placebo, 2 patients from each group. The patients under treatment group stopped the medications due to headache while the 2 patients under placebo group stopped because of muscle pain and palpitations.

Table 1. Baseline Characteristics of Chronic Stable Congestive Heart Failure Patients Under Nicorandil and Placebo Group. (PHC 2011)

Characteristics	Nicorandil 10 mg (n=20)	Nicorandil 20 mg (n=18)	Placebo (n=17)	P value
Age				0.81
Mean	54.95	56.94	55.0	
SD	13.26	9.13	8.64	
SEX				0.58
Male	14	15	16	
Female	6	3	5	
NYHA				
I	0	0	0	
II	20	18	17	
III	0	0	0	
IV	0	0	0	
Any prior surgery	0	0	0	
Coronary Artery Disease	4	5	2	0.49
Diabetes Mellitus	1	2	5	0.09
Chronic Kidney Disease	0	1	1	0.55
Hypertension	2	2	1	0.85
Concomitant Medications:				
ARB	5	5	6	0.78
ACE	13	14	9	0.30
CCB	0	0	1	0.32
Diuretics	15	12	14	0.56
Lanoxin	17	12	15	0.21
BB	10	13	8	0.25
Nitrates	4	8	5	0.26
ASA	16	14	11	0.52
Statin	15	14	13	0.98
Warfarin	3	3	5	0.50
Clopidogrel	3	4	3	0.84
Trimetazidine	1	2	1	0.74
Insulin	0	1	1	0.55
Metformin	0	3	5	0.03

Table 2. Comparison of the Left Ventricular Ejection Fraction of Chronic Stable Congestive Heart Failure Patients Between Nicorandil and Placebo Group at Week 24 (PHC 2011)

Ejection Fraction	Nicorandil 10 mg (n=20)	Nicorandil 120 mg (n=18)	Placebo (n=17)	P value
M Mode				
Baseline				0.45
Mean	28.35	30.17	31.88	
SD	7.92	9.45	8.10	
At 6 months				
Mean	38.56	37.57	35.56	0.75
SD	10.15	11.24	12.87	
Mean Difference	9.50	7.85	3.43	
P-value	0.00	0.02	0.44	
SIMPSONS:				
Baseline				0.45
Mean	29.15	31.17	29.24	
SD	5.18	7.09	7.60	
At 6 months				032
Mean	38.69	32.79	36.69	
SD	11.65	8.65	11.55	
Mean Difference	9.50	2.21	7.00	
P value	0.007	0.37	0.66	

Table 3. Distribution of Major Clinical Outcomes of Chronic Stable Congestive Heart Failure Patients Under Nicorandil and Placebo Group at 24 Weeks (PHC 2011)

Ejection Fraction	Nicorandil 10 mg (n=20)	Nicorandil 120 mg (n=18)	Placebo (n=17)	P value
	No	No	No	
Death due to Coronary Event	0	1	0	0.35
Non Fatal MI	0	0	0	
		0		
Unplanned Hospital Admission for Cardiac Chest pain	0	0	1	0.32
Others:				
Headache	4	4	1	0.36
Muscle pain	0	1	1	0.55
Palpitation	0	1	1	0.32

DISCUSSION

There was no significant difference in the baseline characteristics of the study patients other than the intake of anti-diabetic metformin. Assesment of the change in ejection fraction at baseline showed no significant result for both the M mode and Simpson's method but is statistically significant after 24 weeks in treatment group but not in the placebo group in the M mode method and only in the 10 mg group using the Simpson's method. The main clinical outcome results showed no statistical significance, with an outcome group cross tabulation of placebo group versus nicorandil 10 mg and 20 mg group p value 1.0.

The landmark trial IONA reported significant improvement in clinical outcome in terms of reducing occurrence of events related to acute coronary disease and the associated hospital admission in patients under nicorandil group, however, this was not seen in this study.

CONCLUSION

The study showed a significant improvement in left ventricular ejection fraction among patients with compensated congestive heart failure who are taking Nicorandil as compared to their baseline ejection fraction. On the other hand, treatment with nicorandil, both 10 and 20 mg, showed no significant effects in terms of reducing the occurrence of coronary events such as death due coronary event, non fatal myocardial infarction, and unplanned hospital admission for chestpain. It was noted that the overall withdrawal from the study was more frequent on Nicorandil group than in placebo and was due to headache which known as a very common adverse reaction of nicorandil.

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The Effect of the Philippine Heart Center (PHC) Heart Failure (HF) Clinic Program on the Incidence of Mortality and Hospital Re-admission

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Background **---** The Philippine Heart Center (PHC), in an effort to reduce mortality and re-hospitalization rates and improve quality of life of patients with heart failure, established the PHC Heart Failure (HF) Clinic Program. The aim of this paper is to prospectively evaluate the effectiveness of the Philippine Heart Center Heart Failure Clinic Program in reducing mortality and re-hospitalization 12 months after discharge.

Method **---** This was a prospective cohort study. Subjects were divided into two groups: those who were enrolled with the HF Clinic Program and those who received conventional follow up. Data on the number of read missions, hospital days and time to readmission were prospectively collected from the medical charts. Data were collected at baseline, after 3 and 12 months.

Results **---** There were 150 patients included in the study, 64 of whom were enrolled in the Heart Failure Clinic while 86 patients received conventional care. There was a higher mortality in the non-Heart Failure Clinic group compared to those who were enrolled in the program. More patients in the non-HF Clinic group were re-admitted within 3 and 12 months after inclusion compared to those who were enrolled in the program. Likewise, patients in the non-HF clinic group stayed longer in the hospital compared to those who were enrolled in the program.

Conclusion **---** The Philippine Heart Center (PHC) Heart Failure (HF) Clinic is effective in reducing mortality and re-hospitalization 3 and 12 months after inclusion. ***Phil Heart Center J 2016;21(2):75-79.***

Key Words: Heart Failure Clinic ■ Mortality ■ Re-hospitalization

Despite effective treatments aimed to reduce hospitalizations, heart failure (HF) is still a leading cause of hospitalization in developed and developing countries.[1] It is affecting an increasing number of individuals and is associated with a poor prognosis. One-year survival rates, depending on severity, are lower compared to breast, bowel, bladder, prostate and ovarian cancer.[2] In many industrialized countries, heart failure is a common discharge diagnosis for patients over 65 years of age.[3]

The most recent 2013 American College of Cardiology Foundation/ American Heart Association labels patient education to facilitate heart failure self-care as a Class I recommendation.[6] Studies have demonstrated that education improved knowledge, self-monitoring, medication adherence, time to hospitalization, and days in the hospital. Although provider and patient education is a substantial domain of a heart failure clinic, its domain also encompasses medical therapy, drug evaluation, functional and nutritional assessment as well as follow-up and quality assessment. The latest guideline only elucidates on patient education as a Class I recommendation but has presently no clear-cut recommendation as to enrollment in heart failure clinics.

The Philippine Heart Center (PHC), in an effort to reduce mortality and re-hospitalization rates and improve quality of life of patients with heart failure established the PHC Heart Failure (HF) Clinic Program. The PHC-HF Clinic Program is a specialty care clinic dedicated to medical management, education, and clinical research on patients diagnosed with congestive heart failure. Its primary goal is to reduce mortality, hospitalizations, cost and improve quality

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of life of patients enrolled in the program. The aim of this paper is to prospectively evaluate the effectiveness of the Philippine Heart Center Heart Failure Clinic Program in reducing mortality and re-hospitalization 12 months after discharge.

METHODS

Study Design. This was a prospective cohort study aimed to evaluate the effectiveness of the PHC-HF Clinic Program in reducing mortality and re-hospitalization by examining the time to readmission and overall hospitalization days one year after hospitalization for heart failure. An institutional review board approval and informed consent were obtained.

Setting and Time Period. Patients hospitalized due to heart failure in New York Heart Association (NYHA) Classification I-IV were asked to participate in the study during the predetermined recruitment period of 1 year (March 2014 - March 2015).

Study Population. Included in the study were patients with persistent NYHA FC I-IV symptoms from ages 19 and above; patients recently hospitalized or evaluated at the emergency room for heart failure; patients with HF and with other co-morbidities including those with:

a. Renal Insufficiency
b. Diabetes
c. Chronic Obstructive Pulmonary Disease; patients who are in waiting list category for cardiac surgery but would need assistance for HF management; and post cardiac revascularization patients (PCI/CABG) with signs and symptoms of HF.

Excluded in the study were patients in acute heart failure regardless of etiology; patients with communicable diseases; with HF but with severe psychiatric conditions needing special facilities; who refuse to cooperate with the team management; and patients who cannot visit the clinic for regular check up.

Sample Size Calculation. In a trial conducted by Strombert et al. in Sweden, mortality of patients enrolled in the heart failure clinic is 13.5%. Patients who are not enrolled however have mortality rates recorded at 37%. With a 20% relative error and 95% confidence interval, this study will require an n=45 for patients enrolled in the heart failure, and n=90 for those who are not enrolled in the heart failure clinic.

Study maneuver. Subjects were divided into two groups: those who were enrolled with the HF Clinic Program and those who received conventional follow-up.

The patients enrolled in the program were followed-up at the PHC-HF Clinic staffed by nurses. The first visit was scheduled 2-3 weeks after discharge. All visits last for less than an hour and the PHC-HF staff evaluated the patient's status and if the heart failure treatment was optimized. Patients were educated about heart failure along with social support to the patient and the family. The status taken during the visit included auscultation of the heart and lungs and inspection of edema. If treatment was not optimized, the cardiologist with medical responsibility for the Heart Failure Clinic revised medications in accordance with current clinical guidelines. Patient education was individualized, including both written and verbal information, both based on guidelines. It also included non-pharmacological treatment with dietary changes such as restriction of fluid, sodium and alcohol intake, individually adjusted energy intake in order to reduce overweight or prevent malnutrition, smoking cessation, exercise in stable heart failure and infection prophylaxis with vaccinations. If the patient was unstable with symptoms of worsening heart failure at the time of follow up visit or if further education was needed, the patient was scheduled for another visit to the Heart Failure Clinic.

Patients not enrolled in the HF Clinic Program were managed in accordance with current clinical practice and received conventional follow-up with their attending physicians. The attending physician was free to evaluate and treat the patients according to their own judgment.

Clinical and demographic data were collected from the medical chart of the patient. Clinical

evaluation of the NYHA class and documentation of drug therapy was done on the day of inclusion. Medical charts and/or death certificates verified deaths. Data on the number of readmissions, hospital days and time to readmission were prospectively collected from the medical charts. Data were collected at baseline, after 3 and 12 months.

The primary endpoint was mortality or hospital admission after 12 months for heart failure. Secondary endpoints were mortality, number of readmissions for any reason, and number of days in the hospital.

Identification of Study Variables. The following were the independent or exposure variables that were evaluated: age, gender, co-morbidity (ischemic heart disease, hypertension, diabetes), NYHA Class, number of comorbidities, systolic BP, treatment (ACEI, loop diuretic, beta blockade, digitalis) and length of stay at inclusion whether at the emergency room or admitted in the wards or critical care units.

Dependent or outcome variables. The outcome variables were noted after three and twelve months as compared according to (a) number of deaths, (b) admission for any cause, and (c) mean hospital stay for any cause included all admissions for whatever etiology, whether related to heart failure or not. The patient can thus be admitted several times during the predetermined period of 3 and 12 months. The mean hospital stay refers to the patient's total length of stay in the emergency room, wards or critical care unit whichever is applicable.

RESULTS

There were 150 patients included in the study, 64 of whom were enrolled in the heart failure clinic while 86 patients received conventional care. The mean age of those were enrolled in the clinic was 50 while those who were not enrolled was 47. More than half of the patients in the non-heart failure group were female, while more than half of the patients enrolled in the heart failure are male. Most patients in both groups are married and had at least one co-morbid illness.

