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Original Article

CHARACTERISTICS AND MANAGEMENT OF HEART FAILURE: A RETROSPECTIVE SINGLE CENTER STUDY IN CAMBODIA.

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ABSTRACT

Objective: *The goal of this study is to describe characteristics, clinical features, evaluation and treatment of patients with heart failure (HF) admitted to one public hospital in Phnom Penh, Cambodia.*
Method: *This retrospective study included all patients age ≥ 18 years who were admitted with the diagnosis of HF to the Intensive Care Unit of Preah Ket Mealea Hospital in Phnom Penh from 1st January 2017 to 31st December 2018. Out of 140 cases, 20 were excluded because they did not meet the inclusion criteria. Characteristics, evaluation, and treatment of the 120 remaining patients were analyzed.*
Results: *HF with reduced Ejection Fraction (HFrEF) was present in 15%, with mid-range EF (HFmrEF) in 13.3%, and preserved EF (HFpEF) in 71.7% of patients. Hypertension was more prevalent in HFpEF (89.5%, P <0.001). Diabetes was more common in HFpEF and HFmrEF (52.3% and 43.7%, P = 0.316). Coronary artery disease was more prevalent in HFrEF (72.2%, P = 0.015). Global wall hypokinesia was more common in HFrEF group (72.2%, P <0.001). Only 44% of patients with HFrEF who were given guideline-recommended HF drugs (ACEi/ARB, beta blockers or aldosterone antagonist). This was much lower than those with HFmrEF and HFpEF.*
Conclusions: *HFpEF was the most common types of HF in this population, and was associated with hypertension and diabetes. HFrEF was least common and was associated with CAD. Prevention and treatment of hypertension and diabetes is essential to reduce the incidence of HFpEF while greater use of guideline recommended drugs is needed in HFrEF.*

Keywords: *Heart failure, Cambodia, Left ventricular wall motion.*

1. INTRODUCTION:

An estimated 37.7 million people worldwide have heart failure (HF) [1]. HF is a clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood due to a variety of etiologies [2]. The estimates of HF prevalence in Western countries generally range from 1%–2% of the adult population [3]. The prevalence of HF in 8 countries in Asia (Hong Kong, Indonesia, Malaysia, Philippines, Singapore, South Korea, Taiwan, and Vietnam) has been estimated to be between 1%–3%) and is generally similar to values reported for Europe [4]. The prevalence in China is 0.9% [5]. The prevalence is higher in men than in women, but Asian HF patients are slightly younger than their European and American counterparts, reflecting the generally younger demographic of these countries [4].

HF is associated with a wide spectrum of LV functional abnormalities ranging from patients with normal LV size and preserved ejection fraction (EF) to those with severe dilatation and markedly reduced EF [6]. EF is important in the classification of patients with HF because of differing patient demographics, comorbid conditions, prognosis, and response to therapies [6]. Based on the 2016 Heart Failure Guidelines of the European Society of Cardiology (ESC), HF classified into 3 groups: 1). HF with reduced ejection fraction (HFrEF with EF <40%), 2). HF with mid-range EF (HFmrEF with EF 40%–49%), and 3). HF with preserved EF (HFpEF with EF ≥50%) [7]. The data from the Atherosclerosis Risk in Communities (ARIC) study show that in the United States, HFpEF is by far the dominant form of HF among older adults, representing 65%–75% of cases [8]. In HFrEF, men outnumber women, largely owing to the greater burden of coronary artery disease, while HFpEF is fairly similar in both men and women [9–13].

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The most common etiologies of cardiovascular disease (CVD) in Cambodia included heart failure (52.9%), angina pectoris (11.6%), and acute myocardial infarction (4.11%) [14]. There is, however, a lack of data about the prevalence and types of HF present in these patients. The objective of this study is to describe the characteristics, investigation and treatment of patients with HF admitted to the Intensive Care Unit (ICU) of one referral hospital in Phnom Penh.

2. MATERIALS AND METHODS

2.1 Study population

This retrospective study evaluated patients admitted to the ICU of Preah Ket Mealea Hospital with the diagnosis of heart failure during the 2-year period between January 01, 2017 to December 31, 2018. Entrance criteria included 1) age ≥ 18 years; 2) symptoms and physical signs consistent with HF; 3) performance during the hospitalization of a two-dimensional echocardiogram for evaluation of ejection fraction and structural abnormalities of the heart, and; 4) electrocardiogram.

