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Prevalence of Atrial Fibrillation in Systolic Heart Failure, Pulsed and Tissue Doppler Echocardiographic Abnormalities

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ABSTRACT

Background: Heart failure (HF) is a common clinical syndrome mostly due to the impaired ability of the Left Ventricle (LV) to eject blood with reduced cardiac output. Heart failure is called systolic (SHF) if left ventricle ejection fraction on echo-cardiogram is low (LVEF of ≤50%). **Aim:** To assess the echocardiographic characteristics of patients with SHF with Atrial Fibrillation (AF) and compare with those with Sinus Rhythm (SR) on 12 leads ECG. Furthermore, to evaluate the clinical and biochemical markers for the prediction of AF in SHF. **Method:** Over two years duration, each patient diagnosed with SHF was enrolled in the study (n = 354) based on admission code. AF or sinus rhythm on 12 leads ECG was documented on each patient. Multiple logistic regression analysis was applied to assess the risk ratio of different clinical and Doppler derived variables for the development of AF in SHF. **Results:** Out of the total hospital medical admissions of 14,674 patients, there were 354 patients with diagnosis of SHF, a prevalence of 2.4%. The incidence of AF on ECG was 109 (31%) patients in the whole study population and 245 (69%) in SR. M Mode echocardiogram in patients with SHF and AF compared with those in SR showed significant dilation of LV cavity in systole with LVESD of 5.72 ± 0.63 vs. 5.23 ± 0.76 cm, $P < 0.001$ and in Diastole LVEDD of 6.83 ± 0.51 vs. 6.58 ± 0.63 cm, $P < 0.001$. Pulsed Doppler echocardiogram showed a severe restrictive-pattern with shorter Decellration Time (DT) of 163.73 ± 7.42 vs. 214.9 ± 31.81msec, $P < 0.001$ and higher Pulse to Tissue Doppler ratio of E/Em of 14.26 ± 1.34 vs. 9.99 ± 1.27, $P < 0.001$, and the serum level of Brain Natriuretic Peptide (BNP) hormone of 723.72 ± 13.45 vs. 686.98 ± 72.57 pg/ml, $P < 0.001$. The predictive risks (odd ratio) of different clinical variables for the development of AF in SHF were positive for high BNP > 500 pg/ml of 2.8, history of hypertension of 1.8, history of DM of 1.7, BMI > 28 of 1.4, LV hypertrophy on ECG of 1.3. **Conclusions:** The prevalence of Systolic Heart Failure in the study population was 2.4%. The prevalence of AF in the study population was 31%. The best predictors of AF in SHF were high BNP > 500 pg/ml, history of hypertension, Diabete Mellitus and LV Hypertrophy on ECG.

Keywords: Systolic Heart Failure; Pulse Doppler; Tissue Doppler; Prevalence

1. Introduction

Heart failure (HF) is a common clinical syndrome representing the end-stage of a number of different cardiac diseases [1]. It can result in any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood [2]. There are two mechanisms by which reduced cardiac output and HF occur: Systolic Heart Failure (SHF) with low left ventricle ejection fraction on echocardiogram (LVEF of ≤50%) and diastolic heart failure (DHF) with normal LVEF of >50% [3].

SHF has been classified as very mild, mild, moderate or severe based on echocardiographic derived LVEF% where very mild LVEF% is (<43% - ≥50%), mild (LVEF of <33% - ≥43%), moderate (<23% - ≥33%) and severe with LVEF (<22%) [4]. Systolic Heart Failure has been recognized previously as a risk factor for the development of Atrial Fibrillation (AF) [5]. The overall prevalence of new onset of AF in hospitalized patients with

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SHF is in the range of 8% - 36% [6]. It has been observed that the incidence of AF is proportional to the severity of HF where a higher incidence occurs in severe SHF [7].

Previous reports showed a deleterious impact of AF on top of SHF with poor clinical outcomes in terms of mortality and hospitalization [8,9]. Randomized pathophysiologic studies showed important differences between patients presented with SHF as compared with those of DHF as it seems that the two conditions represent two distinct syndromes rather than a continuous spectrum of one disorder [10,11].

Earlier reports showed the high sensitivity of brain natriuretic peptide (BNP) as a biomarker of detecting a symptomatic SHF with low LVEF on echo of <50% [12]. Further, a serum level of BNP was shown to have prognostic implications in patients with SHF [13]. At present, the relationship between SHF and the development of AF in non white population is not clear.

In this study, firstly, we assess the incidence of AF in patients with SHF; secondly, evaluate the clinical characteristics, causative agents and echocardiographic abnormalities in this group of patients and thirdly, correlate the serum level of BNP with the degree of LVEF% reduction on echo.