The most common comorbid illness in both groups is hypertension, closely followed by both ischemia and diabetes. More than half of the total number of patients was in NYHA functional class II or III. Forty-two percent of the patients in the Heart Failure Clinic were in functional class II, and 8% were functional class IV. Distribution in the non-Heart Failure Clinic group was almost similar. Systolic BP in the non-HF Clinic group was relatively higher with a mean of 123 mmHg compared to the HF Clinic Group which had a mean BP of 112 mmHg. Ninety-eight to one hundred percent of patients enrolled in HF Clinic Group were on guideline directed medical treatment for heart failure on admission and dishcarge. They were all on ACEI or ARB, loop diuretic, beta blocker and digitalis. While the majority of patients on the non-HF Clinic group were on ACEI or ARB and loop diuretic, only half of them were on beta blocker and digitalis. Patients who were enrolled in the HF Clinic were admitted longer on inclusion, staying for a mean of 3.16 days, while patients on the non-HF Clinic group were admitted for 1.93 days.

Four patients enrolled in the HF Clinic and 6 patients in the non-HF Clinic died within 12 months of inclusion in the study. More patients in the non-HF Clinic group were readmitted within the next 3 months with a mean of 1.51 compared to 1.05 in the HF clinic group patients. Twelve months after inclusion, more patients in the non-HF Clinic group were re-admitted with a mean of 2.9 compared to 0.25 in the HF Clinic group. Patients in the non-HF Clinic group stay in the hospital longer compared to those who are enrolled in the program. Patients in the non-HF Clinic group stayed for an average of 4 days in the hospital while those who are enrolled stayed for 1-2 days.

DISCUSSION

There are several studies that demonstrate positive patient outcomes for heart failure clinic programs. Positive results range from lower re-hospitalization rates, fewer hospital days, improved quality of life and functional status, to lower healthcare costs despite the

Table 1. Baseline Characteristics

Variable	Heart Failure Clinic Mean n=64	Non-HF Clinic Group n=86	p-value
Age	50 ±16.13	47.13 ±15.34	0.270
Gender			0.005
Male	41(64.06)	34(39.53)	
Female	23(35.94)	52(60.47)	
Marital Status			0.850
Single	15(23.44)	22(25.58)	
Married	49(76.56)	64(74.42)	
Comorbidities			
Ischemia	28(43.75)	24(27.91)	0.560
Hypertension	28(43.75)	36(56.25)	0.120
Diabetes	15(23.44)	20(23.26)	1.000
NYHA			0.622
1	3(4.69)	2(2.33)	
2	27(42.19)	30(34.88)	
3	29(45.31)	46(53.49)	
4	5(7.81)	8(9.30)	
# of comorbidites	0.84 ±1.10	1.13 ±1.06	0.111
Systolic BP	112.66 ±10.58	123.26 ±28.09	0.005
Medication			
ACEI/ARB	64(100)	72(83.72)	<0.001
Loop diuretic	63(98.44)	70(81.40)	0.001
Beta blocker	63(98.44)	56(65.12)	<0.001
Digitalis	62(96.88)	56(65.12)	<0.001
Length of stay at Inclusion (days)	3.08 ±2.42	1.93 ±0.85	<0.001

Table 2. Clinical Events in the HF Clinic Group and non-HF Clinic Program Group After 3 and 12 Months

Clinical Events	Heart Failure Clinic	Non-HF Clinic Group	p-value
No. of Deaths After 12 months	4(6.35)	6(6.98)	1.000
No. of admission for heart failure After 12 months	0.25 ± 0.52	2.9 ± 3.05	<0.001

Table 3. Secondary Endpoints in the HF Clinic Program Group and Non-HF Clinic Program Group

Clinical Events	Heart Failure Clinic	Non-HF Clinic Group	p-value
No. of Deaths After 12 months	4(6.35)	6(6.98)	1.000
No. of subsequent admission			
After 3 months	0.70 ± 1.09	1.51 ± 1.69	0.001
After 12 months	0.25 ± 0.52	2.9 ± 3.05	<0.001
Lenght of Hospital Stay			
After 3 months	1.36 ± 1.38	4.37 ± 5.71	0.001
After 12 months	1.19 ± 1.34	4.37 ± 5.68	<0.001

increased cost of the programs. This study evaluated the effect of the PHC-HF Clinic in reducing mortality and re-admissions in patients with HF. Results showed that there were more deaths and unplanned re-admissions within 3 and 12 months after inclusion in the non-HF clinic group compared to the HF clinic group. The difference became statistically significant when the re-admissions were extended up to 12 months after inclusion. Among patients who were admitted, those who were enrolled in the HF Clinic had shorter length of hospital stay compared to those in the non-HF Clinic group. After 12 months, there were four and six deaths in the patients enrolled in the HF Clinic and the non-HF Clinic respectively. This is not statistically significant, but there is a trend towards lesser mortality rates in those patients enrolled in the clinic.

There are several explanations for the positive outcome of patients who were enrolled in the clinic. They were re-admitted less because a care team examined factors that exacerbated underlying cardiac dysfunction, preventing an admission. The cardiologist of the team considered active ischemia/infarction, uncontrolled hypertension or heavy alcohol consumption among others. Patients were likewise closely supervised for viral infections and pneumonia which are common causes of exacerbation. A nurse educated the patients on their medications and emphasized the importance of compliance.

Heart Failure Clinic patients were also closely examined for increasing filling pressures. Those who presented with physical evidence of congestion in the clinic had their medications adjusted and were educated on compliance to medications and dietary restrictions. Most unplanned changes in medications are triggered by fluid retention. Treatment plan thereafter depend on their profile. With Profile B patients on standard therapy generally being treated with temporary increase in diuretics while Profile C is sent to the emergency room for admission to improve systemic and renal perfusion from intravenous therapy.[13]

There are several factors that may change patient outcomes, most of which are secondary to suboptimal use of effective therapies, an aging

population, complex patient profiles and inadequate follow-up and support of patients with heart failure. These factors are the emphasis of the PHC-HF Clinic. Optimizing medical management and patient education regarding their disease are proven to prevent mortality and unexpected re-admissions. This is consistent with the results in this study.

A clear and organized plan of patient education and counseling is critical to the achievement of optimal outcomes. Overviews of heart failure and associated symptoms, dietary recommendations, activity and exercise, and medications are taught to patients and families. Given the complexity of the information, the team approach is extremely useful in helping patients to understand and retain information about the treatment regimen. This is particularly evidenced by shorter hospital stay and lesser readmission in this study.

Several reviews have reported the effectiveness of HF Clinics, with reductions in morbidity and mortality and cost-effectiveness in the management of HF. Meta-analysis reveal that disease management programmes that use multi-disciplinary approach potentially reduce hospital re-admission and that HF Clinics are associated with reductions in re-hospitalization and mortality in an unselected HF population, independent of whether they are academic or community-based. The positive results seen in international studies are consistent with our local experience, suggesting that part of the treatment plan for patients with heart failure is enrollment in the HF specialty clinic.

CONCLUSION

The Philippine Heart Center-HF Clinic is effective in reducing readmission, mortality and length of stay in the hospital at 3 and 12 months after inclusion. This is consistent with reports of several randomized controlled trials that a specialty clinic for patients with heart failure does reduce mortality and re-admission rates. This intervention should receive the greatest consideration by systems or providers seeking to implement optimal care interventions for persons with heart failure.

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A Meta-Analysis on the Effects of Tolvaptan in Patients with Chronic Heart Failure

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Background --- Among the recent novel therapies for heart failure are the vasopressin receptor antagonists, "the vaptans" (Tolvaptan, Conivaptan). This meta-analysis will test the hypothesis that Tolvaptan is beneficial and result in clnical improvement in the treatment of heart failure.

Method --- Included in this meta-analysis are randomized controlled trials (RCTs) which compared the efficacy of Tolvaptan with a placebo or an active drug (e.g. Furosemide). Three (3) reviewers independently assessed and abstracted data from the five (5) included studies using the JADAD Quality Scale.[12] Treatment of data was done using the Review Manager 5 software version 5.1.7 to compare the effectiveness of Tolvaptan versus placebo and its mean change in body weight and serum sodium from baseline among heart failure patients.

Results --- There are five randomized controlled trials (RCTs) included in the meta-analysis with a total pooled patient population of 4,899 patients. The outcome of the mean change (Δ) in body weight after 24 hours of treatment demonstrate a statistically significant point estimate that favored the Tolvaptan treatment group compared to the placebo group. The outcome of mean change (Δ) in serum sodium after 24 hours of treatment showed statistically significant outcome favoring the Tolvaptan group.

Conclusion --- This meta-analysis had demonstrated significant weifht reduction and increase in serum sodium in patients with heart failure treated with Tolvaptan during the first day and up to the end of follow-up treatment. ***Phil Heart Center J 2016;21(2):80-87.***

Key Words: Heart Failure Clinic ■ Mortality ■ Re-hospitalization ■ Heart Failure Clinic

According to the American College of Cardiology / American Heart Association (ACC/AHA) Task Force, the definition of Heart Failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.[1] The manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary congestion and peripheral edema. Symptomatic heart failure (New York Heart Association Functional Class 11 to IV), is associated with increased mortality that is due primarily to progression of the myocardial dysfunction.

It is increasingly challenging to manage heart failure given the many pathophysiologic mechanisms in play. Treating heart failure aims to address three main goals, primarily of which is improvement in symptoms - (decreasing hospital admissions), decreasing rate of disease progression, and survival with good functional capacity.

Vasopressin has significant cardiovascular and renal effects. Levels are often elevated in HF patients and LV dysfunction, and it appears to be associated with adverse outcomes in the setting of low ejection fraction after myocardial infarction.[2] In heart failure, elevated vasopressin levels may contribute to the increase in systemic vascular resistance via stimulation of the V1 a receptor, which is found on vascular smooth muscle cells. Renal consequence of elevated vasopressin levels includes enhancement of water retention via the V2 receptor, leading to the development of hyponatremia. Hyponatremia is reported to

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be associated with increased morbidity and mortality among patients with heart disease.[3,4]

Among the recent novel therapies for heart failure are the vasopressin receptor antagonists, "the vaptans" (Tolvaptan, Conivaptan). Tolvaptan is an oral, non-peptide, selective vasopressin V2- receptor antagonist that causes aquaresis by acting on the distal nephron to increase secretion of electrolyte-free waters.[5]

Tolvaptan (Samsca) is the first V2 receptor antagonist in Asia currently being marketed by Otsuka Pharmaceutical Inc. in the USA, Europe, Japan, Canada and China. The company launched the drug on 2013 in the Philippines.

This meta-analysis will test the hypothesis that Tolvaptan is beneficial and result in clinical improvement in the treatment of heart failure. The result of this novel treatment may be translated in the management of our Filipino heart failure patients.

METHODS

Included in this study are randomized controlled trials (RCTs) which compared the efficacy of Tolvaptan with a placebo or an active drug (e.g. Furosemide). The study population included patients with age ≥18 years with chronic heart failure, regardless of the ejection fraction (however most patients have ejection of < 40%) with hypervolemia and hyponatremia.

Type of Interventions. The treatment arm was Tolvaptan 30mg OD as compared to placebo.

Type of Outcome Measure. Outcome measured is (1) change in body weight; and (2) change in serum sodium from baseline within 24 hours of initiating treatment and at the end of follow-up.

Search strategy for identification of studies. We obtained relevant publications from PUBMED, Cochrane and Australasian Medical Index. We used the keywords: Tolvaptan, Heart Failure and Randomized Controlled Trial. Both free text and MeSh terms were used in the search for abstracts, reference lists of reviewed articles and retrieved studies using manual and internet search strategies.

Data Extraction and Quality Assessment of Included Studies. The baseline characteristics of the patients in the individual studies were tabulated (*Table I*). Three (3) reviewers independently assessed and abstracted data from the five (5) included studies using the JADAD Quality scale.[12] This is a commonly used three-item, five-point quality scale that is used to rate the quality of the trials. (*Table 2*)

Assessment was made on the basis of randomization, double-blinding and description of withdrawal or drop-outs. (*Table 3*) Treatment of data was done using the Review Manager 5 software version 5.1.7 to compare the effectiveness of Tolvaptan versus placebo and its mean change in body weight and serum sodium from baseline among heart failure patients.

Analysis utilized continuous data type with inverse variance as the statistical method and random effects for the analysis model and mean difference was used as effect measure. Heterogeneity between comparable trials were tested using the standard chi-square (l) test (significant if $p<0.05$) and I^2 ($I^2 = [(0 - df)/Q] \times 100\%$, where Q is the chi square (X^2) statistic, and *df* is its degrees of freedom). Significant heterogeneity is defined as I^2 greater than 50%. This describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (Chance). A value >50% may be considered substantial heterogeneity. The potential publication bias was examined by constructing a "funnel plot", in which the standard error (SE) of the In OR was plotted against the OR (mortality).

RESULTS

There are five randomized controlled trials (RCTs) included in the meta-analysis with a total pooled patient population of 4,899 patients, the largest proportion of which was from the EVEREST study.[7] From the data extraction, there were 2,281 patients assigned to the tolvaptan (30mg once daily) group and 2,279 patients assigned to the placebo group that was analyzed in the study.

Mean Change in Body Weight. The outcome of the mean change (Δ) in body weight after 24 hours (*Fig. 1*) of treatment demonstrate a statistically significant point estimate that favored the tolvaptan treatment group compared to the placebo group. A mean difference of -0.93 (95% CI: -1.12 to -0.74) using a random effect model was obtained from the forest plot (*Fig. 1*). There was significant heterogeneity, the chi^2 (X^2) is 11.35 with df of 4 ($P_{heterogeneity}$ = 0.02) and I^2 is 65%.

A constructed funnel plot (*Fig. 2)* was done to examine if potential publication bias exist. There was tendency of the studies to cluster towards the apex of the funnel. No outlier studies noted. However, there is asymmetry over the base of the figure. Asymmetry in the funnel plot may be due to small population study designs. The smallest population study in this meta-analysis of Udelson, et.al[8] was located away from the clustered studies. We can say that the skewed distribution may be due to the small population studies and not due to publication bias.

The outcome of the mean change (Δ) in body weight after the end of follow-up (*Fig. 3*) has also showed statistically significant outcome favoring Tolvaptan treatment. The mean difference was -1.34 (95% CI: -1.66 to -1.02) with a X^2 of 2.49 with df of 2 ($P_{heterogeneity}$ = 0.29) and I^2 of 20%, hence a homogenous analysis.

Asymmetry in the funnel plot (*Fig. 4*) may be due to small population study of Udelson, et.al[8], was again located away from the clustered studies.

Mean Change in Serum Sodium. The outcome of mean change (Δ) in serum sodium (*Fig. 5*) after 24 hours of treatment showed statistically significant outcome favoring the Tolvaptan group. Mean difference was 3.05 (95% CI: 1.85 to 4.25). However, the analysis has significant heterogeneity with a X^2 of 5.28 with df of 2 ($P_{heterogeneity}$ = 0.07) and I^2 of 62%.

Asymmetry in the funnel plot (*Fig. 6*) noted with all three (3) studies scattered over the base of the funnel. This may be attributed to the relatively small study population.

The outcome of mean change (Δ) in serum sodium (*Fig. 7*) at the end of follow-up has showed statistically significant outcome favoring the tolvaptan group. Mean difference was 2.25 (95% CI: 0.83 to 3.66). The analysis has significant heterogeneity with a X^2 of 86.83 with df of 3 ($P_{heterogeneity}$ = 0.00001) and I^2 of 97%. The attempted sensitivity analysis to address heterogeneity was futile (did not minimize heterogeneity).

The funnel plot (*Fig. 7*) showed the small population study of Udelson, et.al., J Card Fail 2011, to be lying at the base of the funnel, away from the clustered study groups on the apex.

DISCUSSION

This meta-analysis had demonstrated significant weight reduction and increase in serum sodium in patients with heart failure treated with tolvaptan during the first day and up to the end of follow-up treatment. This further validates the hypothesis that tolvaptan has beneficial cardiovascular effects in heart failure. This may be translated to favorable clinical implications in medical practice. Pulmonary congestion is most commonly noted in patients with Acute Heart Failure Syndromes (AHFS). The major treatment goal is excess fluid removal. Fluid removal can be quantified by the urine output and weight loss during treatment. Loop diuretics had been in the frontline of treatment with its wide acceptance in the management of AHFS. However, treatment with diuretics is associated with electrolyte abnormalities, renal dysfunction, neurohormonal activation and hypotension.[7] The need for aggressive diuresis entails these potential adverse effects. Dobutamine, dopamine, and milrinone improve hemodynamics but are often associated with significant adverse effects that include hypotension, atrial and ventricular arrhythmias, and possibly increased post discharge mortality.[7,14]

Table 1. Summary of Individual Tolvaptan (TLV) Studies included in the Meta-Analysis

Study	Participants	Baseline Characteristics	Intervention	Primary end-point	Secondary end-point
Gheorghiade, M., et.al[6] Circulation. 2003	254	Peripheral edema, mostly mild, was observed in 45% of patients, pulmonary rales in 32%, jugular venous distension in 34%, and hepatomegaly in 51%. The four treatment groups were balanced with regard to age, sex, race, and NYHA functional class. The average furosemide dose was 85 mg/d. The majority of patients were receiving digoxin and ACEi/ARB. Hydralazine and nitrates were used in 24% of patients, whereas 26% were taking a β-blocker.	Study population divided into: Placebo (n=63), TLV 30mg (n=64), TLV 45mg (n=64), TLV 60mg (n=63)	Change in body weight	The secondary efficacy variables included edema size measurements, urine sodium excretion, urine osmolality, and urine volume. Change in serum electrolytes and renal function (Na, K, BUN, Crea), change in heart rate, SBP and DBP
Konstam, MA, t.al[7] (EVEREST) JAMA 2007	4133	There were no significant differences between the 2 groups at baseline. At baseline, the majority of patients were receiving standard therapies for HF, including diuretics in 4002 (96.8%), ACEi or ARB in 3479 (84.2%), andβ blockers in 2903 (70.2%). Nine patients in the TLV group and 6 in the placebo group did not take any study medication.	Study population divided into: Placebo (n=2061), TLV 30mg (n=2072)	Dual primary end points were all-cause mortality (superiority and noninferiority) and cardiovascular death or hospitalization for heart failure (superiority only).	Secondary end points included changes Body Weight, Patient-Assessed Dyspnea, Serum Sodium Concentration, Edema, and KCCQ Overall Summary Score
Udelson, J.E., et.al[11] Card Fail 2011	83	There were no statistically significant differences in the demographic and baseline characteristics between the treatment groups.	Study population divided into: Placebo = 21 TLV30mg = 20 Furosemide = 22 TLV + Furo = 20	The primary end point of the trial was the change in body weight from baseline to day 8, or if the study drug was prematurely discontinued, to the last observation on treatment.	Secondary end points included 24-hour urine volume (measured on day 1 and day 7 of the study), urine sodium and potassium excretion, selected neurohormone levels, and safety measurements.
Gheorghiade, M., et.al[9] (ACTIV in CHF) JAMA 2004	319	There were no significant difference between groups at randomization, except for PCI/CABG (P=0.02) and sex (P=0.04).	Study population divided into: Placebo = 80 TLV30mg = 78 TLV60mg = 84 TLV90mg = 77	The in-hospital end point was change in body weight at 24 hours after the administration of the first dose of study drug. The outpatient end point was worsening heart failure at 60 days after randomization, defined as hospitalization for heart failure, unscheduled visit for heart failure to an emergency department or outpatient clinic associated with need for either increased therapy or new therapy for heart failure, or death.	Secondary end points included changes in dyspnea, JVD, rales, edema, body weight (at discharge and in the outpatient setting), urine output (inpatient), serum electrolyte levels, length of hospital stay after randomization, use of diuretics, and patient and physician-assessed symptom scales
Matsuzaki, M., et.al[10] (QUEST Study) Cardiovasc Drugs Ther 2011	110	No significant difference was found in sex, age, height, EF, causes of HF, types of HF, cardiovascular complications and pacemaker and implantable ICD implantation between the two groups. Body weight was slightly higher and cardiothoracic ratio was slightly lower in the tolvaptan group compared with placebo (p=0.12, 0.10 respectively). No intergroup differences were seen in baseline NYHA functional class, daily urine volume, creatinine level, plasma AVP, lower 11mbedema, hepatomegaly, pulmonary rales, or third heart sounds, whereas pulmonary congestion and jugular venous distention were slightly higher in the tolvaptan group (p=0.15, 0.06 respectively). The amount of used loop diuretics was insignificantly lower in the tolvaptan group (p=0.08), however, the combination therapy with the other diuretics was not different between the two groups.	Study population divided into: Placebo = 57 TLV = 53	The primary endpoint of the current study was body weight change from the baseline at the end of treatment	The secondary endpoints were changes in congestive symptoms, including lower limb edema, pulmonary congestion, jugular venous distention hepatomegaly, pulmonary rales and third heart sound induced with fluid retention. To study the pharmacological effects of tolvaptan, serial changes in daily urine volume and daily water intake, serum electrolyte concentrations (Na+ and K+), serum osmolality and endocrine parameters i.e. AVP, BNP, and plasma renin activity were assessed. To evaluate the safety of tolvaptan, adverse events, laboratory data, vital signs and ECG were assessed