2. Material and Methods

Out of the 14,674 patients admitted to the Salmaniya Medical Complex (SMC) in the medical department with acute medical problems. There were 354 patients diagnosed of systolic heart failure. SMC is a governmental hospital with a catchment area of 900,000 populations. All patients' data of clinical history, physical examination, and laboratory results were obtained. The results of echocardiogram and 12 leads electrocardiogram were available for all patients on admission or during hospital stay. The clinical and biochemical data were extracted from patient's files. The study duration for medical admission was of two years, spanning from 1 January 2010 - 31 December 2011. A constitutional ethical committee approval was obtained prior to the data extraction and analysis.

The history of SHF class was obtained based on New York Heart Associations (NYHA) functional classification [14]. The clinical findings on examination of third sound gallop, pulmonary crackles, and raised jugular venous pressure, hepatomegaly and ankle edema were all recorded. Height and weight, goiter, murmur suggestive of aortic or mitral or pulmonary valve disease were all recorded. Demographic data for previous attacks of heart failure, hypertension and diabetes mellitus (DM) prior to admission were all recorded. History of smoking and previous history for the development of AF were extracted from the patients' files. Twelve leads ECG was analyzed for voltage criteria of left ventricle hypertrophy using Perugia score [15].

Atrial fibrillation was defined as absence of P wave on 12 leads electrocardiogram (ECG), with irregular ventricular rhythm that lasting for >30 seconds [16]. The presence of Q wave and conduction abnormality with ST segment elevation or depression or T wave changes were all recorded. Echocardiographic data of the M mode, 2-D echo, Pulsed and Tissue Doppler were all tabulated regarding the M mode of LV cavity dimensions and LV wall thickness. The calculated LV mass index, indices of left ventricle diastolic fillings such as deceleration time (DT) in msec, E wave velocity in early diastole in cm/sand the ratio of early diastolic pulsed to Tissue Doppler wave (E/Em) were recorded [17].

Based on LVEF% using two dimension echo formula [18], patients were defined as those SHF with reduced (LVREF%) of ≤50% and DHF with preserved (LVPEF%). Further,those SHF patients were subgrouped as very mild SHF (LVREF% <43 - ≥50%), mild (LVREF of <33 - ≥43%), moderate (<23 - ≥33%) and severe (<22%) [19,20].

The diastolic dysfunction of LV was regarded as severe if deceleration time (DT) of E wave was <160 msec and the early E Pulsed wave to Tissue Doppler wave (E/Em ratio) was >12 [21]. The estimated LV mass index on echo of >131 g/m2 for men and >113 g/m^2 for women was defined as cut off points for severe LVH [22].

The results of available serum level of brain natriuretic peptide (BNP), uric acid, estimated glomerular filtration rate (eGFR) and serum potassium were tabulated.

3. Statistical Analysis

The data were analyzed using the statistical package of social sciences (SPSS) version 20. All data were presented as mean ± SD. Student's t-test was used to test the differences between the mean variables of M mode for septal wall thickness, LV cavity and LV mass index in the two groups of heart failure and Chi-square analysis was used to test the differences between proportions of categorical variables.

Multiple logistic regression analysis was applied to calculate the odds ratio for different clinical and biochemical variables for the development of AF in patients with SHF. All reported p-values are two tailed and p-value was regarded as significant at level of <0.05.

4. Results

Three hundred and fifty four patients with clinical diagnosis of systolic heart failure were enrolled. There were 354 defined as SHF with LVEF <50% on echocardiogram. Among the 354 patients with SHF, 12 leads ECG showed AF in 109 (31%) patients and 245(69%) were in

sinus rhythm (SR).

The mean age of patients in the study was 60.47 ± 11.43 years. There were 191 (54.0%) female patients. There were 30 (8.5%) patients with history of hypertension, 60 (16.9%) with history of smoking, BMI was >28 in 35(9.9%), history of hyperlipidemia was in 53 (15.0%), patients, DM in 56 (15.8%) and history of myocardial ischemia in 40% (11.2%).

5. ECG

In the whole study, there were 109 (31%) who had AF on admission and sinus rhythm was seen in 245 (69%).

Among those who had AF (n = 109) on 12 leads ECG there were 34 (31%) patients with no history or documents of previous AF and they were regarded as new onset of AF, 26 (24%) patients had history of persistent AF and 49 (45%) patients had history of recurrent or paroxysmal AF.

Patients with left ventricle hypertrophy based on ECG criteria were 73 out of 354 (20.6%). Among those with LVH there were (25.5%) patients with AF and (74.5%) were in sinus rhythm. The overall sensitivity and specificity of ECG for detection of LVH compared with LV mass index derived by echo as gold standard was 79% and 63% respectively.