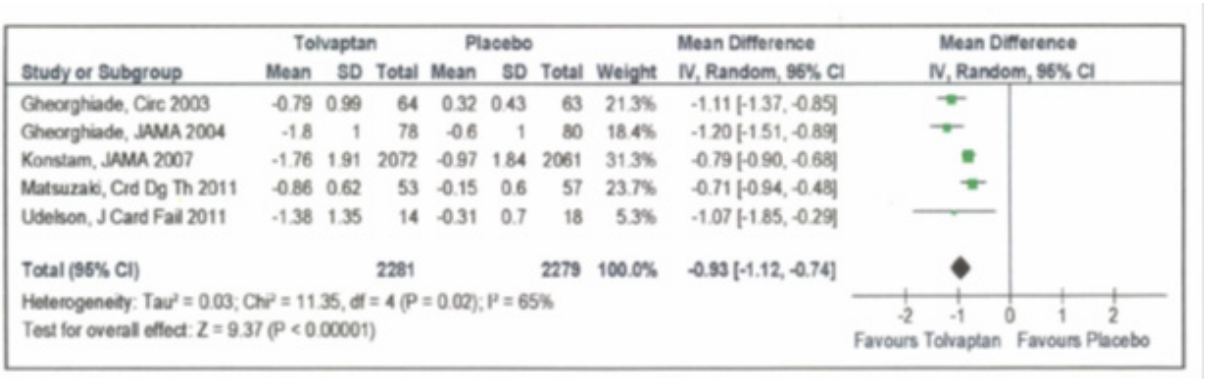

Figure 1. Forest Plot for Mean Change in Body Weight at Day 1

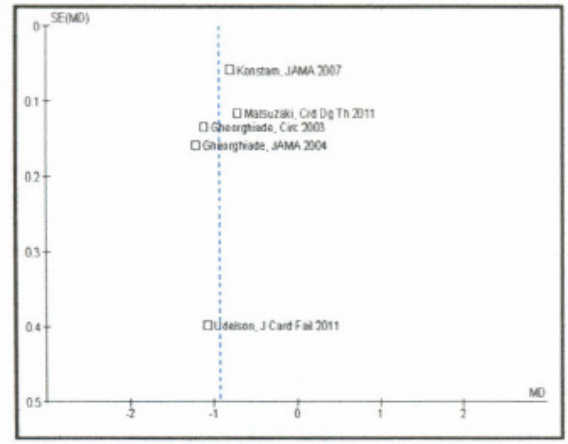

Figure 2. Funnel Plot for Mean Change in Body Weight at Day 1

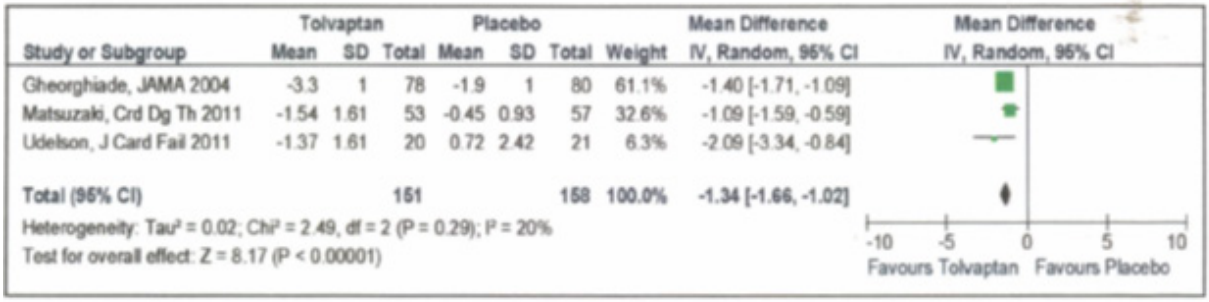

Figure 3. Forest Plot for Mean Change in Body Weight at End of Follow-up

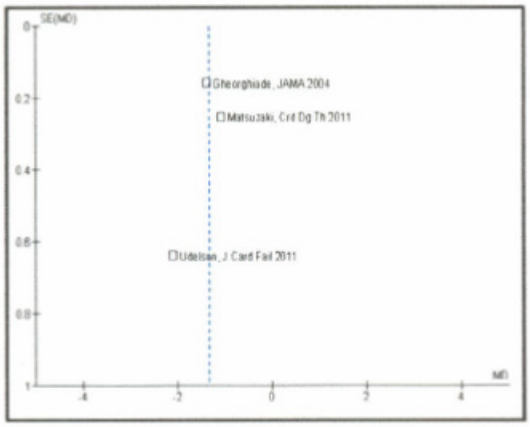

Figure 4. Funnel Plot for Mean Change in Body Weight at End of Follow-up

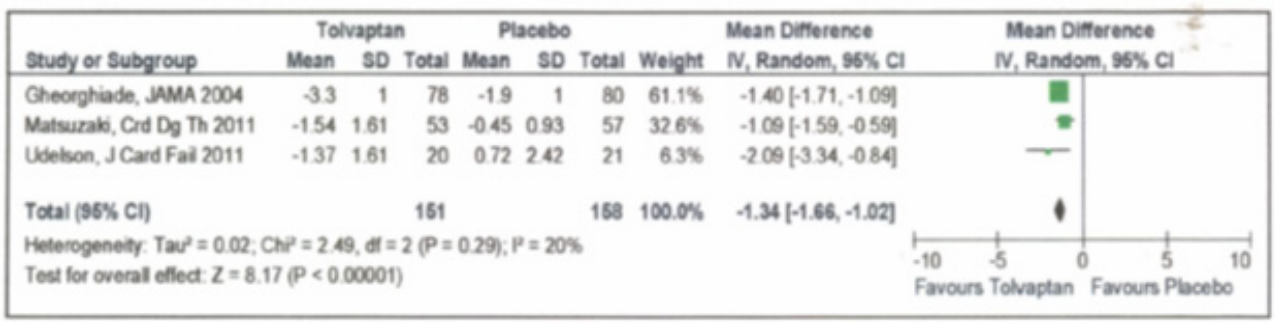

Figure 5. Forest Plot for Mean Change in Serum Sodium at Day 1

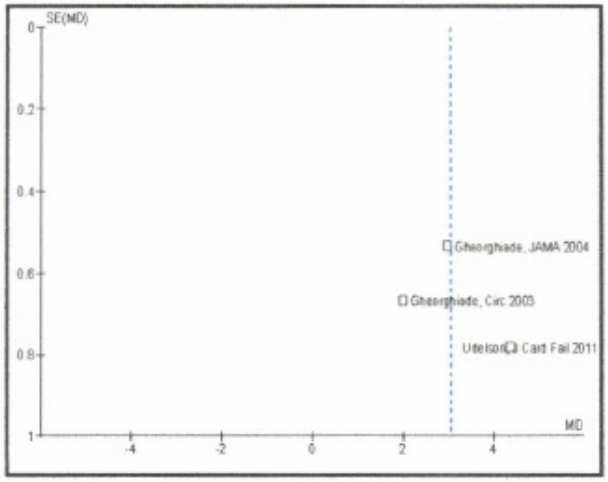

Figure 6. Funnel Plot for Mean Change in Serum Sodium at Day 1

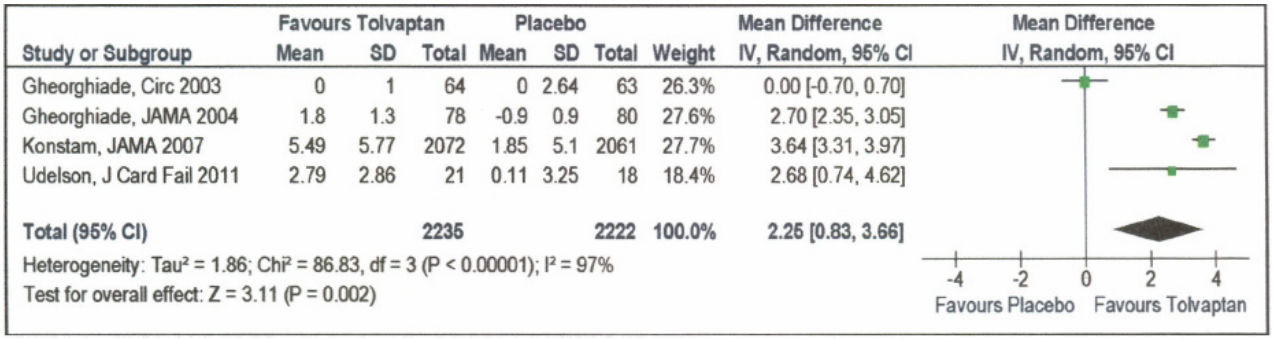

Figure 7. Forest Plot for Mean Change in Serum Sodium at End of Follow-up

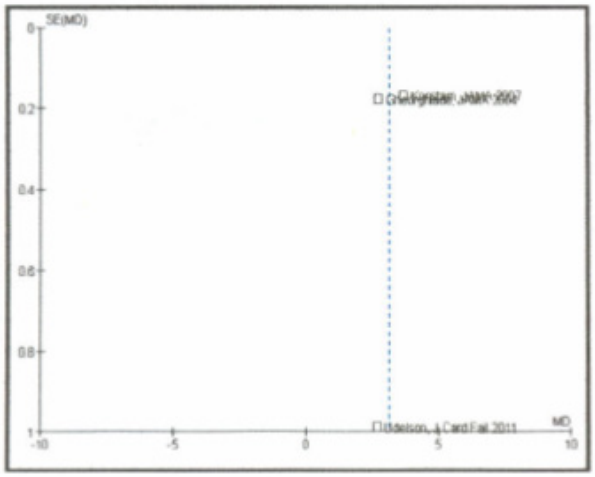

Figure 7. Funnel Plot for Mean Change in Serum Sodium at End of Follow-up.

Table 2. JADAD Quality Scale Point System

(1) Is the study randomized?	If YES	+1 point
Is the randomization procedure appropriateand reported in the study?	if YES	+1 point
	if NO	Delete all points awarded for randomization
(2) Is the study double blind?	if YES	+1 point
Is the double blinding method appropriate and reported in the study?	if YES	+1 point
	if NO	Delete all points for double blinding
(3) Are the reasons for patient withdrawals and dropouts described for each treatment group?	if YES	+1 point
***Maximum 5 point**		

Jadad AR, Moore RA, Carroll D et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clinical Trials 1996; 17:1-12.

Table 3. Tabulated Quality Assessment of the Included Studies in the Meta-Analysis

Author/Publication	Design	JADAD	Allocation Concealment	Follow-up	ITT	Blinding
Gheorghiade M, et al Circ 2003	randomized, double-blind, placebo-controlled study	4	YES	Adequate	YES	YES
Konstam MA et al (EVEREST) JAMA 2007	randomized, double-blind, placebo-controlled study	5	YES	Adequate	YES	YES
Udelson et al. J Card Fail 2011	multicenter, randomized, double-blind, placebo-controlled, parallel group study	4	YES	Adequate	NS*	YES
Gheorghiade M, et al. (ACTIVE in CHF) JAMA 2004	multicenter, randomized, double-blind, placebo-controlled, parallel group, dose ranging	4	YES	Adequate	NS*	YES
Matsuzaki M, et al. (QUEST Study) Cardiovasc Drugs Ther 2011	multicenter, randomized, double-blind, placebo-controlled, parallel study	5	YES	Adequate	YES	YES

*NS = not stated

Vasopressin is inappropriately elevated in heart failure[7] mediating the unfavorable consequences of fluid retention resulting to pulmonary congestion and hyponatremia. Tolvaptan was effective in this regard by addressing the problem on fluid balance and was consistent with the results of our meta-analysis mainly reducing body weight and increase in serum sodium levels.

Furthermore, the additional potential cardiovascular beneficial effects had been shown in the ECLIPSE study.[13] The ECLIPSE (**E**ffe**C**t of to**L**vaptan on hemodynamIc Parameters in Subjects with h**E**art failure) study, a randomized controlled trial, evaluated the hemodynamic effects of vasopressin V2 receptor inhibition and showed modest changes in filling pressures associated with a significant increase in urine output and including concomitant reduction of the pulmonary capillary wedge pressure (PCWP).

Study Limitations. There was significant heterogeneity documented in the meta-analysis of the mean change in serum sodium that was not addressed with sensitivity analysis. This is an inherent weakness in this regard when combining heterogenous data sets.

CONCLUSION

Tolvaptan, a vasopressin V2-receptor antagonist, is effective in the reducing the body weight and increasing the serum sodium from baseline on patients with chronic heart failure. These are important properties that are useful to the armamentarium for the treatment of heart failure.

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Cardiac Resynchronization Therapy for the Treatment of Chronic Heart Failure: a meta-analysis

Geraldine G. Garrido-Pon, MD

Background ---Cardiac resynchronization therapy by means of biventricular pacing is a fairly new procedure that has recently been approved by the US-FDA. Studies have shown that there was a high incidence of left bundle branch block (LBBB) or intraventricular conduction delay in congestive heart failure (CHF) resulting in interventricular dyssynchrony. This then leads to a prolonged delay between the onset of left ventricular and right ventricular conduction as well as a decrease in the duration of left vetricular diastole. By simultaneously pacing the left ventricle along with the right ventricle, a more synchronous ventricular contraction pattern could be achieved resulting in the reduction in QRS duration and thereby a reduction in intraventricular asynchrony.
Methods --- A MEDLINE search of eligible studies were done. Included in the review of literature were studies conducted in humans, randomized controlled trials on cardiac resynchronization therapy without implantable cardiac defibrillator (ICD) implantation in the management of congestive heart failure patients in sinus rhythm. Four full text articles were retrieved and were analyzed using the Review Manager 4.2.
Results --- At pooled analysis, cardiac resynchronization therapy appears to improve significantly the outcome of patients in chronic heart failure compared to patients given medical therapy alone in terms of the following variables: mortality rate was significantly lower for patients on both medical therapy and CRT compared to those on medical therapy alone. In all variables, cardiac resynchronization therapy significantly improve both the clinical symptoms as well as the multiple measures of functional status of patients in chronic heart failure.
Conclusion --- Cardiac resynchronization therapy offers significant improvement in the quality of life and functional capacity of patients in advanced heart failure. In these subset of patients. It has effectively reduced the morbidity and mortality compared to those with optimal medical management only. ***Phil Heart Center J 2016;21(2):88-90.***

Key Words: Cardiac Resynchronization ■ Congestive Heart Failure

Cardiac resynchronization therapy by means of biventricular pacing is a fairly new procedure that has recently been approved by the US-FDA. Studies have shown that there was a high incidence of left bundle branch block (LBBB) or intraventricular conduction delay in congestive heart failure (CHF) resulting in interventricular dyssynchrony. This then leads to a prolonged delay between the onset of left ventricular and right ventricular conduction as well as a decrease in the duration of left vetricular diastole. By simultaneously pacing the left ventricle along with the right ventricle, a more synchronous ventricular contraction pattern could be achieved resulting in the reduction in QRS duration and thereby a reduction in intraventricular asynchrony.

The objective of this study is to do meta-analytic review of four (4) randomized controlled trials on cardiac resynchronization therapy for the management of chronic heart failure.

METHODS

The criteria for considering studies for this review were all randomized controlled trials of which participants are patients with congestive heart failure with New York Heart Association (NYHA) functional class III and IV in sinus rhythm; while intervention is only cardiac resynchronization therapy without implantable cardiac defibrillator (ICD).

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The types of outcome measures were as follows:

1. death from any cause
2. death or unplanned hospitalization due to heart failure
3. Number of hospitalizations for worsening heart failure
4. Quality of life score
5. Distance walked in six (6) minutes
6. Improvement in NYHA functional class

Studies were reviewed using the Quality Scale for Meta-Analytic Review and were assessed based on the presence of bias, exlusion bias and detection bias. Studies graded A and B were included.

RESULTS

At pooled analysis, cardiac resynchronization therapy appears to improve significantly the outcome of patients in chronic heart failure compared to patients given medical therapy alone with unplanned hospitalization for worsening heart failure at only 14% in those on CRT compared to 26% on those on medical therapy alone (P<00004).

There is also significant improvement in NYHA functional class among patients on CRT at 66% compared to only 42% on those on medical therapy alone (P = 0.41).

Mortality rate was significantly lower for patients on both medical therapy and CRT compared to those on medical therapy alone at 16% vs. 26% (P = 0.79).

In all variables, cardiac resynchronization therapy appears to significantly improve both the clinical symptoms as well as the multiple measures of functional status of patients in chronic heart failure.

DISCUSSION

Cardiac resynchronization therapy is a fairly new approach for treating patients with moderate to severe heart failure and ventricular dyssynchrony.

Early observational studies supported the concept of cardiac resynchronization therapy for the treatment of heart failure by demonstrating improvement in hemodynamics, echocardiographic measures of cardiac performance and functional status.

In the Multicenter InSync Randomized Clinical Evaluation (MIRACLE) trial, patients randomized to CRT demonstrated significant improvement in quality of life score, 6-minute walk distance, NYHA functional class ranking, treadmill exercise time, peak V02 and LV ejection fraction compared with the control group.[1]

The Multisite Stimulation in Cardiomyopathies (MUSTIC) study evaluated the safety and clinical efficacy of CRT in patients with dilated ischemic or non-ischemic cardiomyopathy and ventricular dyssynchrony. This study showed a 23% greater mean distance walked in 6 minutes for patients in the active pacing phase than in the inactive pacing phase.[2]

The COMPANION study which was initiated in early 2000 compared drug therapy alone with drug therapy in combination with CRT in patients with dilated cardiomyopathy. This study has shown nearly 20% significant reduction in all-cause mortality and all-cause hospitalization and also in a variety of measures of cardiac morbidity.[3]

Table 1. Overview of Included Studies

Authors	Study	Population	NYHA CI	Rhythm	ICD?	Inter-vention
Abraham W, et al	MIRACLE	524	III, IV	Sinus	No	CRT
Cazeau C, et al	MUSTIC	58	III	Sinus	No	CRT
Krueger S, et al	COMPANION	1520	III, IV	Sinus	No	CRT
Christ G, et al	CARE-HF	800	III, IV	Sinus	No	CRT

Another randomized, controlled morbidity and mortality trial, CARE-HF which also compared optimal medical therapy alone with optimal medical therapy and resynchronization has shown significant improvement in different outcome parameters for those on CRT.[4]

All together, significant improvement in mortality from any cause, worsening heart failure, number of hospitalizations, NYHA functional class, quality of life score and distance walked in 6 minutes has been shown by these studies reviewed here. These studies justify the recent ACC/AHA/NASPE guidelines for pacing recommending biventricular pacing in medically refractory, symptomatic NYHA Class III/IV patients with dilated or ischemic cardiomyopathy, prolonged QRS interval (>130ms), LVEDD of 55mm or more and LV ejection fraction of 0.35 or less as Class IIa indications.

CONCLUSION

Cardiac resynchronization therapy is a safe and effective approach in the management of patients with moderate to severe heart failure and ventricular dyssynchrony. Clinical trials demonstrate significant improvement in both clinical symptoms as well as in the different measures of functional status and exercise capacity. Studies have shown that it significantly reduces mortality and morbidity thus it must be offered as an option to eligible heart failure patients.

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Comparison of Low and High Dose Angiotensin Converting Enzyme Inhibitors in Congestive Heart Failure: a meta-analysis

Kenneth C. Oporto, MD

Angiotensin converting enzyme (ACE) inhibitors have been proven in several major clinical trials to improve symptoms and prolong life. Yet the dosages used in these trials are oftentimes not attained in clinical practice. A meta-analysis was done to determine if low dose and high ACE inhibitors confer similar benefits in heart failure patients. Two randomized controlled trials comparing low and high dose ACE inhibitors, enalapril (NETWORK study) and lisonopril (ATLAS study), were analyzed. Results showed although there was a tendency towards higher all cause mortality in low dose groups. In contrast there was a tendency toward more heart failure related hospitalisation and higher incidence of side effects in the high dose group. All these differences however, were found to be not statistically significant. Therefore both low dose and high dose ACE inhibitors can give similar benefit in the treatment of heart failure. ***Phil Heart Center J 2016;21(2):91-94.***

Key Words: Angiotensin Converting Enzyme (ACE) Inhibitors

The impact of angiotensin converting enzyme (ACE) inhibitors, in the treatment of congestive heart failure have been validated in several large scale trials. They have been shown to decrease symptoms, morbidity and mortality. Thus, many treatment guidelines highly recommend the use of ACE inhibitors in all heart failure patients with left ventricular dysfunction.

The dose of ACE inhibitors used in most heart failure trials are relatively high. For instance, the target dose of enalapril in CONSENSUS was 20 mg twice daily, in SOLV 10 mg twice daily and V-HeFT 20 mg once daily. In SAVE, the daily dose of Captopril was 150 mg and in ISIS-4 100 mg daily. The GISSI-3 and AIRE studies, each recommend a l0 mg daily dose of lisinopril and fosinopril respectively.[5,8]

In actual practice, not all heart failure patients are receiving ACE inhibitors and when they do, they are oftentimes receiving doses much lower than the recommended dose. In one study in Europe, the mean daily dosing were as follows: enalapril 10 mg, captopril 3.5 mg· and lisinopril 5 mg.[5] These are way below the recommended dosages. Considering the economic status of Filipinos, a much larger proportion of heart failure patients could be expected to be receiving even lower doses of ACE inhibitors or even none at all. However, economic considerations is not the only reason. Many physicians, may actually prefer prescribing lower doses of ACE inhibitors with the belief that they are as good as the high doses. Compounding this problem is the fear of some doctors and patients of more side effects with high dose.

It is important to know if the low dose ACE inhibitors actually confer the same beneficial effects as the recommended or high dose. This is because, if the they do not, patients might just be wasting their money, aside from the added risk of adverse effects.

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The objective of this study was to assess whether low dose and high (standard) dose angiotensin converting enzyme inhibitors share comparable benefits in congestive heart failure.

METHODS

An internet search using Medline, Pubmed, Cochrane library and cross references was used to identify relevant studies. The key word used were: angiotensin converting enzyme inhibitors (ACEI), ACE inhibitors, dose, the names of the different types of ACE inhibitors (i.e. Captopril, quinalapril, fosinopril, etc.) and heart failure. The reference lists of identified trials were checked with the related articles featured. Articles are included if it met the following criteria: prospective, randomized, controlled trials, published as an article, involving patient with heart failure. The primary endpoints were all-cause mortality and heart failure related hospitalisation. Trials that were retrospective, non-randomized or quasi-randomized were excluded. A total of 6 trials were obtained. All but one are full text articles. The five were RCT's but only 2 were comparable in terms of subjects and clinical outcome.[5,6] The outcome measures were overall mortality and hospitalisations due to heart failure.

Study Population. The baseline characteristics of the subjects in both trials were comparable.

Exclusion criteria. Patients excluded were those with significant valvular disease, unstable angina, recent myocardial infarction, uncontrolled hypertension, hypotension, advanced pulmonary disease, serum potassium <3.2 or >5.5 mmol/L, serum creatinine >200umol/l or contraindication to ACE inhibitors. Patients are also excluded if they have an acute coronary ischemic event or revascularization procedure within 2 months, had a history of sustained or symptomatic ventricular tachycardia, were known to be intolerant of ACE inhibitors, had serum creatinine >2.5mgldL or had any non-cardiac disorder that could limit survival.

Statistical Analysis. A meta-analysis software was used to calculate for statistical significance. Data were compared using the Mantel-Haenszel chi-square test with a 0.05 level of significance and 95% confidence interval.

Table 1. Characteristics of Trials Included in Meta-Analysis

	Patient	ACE inhibitor		Endpoints
		Low Dose	High Dose	
		Enalapril		
NETWORK Investigators	1532	2.5mg BID	10mg BID	Death, hospitalization
		Lisinopril		
Packer, et al (ATLAS)	3164	2.5-5mg OD	32.5-35mg OD	Death, hospitalization

Table 2. Baseline characteristics in NETWORK trial

	Low Dose (n=506)	High Dose (n=516)
Age in years (mean)	70 (range 38-86)	70 (range 27-86)
Sex male:female	63:37	66:34
NYHA Class		
II	64	66
III	33	32
IV	2	2
Systolic blood pressure	139 ±20	138 ±19
Heart rate	89±13	79 ±14

Table 3. Baseline characteristics in ATLAS trial

	Low Dose (n=1596)	High Dose (n=1568)
Age in years	63.6 ± 10.3	63.6 ± 10.5
Sex male:female	1265:331	1251:317
NYHA Class		
II	231	262
III	1252	1194
IV	11	112
Systolic blood pressure	126 ±20	125 ±19
Heart rate	80±15	80 ±14

RESULT AND DISCUSSION

Results showed a tendency towards higher mortality in low dose ACE inhibitors but this is not significant as shown in Table 4. In contrast there was tendency of higher incidence of hospitalisation in the high dose in the second trial but overall, the difference was not significant. (*Table 5*)

On the other hand, incidence of adverse events were noted to be more common in the high dose, although they are not statistically significant. *(Table 6 and 7)* However it must be mentioned, that these side effects as cited in the studies are minor and did not lead patients to stop the study medications.

The combined endpoints of all cause mortality and heart failure related hospitalization have shown no significant difference between low dose and high dose inhibitors in the treatment of heart failure. Although there was a tendency to higher mortality in the low dose group, this was not significant.

There have been several postulates why low dose ACE inhibitors are able to impart comparable benefits to high dose. Angiotensin converting enzyme (ACE) inhibitors suppress the formation of angiotensin II by binding reversibly to angiotensin converting enzyme. It has a high affinity for the enzyme and dissociate slowly. This has led some investigators to believe that higher doses of ACE inhibitors may not be necessary to suppress the formation of angiotensin II to exert its clinical benefit. Some studies have shown that small doses of ACE inhibitors like Captopril (1mg) can enhance renal salt and water excretion without affecting the circulating hemodynamic factors.[1-4] Furthermore the dose response of some ACE inhibitors (lisinopril, enalapril) may be flat such that a low dose could inhibit plasma ACE for up to 24 hours.[7] In contrast a study on Imidapril have shown that within 3 months after initiating ACE inhibitor treatment, a higher dose was more effective than low dose in increasing exercise capacity. This is also associated by a dose-related effect on plasma neurohormones.

Now the question is not whether low dose ACE is effective but by how much. In view of the available results it seems prudent to try to maximize ACE inhibitor dosages if the patient tolerates.

As was shown in Table 5 and 6, adverse events such as dizziness, increase in serum creatinine levels and hyperkalemia were more common in the high dose group. However, these are minor and well tolerated as to suggest that these should not be made the sole basis of withholding ACE inhibitors.

Despite the large number of subjects, this meta-analysis is hampered by the limited number of trials and type of ACE inhibitors used. Indeed, short acting ACE inhibitors may behave differently than long-acting ones at low doses. Results of ongoing studies on ACE inhibitors in heart failure, might further support the benefit of ACE inhibitors even at low doses, in the near future.