6. Clinical Findings

There were 141 (40%) patients with left ventricle failure manifested with pulmonary odema, 123 (35%) patients had both left ventricular and right ventricular failure (biventricular) and 88 (25%) had right sided heart failure.

The history of functional (NYHA) class on admission was as follow: 70 (20%) patients had functional class IV, 130 (37%) had class III, 152 (43%) patients had functional class II and none had class I.

7. Medication Prior to Admission

There were 336 (94.9%) patients using angiotensin-converting enzyme blocker (ACE) medication, 239 (67.5%) were on diuretics, 127 (35.9%) on beta blocker, and 56 (16.9%) were on digoxin medication.

8. Systolic Heart Failure and Patient's Age

Figure 1 shows the age distribution in patients with SHF. There were 95 (26.8) patients in the young age category of <50 years, 114 (40.6%), in age category of between 50 - 65 year and 115 (32.4%) patients in age category of >65 year.

9. Echocardiographic and Biochemical Variables

Table 1 shows biochemical, M mode, pulsed and tissue Doppler echocardiogram results in patients with SHF.

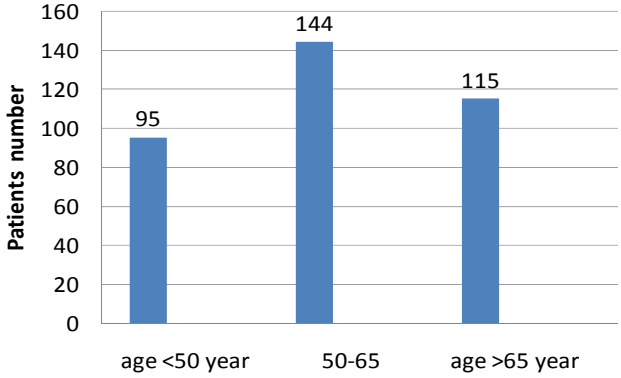

Figure 1. Distribution of patients according to age in patient with systolic heart failure, n = 354.

Table 1. The mean value standard deviation (SD) of Biochemical markers and echocardiographic indices in all patients presented with SHF, N = 354.

ECG	AF N = 109	SR N = 245	P value
IVS cm	0.98 ± 0.22	0.97 ± 0.94	0.083
PW cm	0.89 ± 0.12	0.88 ± 0.12	0.071
ESD cm	5.72 ± 0.63	5.23 ± 0.76	0.001
EDD cm	6.83 ± 0.51	6.58 ± 0.63	0.001
LV Mass Index	111.58 ± 2.81	112.20 ± 3.05	0.063
DT msc	163.73 ± 7.42	214.90 ± 31.81	0.001
E/Em ratio	14.26 ± 1.34	9.99 ± 1.27	0.001
BNP in (pg/ml)	723.72 ± 13.45	686.98 ± 72.57	0.001
Uric acid (mmol/L)	472.25 ± 34.14	397.62 ± 92.08	0.001
eGFR	56.21 ± 12.59	76.65 ± 10.57	0.001
Potassium (mmol/L)	3.43 ± 0.27	3.78 ± 0.24	0.001

Abbreviations: SHF: Systolic heart failure; IVS Interventricular septum; PW: posterior wall; ESD: end systolic Dimension; EDD: end diastolic dimension; DT: Deceleration time; eGFR: estimated glomerular filtration rate; AF: Atrial fibrillation; SR: Sinus rhythm; E/Em: ratio of E velocity to Tissue Doppler velocity of septum; BNP: Brain Natriuretic Peptide.

In patients with SHF and AF compared with SR on 12 leads ECG. Echocardiographic M mode measurement showed no significant difference in LV wall thickness or LV mass index of P = 0.083 and P = 0.063 respectively. However LV cavity showed significant dilation in both systole and diastole. Pulse and tissue Doppler showed significantly shorter DT of E wave of 163.7 ± 7.4 vs. 214.9 ± 31 msec, P < 0.001, higher E/Em ratio of 14.26 ± 1.34 vs. 9.99.1 ± 1.27, P < 0.05.

10. Biochemical Markers

In SHF patients with AF compared with those in SR, there was significantly higher level of uric acid, BNP level but a lower eGFR and low serum potassium. Furthermore, Two D segmental wall motion abnormallities suggesting ischemia were detected in 38 (11.9%) in pa-

tients with AF patients versus 22 (6.7%) in those with SR.

11. Etiological Diagnosis

In patients with SHF (n = 354) there were 113 (31.9%) patients with dilated cardiomyopathy with global hypokinesia, 31 (8.7%) had hypertension heart failure, 74 (20.9%) had ischemic heart disease with old myocardial infarction in 36(10.1%) patients, 67 (18.9%) had significant valve disease with 28(7.9%) of severe mitral valve regurgitation and 18(5.0%) had severe aortic regurgitation, 17 (4.8%) patients had thyroid disease and 35 (9.9%) were of unknown etiology.