Table 4. Comparative All-Cause Mortality

Trial	Low Dose (%)	High Dose	Odds Ratio	CI	P-Value
NETWORK Trial	21/156 (4.2)	15/516 (2.9)	1.45	.70,2.99	0.364
ATLAS Trial	717/1596 (42.5)	666/1568 (42.5)	1.10	.96,1.27	0.176
Overall			1.12	.97,1.28	0.122

Table 5. Comparative Heart Failure Related Hospitalization

Heart Failure related hospitalization	Low Dose (%)	High Dose	Odds Ratio	CI	P-Value
NETWORK Trial	26/506 (4.2)	15/516 (2.9)	0.72	.42, 1.25	0.364
ATLAS Trial	247/1596 (42.5)	198/1568 (42.5)	1.29	.1.03, 1.56	0.176
Overall			1.18	.98,1.48	0.099

Table 6. Clinical and Laboratory Adverse Events in NETWORK Trial

	Low Dose (n=506)	High Dose (n=516)
Dizziness	99	105
Cough	78	71
Increase in creatinine	15	31
Hyperkalemia	8	17

Table 7. Clinical and Laboratory Adverse Events in ATLAS Trial

	Low Dose (n=1596)	High Dose (n=1568)
Dizziness	193	297
Cough	211	166
Increase in creatinine	112	155
Hyperkalemia	56	100

CONCLUSION

This meta-analysis have shown that low dose and high dose ACE inhibitors have no significant differences in terms of overall mortality and hospitalizations, in the treatment of heart failure. Nevertheless, in view of a tendency of a more favorable outcome in the high dose ACE inhibitor, a higher dose should still be the aim.

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A Very Rare Variant of Cor Triatriatum Sinister in an 18-Month Old Child With Congestive Heart Failure

Maria Rosita S. Quitola, MD; Glenda T. Tubianosa, MD

Background: Cor triatriatum sinistrum is a rare congenital heart disease that can present with a wide range of symptoms due to its different anatomic variants and possible association with other structural cardiac defects. *Case*: This is the case of an 18 month old child who presented with signs of congestive heart failure which started at 3 months of age. Pertinent physical examination showed acyanotic, irritable, tachypneic, tachycardic, severely wasted and stunted child, oxygen saturation of 96-97% with cardiac findings of adynamic precordium, right ventricular heave, apex beat at the 4th intercostals space left midclavicular line, normal SI, physiologically split S2, loud P2, grade 3/6 pansystolic murmur at the left lower sternal boarder. Chest radiography showed pulmonary arterial congestion, right ventricular prominence and prominent main pulmonary artery segment. Electrocardiogram showed sinus tachycardia, right axis deviation, right ventricular hypertrophy. The 2D echocardiography result was congenital heart disease, cor triatriatum with decompressing vertical vein to the left innominate vein. The diagnosis was established clinically and further confirmed with non-invasive diagnostics like chest x-ray, electrocardiography and echocardiography. Intraoperative findings include left atrium noted to have two chambers, all pulmonary veins draining into the upper chamber, with decompressing vertical vein, no other anomalous structures were noted. The patient underwent repair of the cor triatriatum.
Conclusion: Fully establishing the diagnosis of a rare variant of cor triatriatum sinistrum is possible with non-invasive cardiac imaging modality like transthoracic echocardiography. This valuable diagnostic tool helps to optimise the management of this congenital heart disease whose rarity may frequently lead to misdiagnosis, but when adequately evaluated and treated the clinical outcome is excellent. ***Phil Heart Center J 2016;21(2):95-101.***

Key Words: Cor Triatriatum ■ Congenital Heart Disease ■ Congestive Heart Failure

Cor triatriatum is a rare congenital cardiac anomaly which comprises of 0.1-0.4% of all the patients with congenital heart disease. This anomaly has several anatomic variants that can present with a wide range of symptoms that may lead to improper or late diagnosis.[1]

Due to the rarity of Cor Triatriatum, the number of cases reported in the literature is relatively sparse. Very limited data are available regarding the different anatomic variants of the disease, its residual morbidity following surgical correction and long-term follow up in children.

This report discussed the embryology and anatomical variations of Cor Triatriatum, the approach in the diagnosis and the management and prognosis of the disease. This report emphasized the detailed echocardiography approaches to come up with the diagnosis and detailed anatomic characterization of a rare complex congenital heart disease.

Case

This is a case of an 18 months old, female who was born term with unremarkable birth and neonatal history until she started to have recurrent lower respiratory tract infections at 3 months old. Following routine investigations, patient was diagnosed with bronchial asthma and commenced on bronchodilator and inhaled steroid therapy. The patient then had frequent episodes of lower respiratory tract infections unrelieved by antibiotics. During this

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time, she was noted to have diaphoresis and failure to gain weight. Until at 1 year and 3 months old, an incidental finding of a murmur led to a 2D echocardiography. Result showed congenital heart disease, partial anomalous pulmonary venous connection to superior vena cava (PAPVC to SVC), hence the advice for surgery. However, due to financial constraints, it was not done. A second opinion was sought by the parents and another 2D-echocardiography was done with the same diagnosis as the first. Again, the patient was advised for surgical intervention. During another check-up for cough and fever with another pediatric cardiologist, a 2D echo was done with a diagnosis of congenital heart disease, cor triatriatum, total anomalous pulmonary venous connection to superior vena cava (TAPVC to SVC) versus PAPVC to SVC. The patient was advised cardiac catheterization for hemodynamic studies but due to financial constraints, it was not done. Rather, another 2D echo was requested for it was a cheaper option. The patient was then admitted for surgical intervention.

On physical examination, the patient is acyanotic, irritable, tachypneic, tachycardic, oxygen saturation of 96-97%, severely wasted and stunted, with shallow subcostal retractions, clear breath sounds, with Harrisons groove, adynamic precordium, right ventricular heave, apex beat at the 4th intercostal space left midclavicular line, SI normal, S2 physiologically split, accentuated P2, 3/6 pansystolic murmur at the left lower sternal border with noted hepatomegaly about 3 finger breadths below the subcostal margin.

Chest radiography showed pulmonary arterial congestion, right ventricular prominence, main pulmonary artery segment is slightly prominent (*Fig. 1*). Electrocardiogram showed sinus tachycardia, right axis deviation, right ventricular hypertrophy (*Fig. 2*).

These salient features of increased pulmonary blood flow and right ventricular hypertrophy in acyanotic patients are seen most commonly in cases of Atrial Septal Defect, Partial Anomalous Pulmonary Venous Return and Left to Right shunt with Pulmonary Hypertension. Any or all of the differential diagnoses listed above may represent the patient's condition, thus echocardiography study was requested.

Echocardiographic assessment requires a careful step-by-step analysis of the anatomy from multiple imaging views. Questions with pulmonary venous anomalies start with the subxiphoid views. The subxiphoid view is the best view for the evaluation of pulmonary veins in infants and young children. On color doppler flow mapping, the right upper pulmonary vein is seen to drain to the left atrium. The interatrial septum is intact and there is no color drop out. A membrane is noted to divide the left atrium into 2 chambers (*Fig. 3*). This membrane moves throughout the cardiac cycle. The closest diagnosis for this membrane is cor triatriatum and the differential is a supramitral stenosing ring. The left atrial appendage is seen on the distal side of the membrane and the septum primum is in normal position, thus, establishing the diagnosis of cor triatriatum. In contrast with a supramitral stenosing ring, it is located on the immediate atrial side of the mitral annulus, does not encompass the left atrial appendage, is frequently more immobile and may cause restriction of mitral leaflet excursion due to valvar attachments. In this case, the mitral valve leaflets are freely moving. Next standard view in pediatric echocardiogram is apical. This view easily demonstrates the curvilinear membrane in the mid-portion of the left atrium separating pulmonary venous portion from the true anatomic left atrium. (*Fig. 4*) There is a communicating orifice between these chambers measuring 0.5 cm causing turbulence with maximum gradient of 30 mmHg. During diastole, the membrane moves toward the mitral valve. The mitral valve is also normal-looking and moves normally. All 4 pulmonary veins were seen to connect to the upper chamber of the left atrium. The right atrium and right ventricle are seen enlarged, with the interventricular septum bowing to the left. Again, the left atrial appendage is noted below the membrane, making the diagnosis of cor triatriatum stronger. Because, on the contrary, a supramitral stenosing ring membrane is usually adherent to the mitral valve, moves away from the valve in diastole, and has the left atrial appendage located proximal to the membrane. The mitral valve domes during diastole and has

decreased excursion of the posteromedial leaflet. Another standard view is suprasternal notch, the dilated right superior vena cava is seen to connect to the dilated left innominate vein and a vertical vein is connecting to the latter. On color flow mapping, the vertical vein shows a red color flow, meaning its flow is heading towards the transducer (*Fig. 5*). Its flow then is ascending to join the leftward aspect of the innominate vein. The presence of a vertical vein, dilated superior vena cava and left innominate vein are clues to anomalous pulmonary venous drainage. So, at this point, are we dealing with a case of cor triatriatum plus anomalous venous drainage? Careful inspection should be done to assess the pulmonary venous drainage. At the apical view, the 4 pulmonary veins were seen to drain to the left atrium. However, we need another view to confirm this. Repositioning the transducer to the left infraclavicular area at 3o'clock position, the "crab view" is shown (*Fig. 6*). This view shows 2 left and 2 right pulmonary veins normally draining into the left atrium - the "legs of the crab"; and the right superior vena cava and the left atrial appendage are the "claws". On left parasternal view, the linear echo membrane is noted above the mitral valve in the left atrium. The right ventricle is enlarged with the interventricular septum bulging to the left.

With the following echocardiograhic findings, the present working impression is Congenital Heart Disease - Cor Triatriatum with decompressing vertical vein to the left innominate vein, Pulmonary Arterial Hypertension with Congestive Heart Failure.

The patient underwent repair of the cor triatriatum and patient tolerated the procedure well. Intraoperative findings include the following: left atrium
noted to have two chambers; all pulmonary veins draining into the upper chamber, with decompressing vertical vein no other anomalous structures were noted, excision of left atrial septum done. The patient made an uneventful recovery following surgery and was discharged home on the 7th post-operative day.

DISCUSSION

Cor triatriatum sinistrum is characterized with the division of the left atrial chamber into two parts by a fibromuscular membrane, the proximal posterosuperior venous chamber which receives pulmonary venous connections and the distal anteroinferior left atrium proper which contains LA appendage as well as the atrial septum containing fossa ovalis. These two chambers communicate via a defect in the membrane.[2]

Cor triatriatum accounts for approximately 0.1-0.4% of all congenital heart diseases.[1] In our institution, there are 18 pediatric cases diagnosed with cor triatriatum since 2000. There is an equal frequency in both sexes. This malformation is usually isolated, but it may be associated with other congenital heart diseases in up to 80% of the cases in the pediatric population, most frequently with atrial septal defect and anomalous pulmonary vein return. No genetic linkages was been known to be associated with cor triatriatum. Our patient has no other associated congenital heart disease noted.

Cor triatriatum is considered as one of the pulmonary venous anomalies (*Fig.7*).[1] It is the result of stenosis of the common pulmonary vein (*Fig. 8*).

Because of its great variability in certain details, several classifications of cor triatriatum sinister have been suggested. In Moss and Adams, several classifications of cor triatriatum had been described by different authors. One author classified cor triatriatum according to the presence and size of openings in the intra-atrial membrane. One author described three types of cor triatriatum sinister according to morphology. Another group of authors suggested a more complex classification of subdivided left atrium, considering the kind of connection between the two chambers and associated lesions. The most recent classification was proposed by Lucas and Krabill because of its simplicity with regards to the wide range of complex morphologies. [1]

Our patient on 2D echo showed the type C anatomic variant where the accessory left atrial receives all pulmonary veins and communicates

with the true left atrial chamber through an orifice, plus an indirect communication with the right atrium through anomalous venous connections.

In the usual case, the stenosis occurs late, after collateral venous connections have been lost, or else the severity of the obstruction produced by cor triatriatum is not sufficient to stimulate maintenance of the primitive routes of venous drainage. However, in the case of our patient, the stenosis might occurred early producing severe obstruction to favor persistence of one of the primitive drainage channels such as the levoatriocardinal vein.

A wide spectrum of presentations is encountered in cor triatriatum and are determined by the degree of hemodynamic obstruction and presence or absence of other structural cardiac defects. The time of presentation for cor triatriatum can vary depending on the size of the ostium in the membrane and the presence of coexisting cardiac anomalies.[4] If the ostium is wide enough (>1 cm) to not obstruct incoming pulmonary venous blood flow, cor triatriatum may be only an incidental finding in adulthood. Delayed presentation may also be secondary to chronic flow disturbances that lead to calcification or fibrosis of the opening. If the membrane is moderately restrictive (3 mm to 9 mm), cor triatriatum may present clinically 2 months or later after birth as the pulmonary vascular resistance falls and lung congestion develops. These patients may develop respiratory symptoms, poor pulses, and feeding intolerance. In cases of severe obstruction (<3 mm), cor triatriatum will present during the newborn period and will appear pale and clammy, and the presentation may be similar to that of critical aortic or mitral stenosis.[1] Our patient's hemodynamics is congestive heart failure which started at age 3 months which points out that there is a moderately restrictive opening as evidenced by 2D echo results of 0.5 cm communicating orifice between intraatrial chambers.

Diagnostic modalities utilized in cor triatriatum include chest radiography, electrocardiography, echocardiography and cardiac catheterization. Electrocardiogram in cor traitriatum will show right ventricular hypertrophy, right axis deviation and SIQ3 pattern are found with pulmonary artery hypertension.

The routine chest radiogram reflects pulmonary venous obstruction. Fine, diffuse, reticular pulmonary markings fan out from the pulmonary hilum to involve the lower lung fields. It also reveals enlargement of the main pulmonary artery and right ventricular hypertrophy. However in our patient, it showed more of pulmonary arterial congestion rather than venous congestion because of the presence of the decompressing vertical vein which indirectly connects the left atrium into the right atrium.

Since the 1990s, echocardiography has become the imaging modality of choice for the diagnosis of cor triatriatum. With echocardiography, demonstration of the membrane, determination of any gradient across the membrane and coexisting congenital anomalies can also be well characterized. Series of 2D echocardiography was done in our patient with a diagnosis torn between cor triatriatum and total versus partial anomalous pulmonary venous connection to superior vena cava. The last 2D echocardiography result was congenital heart disease, cor triatriatum with decompressing vertical vein to the left innominate vein; tricuspid regurgitation, mild; pulmonary arterial hypertension. The apical view clearly demonstrates the cor triatriatum membrane, the 4 pulmonary veins draining to the accessory left atrial chamber, membrane orifice with mild obstruction and the true left atrial chamber. The apical and subxiphoid views also show the mitral valve appearance and motion, left atrial appendage which are helpful in differentiating cor triatriatum membrane from supramitral stenosis ring membrane. The dilated superior vena cava is noted in the subxiphoid view giving a hint of an anomalous venous drainage. And in the suprasternal notch view, the presence of the anomalous venous drainage is confirmed by the sight of the vertical vein ascending to the dilated left innominate vein connecting to the dilated superior vena cava. This vertical vein decompresses the pulmonary venous confluence.

A recently published, retrospective review demonstrated that of a total of 28 patients 96%, 27 patients with cor triatiratum underwent trans-

thoracic echocardiography, the correct diagnosis was made preoperatively.[5] Also a study done by Ostman-Smith et al[6] the use of echocardiography is sufficiently accurate in the diagnosis of cor triatriatum and that other invasive diagnostic procedures need not always be performed.

Cardiac catheterization is seldom necessary in the current era except when there is suspicion of irreversible pulmonary vascular disease or the diagnosis is unclear from noninvasive investigations.

The medical treatment in cor tratriatum depends on symptoms. If with signs of pulmonary congestion occur, diuretics, digoxin and preload reduction are the mainstay of medical therapy. On the other hand, surgical treatment is indicated on the following basis: significant intra-atrial flow obstructions, in older patients with chronic symptom and in complex cor triatriatum.[7] Our patient presented with signs of congestive heart failure hence immediate surgical management was warranted. In a study done by Alphonso, et al.[5] it was concluded that surgery offers good early and long-term results for both classic and atypical variants of cor triatriatum.[6]

Successful balloon catheter dilatation of the communication between the two chambers has been reported in few cases.[7]

The immediate post-operative outcomes include early deaths due to the following reasons, patients are already at the critical presentation upon diagnosis, with associated congenital heart diseases and due to misdiagnosis/late diagnosis. The long term surgical outcome is favourable with the reported overall survival above 90% at 5 years, unless the surgery is performed for complex congenital heart diseases.[8] Other long term postoperative outcomes include reversible pulmonary hypertensive changes, residual obstruction in the atrium and restenosis.[5] In the Mayo Clinic 50-year experience of surgical repair of cor triatriatum, they have reported 50 years of operative experience and long-term follow-up of cor triatriatum sinister. Surgical treatment leads to satisfactory early and long-term results. The defect is associated with a number of congenital cardiac abnormalities in a majority of patients.[9]

Clinical presentation and complexity of cardiac anomalies seem to have an adverse effect on survival after repair. The risk of recurrent intraatrial obstruction postoperatively is low in the study.[10] In our institution, we still recommend further researches on presentation, diagnosis and long-term surgical results of pediatric patients diagnosed with cor triatriatum.

The natural history of cor triatriatum without surgical intervention is related to the size of the orifice in the obstructing membrane. In a survey done by Niwayana,[11] the average survival was 3 1/3 months when the opening was <3 mm and 16 years when the opening was >3mm. Also in a study done by Alphonso, et al.[5], the natural history of the disease depends on effective size of hole in the partition between the common pulmonary venous chamber and left atrium. Mostly, the hole is severely restrictive and about 75% die in infancy without treatment. When communicates with right atrium through ASD, the prognosis is better. However, at least one series has reported no decrease in the severity of symptoms in the presence of ASD.[5] Pulmonary hypertension as a result of elevated left sided pressures usually indicates severity of the lesion and worsening pulmonary hypertension is associated with poor prognosis. Our patient made an uneventful recovery following surgery and was discharged home on the 7th postoperative day and at present, the patient is thriving well.

CONCLUSION

This case reports the dilemma encountered in the clinical diagnosis and in the use of a limited diagnostic modality as a confirmatory in the diagnosis of a rare variant of cor triatriatum in children.

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APPENDICES

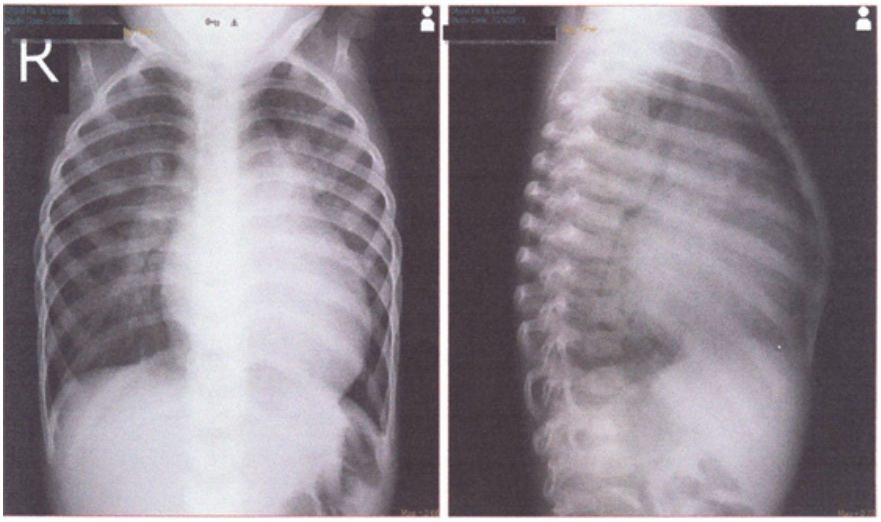

Figure 1. Electrocardiogram showed sinus tachycardia, right axis deviation, right ventricular hypertrophy.

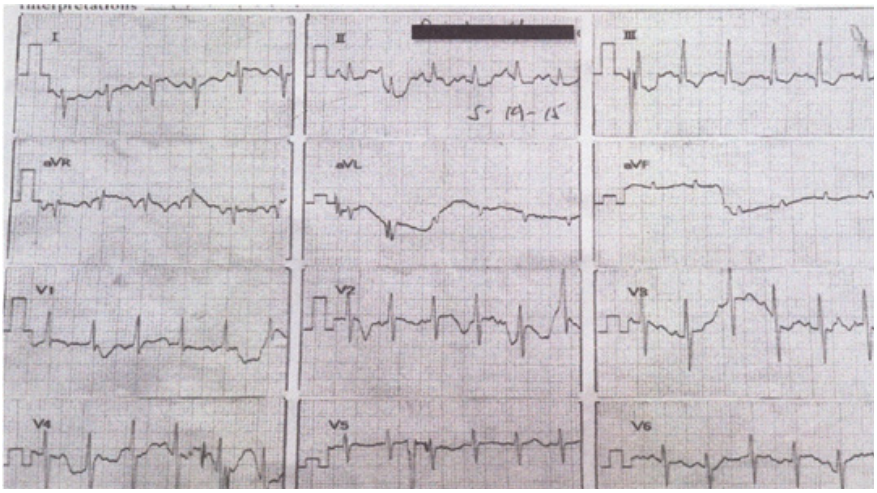

Figure 2. Chest radiography showed pulmonary arterial congestion, right ventricular prominence, main pulmonary artery segment is slightly prominent ventricular hypertrophy

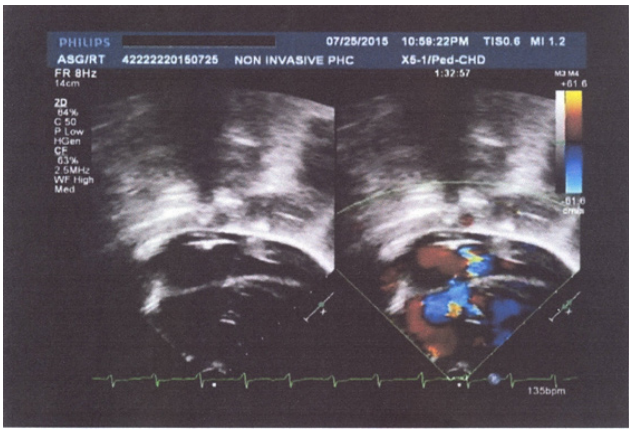

Figure 3. The subxiphoid view is the best view for the evaluation of pulmonary veins in infants and young children. On color doppler flow mapping, the right upper pulmonary vein is seen to drain to the left atrium. The interatrial septum is intact and there is no color drop out. A membrane is noted to divide the left atrium into 2 chambers, deviation, right ventricular hypertrophy

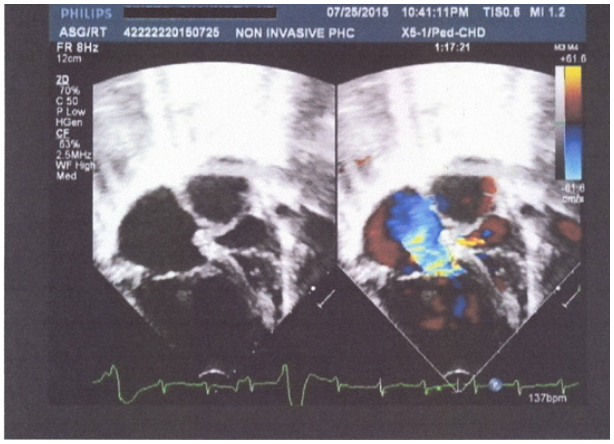

Figure 4. This apical view easily demonstrates the curvilinear membrane in the midportion of the left atrium separating pulmonary venous portion from the true anatomic left atrium. There is a communicating orifice between these chambers measuring 0.5 cm causing turbulence .with maximum gradient of 30 mmHg