12. The Odds Ratio for Risk of AF in SHF Patients

Table 2 shows the hazard ratio of clinical and biochemical variables in the study for the developing of AF in patients with SHF. After adjusting for age and sex multiple logistic regression analysis showed positive predictive value for: history of hypertension of 1.8, history of DM of 1.7, for BMI >28 of 1.4, LVH on ECG of 2.4.

The positive predictors biomarker were hyperuricemia >420 mmol/l of 2.1 higher BNP >500 pg/ml of 2.8 and low estimated glomerular filtration rate (eGFR) <50 of 2.1, LVH of 1.3 and hypokalemia of <3.4 mmol/l of 1.2.

13. Discussion

Patients with heart failure in this study were evaluated with echocardiogram and ECG for the development of AF. Patients who had systolic heart failure on echo had reduced EF ≤50%. SHF patients had high female distribution and mostly age of between 50 - 65 years. This finding is in keeping with previous report, where 49% of patients with systolic heart failure were below the age of 70 year [10].

The overall prevalence of systolic heart failure in the study in two years was 2.4%. This was lower than other studies with prevalence of 4.1% and 4.2 respectively [23,24]. The prevalence in of SHF was 2.4% is similar to one study by Mureddu GF *et al.* [25].

Table 2. The hazard ratio for the development of AF in patients presented with systolic heart failure using multiple logistic regression analysis in patients presented with systolic heart failure, n = 354.

Variable	Odds ratio	95% Confidence interval	P value
History of hypertension	1.8	(1.2 - 2.4)	0.036
History of DM	1.7	(1.2 - 2.2)	0.037
BMI > 28	1.4	(0.9 - 1.9)	0.028
LV hypertrophy on ECG	1.3	(1.0 - 1.6)	0.021
K < 3.4 mmol/L	1.2	(0.9 - 1.5)	0.043
Uric acid > 420 mmol/L	2.1	(1.7 - 2.4)	0.021
eGFR < 50	2.1	(1.5 - 2.8)	0.013
BNP > 500 pg/ml = pg/L	2.8	(2.1 - 3.5)	0.001

Abbreviations: BNP: Brain Natriuretic Peptide; eGFR: estimated Glomerular Filtration Rate; K: Potassium; BMS: Body Mass Index.

The rate of occurrence of AF patients with HF in whole the study was of 31% which was higher than previous report found in occurrence of 25% [26].

In different clinical trials, the use of different diagnostic criteria and different age groups leads to variation of prevalence of HF. In one study by Grewal J, *et al*., the prevalence of HF was 1.9% [27] and in another study by Phillips SJ *et al.*, [28] as the prevalence of HF was of 1.7%. In both studies the prevalence was lower compared with this study although the prevalence was increasing as the patient's age increased.

In this study the percentage of female gender was high in SHF. In previous studies female gender in SHF accounting to 25% - 35% of systolic heart failure [29]. In another report male gender had doubled the risk of developing blood-pumping problems (SHF) compared with female [30].

The age distribution in SHF showed increment in the rate of SHF mostly between 50 and 65 year. In one study the estimated prevalence of systolic dysfunction among patients was different where 15%, were at ages <50 year, 33% at age of 50 - 70 year, and 50% > 70 years, [31]. In one report, a higher incidence of SHF was observed in patients aged <65 years due to ischemia and hypertension [32].

The level of BNP was significantly higher in SHF with AF. This finding had been shown previously, where BNP was significantly high in dilated SHF [27]. In one report higher level of BNP >100 pg/ml was shown as an independent predictor of adverse cardiovascular outcome in patients with DHF [33].

The serum level of potassium in AF patients in patients with SHF was lower than those with Sinus rhythm. Previous studies showed the incidence of AF compared with SR is inversely related with level of serum Potassium [34].

In this study a higher rate of segmental wall motion abnormality on echo was detected in patients with AF. The causative agents of SHF were mainly idiopathic dilated myopathy followed by valvular heart disease. In one report by Topol *et al*., hypertension and ischemia were the main etiology of DHF [35].

Patients in SHF with dilation of LV on echo, tachycardia-mediated cardiomyopathy were presumed to be the causative agent in 29% of patients with HF however. In this subset of patients improvement of LV function is expected to improve as patient revert to sinus rhythm [36, 37].

14. Conclusion

The prevalence of SHF was 2.4% in the study population,

with the incidence of AF being 31% in the whole study. The best predictors of AF in HF were high BNP >500 pg/ml, left ventricle hypertrophy on ECG followed by history of hypertension and DM.

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