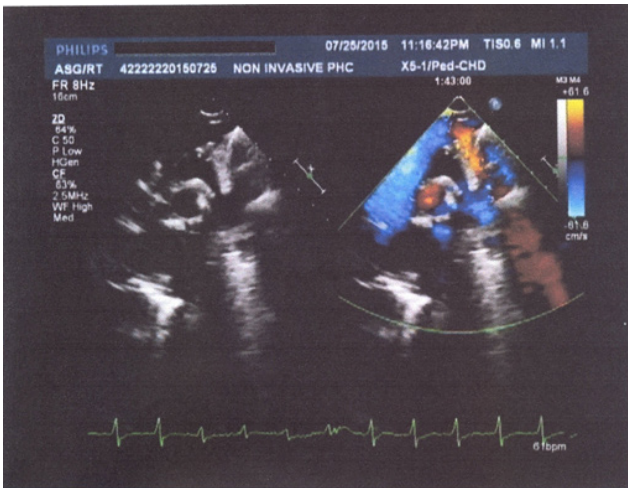

Figure 5. Another standard view is suprasternal notch, the dilated right superior vena cava is seen to connect to the dilated left innominate vein and a vertical vein is connecting to the latter. On color flow mapping, the vertical vein shows a red color flow, meaning its flow is heading towards the transducer (*Fig. 5*). Its flow then is ascending to join the leftward aspect of the innominate vein

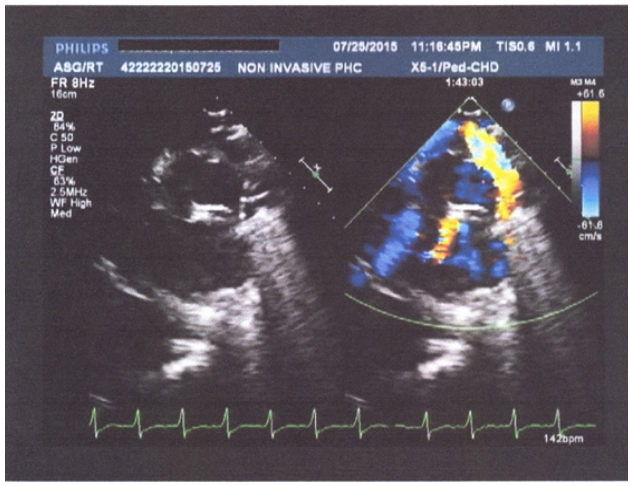

Figure 6. The "crab view". This view shows 2 left and 2 right pulmonary veins normally draining into the left atrium - the "legs of the crab"; and the right superior vena cava and the left atrial appendage are the "claws".

Critically Appraised Topics

Citation: Shaddy RE, Boucek MM, Hsu DT, Boucek RJ, Canter CE, Mahony L et al. Carvedilol for Children and Adolescents with Heart Failure. JAMA. 2008 Sept. 298 (10):1171-1178.

Topic: Treatment for Children with Heart Failure

Reviewer: Suzette M. Perfecto, MD

Case Scenario: An 8-year old boy was brought to the ER due to edema and easy fatigability. He was diagnosed to have Congenital Heart Disease, Tricuspid Valve Atresia, Type 1-A and underwent Balloon atrial septostomy and Modified Blalock Taussig Shunt at 2nd day of life but was lost to follow up since then. After patient's mother demise at 1 year of age, patient was under the care of his aunt. As claimed by the caregiver, patient was apparently well, a Grade 2 average student, until 4 months prior to consult, when patient experienced easy fatigability during Physical Education activities. Bipedal edema was first noted 1 month prior, with gradual progression, now observed up to the scrotal area. Emergency physician diagnosed the patient with heart failure, he was thinking of what oral medications he may give just in case the aunt would not consent for an admission?

Evaluating Directness:

1. **Patients included** - Patients were recruited from 26 centers in the US included which include 161 children and adolescents with symptomatic systolic heart failure.
2. **Interventions compared** - Patients were ran domized into a 1:1:1 ratio to twice dosing with placebo, low dose and high dose Carvedilol. Groups were stratified accor-ding to their systemic ventricle. Low dose Carvedilol was computed at O.2mg/kg/dose for patients below 62.5kilos or 12.5mg per dose if weighed 62.5kg or more. High dose Carvedilol, on the other hand was prepared at O.4mg/kg/dose for patients below 62.5kg or 25 mg/kg/dose if weighed 62.5kg or more.
3. **Outcomes monitored** - Heart failure was the primary outcome measured in this study. Secondary outcomes monitored included echocardiographic measures and plasma b-type natriuretic peptide levels.

Validity Criteria:

A. Were the patients randomly assigned to treatment groups? **Yes**
B. Was allocation concealed? **Yes**
C. Were the baseline characteristic similar at the start of the trial? **Yes**
D. Were patients blinded to treatment assignment? **Yes**
E. Were caregivers blinded to treatment assignment? **Yes**
F Were outcome assessors blinded to treatment assignment? **Yes**
G. Were all patients analyzed in the groups to which they were originally randomized? **Yes**
H. Was follow up adequate? **Yes**

Applicability:

A. Are the study patients similar to the patients in my practice? **Yes**
B. Were all clinically relevant outcomes reported? **Yes**
C. Are the likely treatment benefits worth the harm? **Yes**

Table 1. Primary Endpoint and Prespecified Subgroup Analysis

All Patients	+	_	To - tal	RR	95% CI	P value	ARR	RRR	NNT
Carvedilol	45	58	103	0.98	0.68, 1.42	0.937	10%	2%	1000
Placebo	24	30							
Dilated CMP									
Carvedilol	19	41	60	0.70	0.41, 1.18	0.273	138%	30%	72
Placebo	15	18	33						
CHD with systemic LV									
Carvedilol	9	8	17	0.79	0.39, 1.63	0.660	138%	30%	72
Placebo	4	2	6						
CHD without Systemic LV									
Carvedilol	17	9	26	1.96	0.91, 4.23	0.097	321%	96%	31
Placebo	5	10	15						
Systemic LV									
Carvedilol	28	49	79	0.75	0.48, 1.16	0.280	123%	25%	81
Placebo	19	20	39						

Author's Conclusion:

The author's preliminary report concluded that Carvedilol does not significantly improve heart failure in children and adolescents with symptomatic systolic heart failure, although there may be a differential effect of Carvedilol based on ventricular morphology.

Reviewer's Conclusion:

In concurrence with the author's conclusion, the reviewer concluded that Carvedilol did not significantly improve patients' heart failure states compared to the placebo group with all p values above 0.05.

Citation: Deedwania PC, Gottlieb S, Ghali JK, Waagstein F, Wikstrand JC; MERIT-HF Study Group. Efficacy, safety and tolerability of beta-adrenergic blockade with metoprolol CR/XL in elderly patients with heart failure. Eur Heart J. 2004 Aug;25(15):1300-9.

Reviewer: Thad S. Ciocson, MD

Case Scenario: Your 70-year-old uncle has been diagnosed with chronic heart failure. He is maintained on diuretics and ACE-inhibitor in optimal dosage. Despite this, he still complains of easy fatigability and shortness of breath. His blood pressure is 130/70 and cardiac rate of 72/min. He heard from another patient of the benefit of beta-blockers like metoprolol on such patients. He then asks for your recommendation.

Evaluating Directness:

1. **Patients included** - heart failure patients who are elderly.
2. **Interventions compared** - to evaluate the benefit of beta-blockers in addition to optimally managed patients of standard therapy (e.g. ACEI, digitalis, diuretics)
3. **Outcomes monitored** - total mortality and the combined end point of all cause death and hospitalization.

Validity Criteria:

A. Were patients randomly assigned? **YES**

B. Was allocation concealed? **YES**

C. Were the baseline characteristic similar at the start of the trial? **Yes**

D. Were patients blinded to treatment assignment? **Yes**

E. Were caregivers blinded to treatment assignment? **Yes**

F. Were outcome assessors blinded to treatment assignment? **Yes**

G. Were all patients analyzed in the groups to which they were originally randomized? **Yes**

H. Was follow up adequate? **Yes**

The MERIT HF is by far the largest prospective placebo-controlled double blind trial (n= 3991 patients) that investigated the role of b-blockers added to standard therapy (ACEI, ARB, digitalis and diuretics) in congestive heart failure patients. A sub-study that was pre-specified is the focus of this analysis; investigating the use of β blockers in 1982 elderly patients, defined as age >65. The mean age of the population was 72 years, 75% of whom were males. Mostly were in NYHA III (60%) and 11 (35%) with a mean LVEFmeasured 28% (20-36%). Compared to the non-elderly population, they were also less likely to be on ACEI (91% v 87%). Diuretics were used in 90% of all patients, lanoxin in 65%, ASA in 45% and statins in 25%. (*Table 1*). The study drug metoprolol CR/XL was started at 25 mg OD and 12.5 mg OD for patients in NYHA 11 and III/IV, respectively. The dose was then doubled every 2 weeks until tolerable or a total dose of 200 mg was achieved. The mean follow up was 12 months.

Primary endpoints:

1. total mortality and
2. all-cause mortality and hospitalization.

Pre-specified secondary endpoints:

1. cardiac death or non-fatal MI,
2. death from heart failure,
3. sudden death,
4. total hospitalization due to cardiovascular causes,
5. hospitalization for worsening heart failure,
6. withdrawal of the drug for any cause

The mean follow-up duration was 12 months.
No patient was lost on follow-up. Mean daily dose of metoprolol was 146 mg.

The addition of metoprolol to standard therapy resulted in a 35% reduction in all-cause death (primary endpoint total mortality). The combined endpoint of total mortality and all cause hospitalization was reduced by 15%. 8 events were prevented for every hundred patients treated. Again, only 21 patients needed to be treated to prevent an outcome. With regards to the pre-specified secondary endpoints, cardiac death/non fatal MI and sudden death were both reduced by 40% while death from CHF progression was reduced by a significant 60%.

There was a significant 20% reduction in all cardiovascular related admissions. A reduction by 36% was noted in worsening CHFadmissions. Approximately 18% of patients in the study group and 20% in the placebo group (1 out of 6) stopped taking the drug with the most common reasons: worsening heart failure, hypotension, bradycardia and dizziness. There was no statistically significant difference between groups.

Assessing Applicability:

1. Are there issues that may affect the result? - **NO**
2. Are there factors affecting applicability of the result - **YES**

The hesitation of clinicians cardiologists regarding the risk of starting beta blockers in the elderly CHFpatient.

OUTCOME (12 MONTHS)	Placebo (n=992)	Metoprolol (n=990)	P	RRR 95% CI	ARR 95% CI	RR 95% CI	NNT 95% CI
Total Mortality	13.5% (134)	8.8% (88)	0.008	35% (14-55)	4.7% (1.9-7.5)	0.65	21 (13-52)
Total Mortality or all -cause hospitalization	57% (428)	48.6% (376)	0.05	14.7% (1-21)	8.4% (0.5-9.1)	0.85	21 (11-206)
Cardiac death or non fatal MI	13.8% (138)	8.5% (82)	0.0001	40% (20-60)	5.5% (2.8-8.2)	0.61	18 (12-36)
Death from worsening CHF	4.7% (45)	1.8% (18)	0.005	60% (26-94)	2.7% (1.2-4.2)	0.38	37 (24-86)
Sudden death	7.6% (72)	4.3% (42)	0.0032	42% (14-70)	3.1% (1.1-5.1)	0.56	32 (19-95)
Hospitalization for CV cause	42.8% (425)	33.6% (333)	0.015	21% (12-31)	9.2% (4.9-14.5)	0.78	11 (7-20)
Hospitalization for worsening CHF	25.4% (252)	16.3% (161)	0.0009	36% (22-50)	9.1% (5.5-12.7)	0.64	11 (8-18)
Withdrawal of study drug	20.3% (199)	17.8% (176)	0.2*	11%*	2.3%*		

Reviewers Conclusion:

While clinicians are still hesitant to use beta-blockers in elederly CHF patient, this study can assure us that beta-blockers are safe, effective and can be tolerated amongst these sub-set of patients. This is reflective on the significantly higher risk reduction compared to <65 year old patients. There is need however for careful dosage titration on patients who have more severe CHF.