Patients were categorized as one of the 3 types of HF per ESC guidelines [7]. Variable for patient characteristics included age (years), gender (female/male), pulse (bpm), systolic blood pressure (mmHg), diastolic BP (mmHg), atrial fibrillation on ECG, left ventricular ejection fraction (LVEF) by echocardiogram, two-dimensional echocardiographic characteristics (LV wall motion abnormalities, left ventricular hypertrophy, others), serum creatinine, lipid profile (total cholesterol, HDL, LDL). The etiologies of HF were determined from the medical history of documented hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), or valvular heart disease. 2D-echocardiograms were used to determine regional wall abnormalities (global and segmental). Medications prescribed at the time of discharge were recorded.

2.2 Statistics

The characteristics, evaluation, and treatment of the three types of HF patients were compared using a Chi-square test. Continuous variables are shown in mean±SD and analyzed using an independent t – test. A probability of type I error of <0.05 was considered significant. Data entry was conducted using Microsoft Excel, and data analyses were performed by using IBM SPSS Version 23.0 (SPSS Inc.) software program.

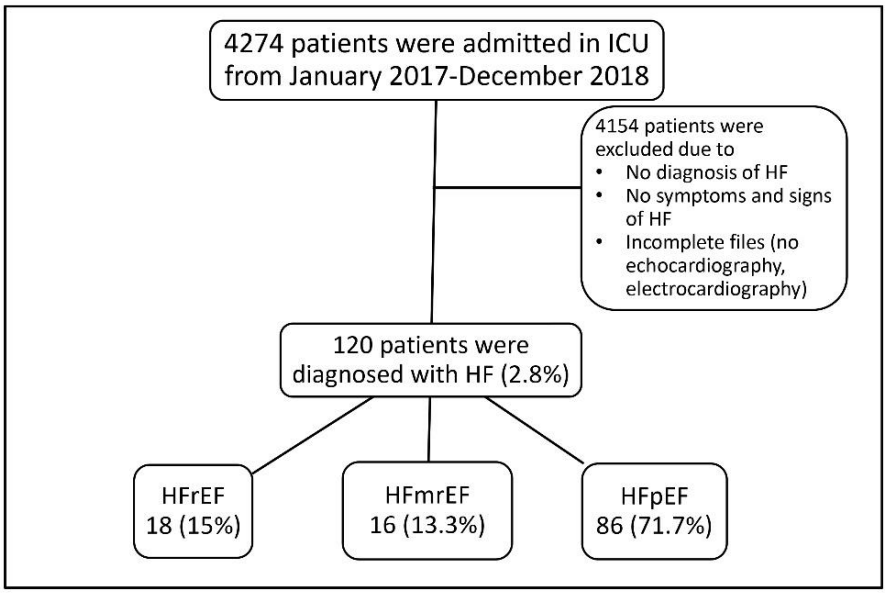

FIGURE 1: Patient inclusion flow chart of heart failure in ICU-PKMH. HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with persevered ejection fraction; LVWM, left ventricular wall motion; ICU, intensive care unit.

3. RESULTS

There were 140 cases of HF among 4274 patients admitted to the ICU (figure 1). Twenty of these patients were excluded because no two-dimensional echocardiography or electrocardiogram records were available. Thus, 120 cases met the inclusion criteria. The prevalence of HF among all admissions in ICU was 2.8% (figure 1). HFrEF was present in 15%, HFmrEF in 13.3%, and HFpEF in 71.6% of patients. Table 1 shows the characteristics of the HF subtypes. Over 50% of the patients were male. There was no significant difference in age between the 3 types of HF.

The HF patients presented with hypertension (79.2%), diabetes mellitus (48.3%), coronary artery disease (45.8%), mitral regurgitation (43.3%) and/or atrial fibrillation (15.8%). The etiologies of HF were markedly different between the types of HF. Hypertension and LV hypertrophy were

significantly more common in HFpEF (Table 1) while diabetes was more common in HFpEF, it did not reach statistical significance. In contrast, CAD was significantly more common in the HFrEF group (Table 1).

3.1 Echocardiographic evaluation

By definition, the mean LVEF was significantly reduced in patients with HFrEF. Figure 2 shows that global left ventricular wall motion abnormalities (LV WMA) were significantly more common in patients with HFrEF. In contrast, the borderline reduction in EF in the HFmrEF group was due to mild segmental hyperkinesia (Figure 2).

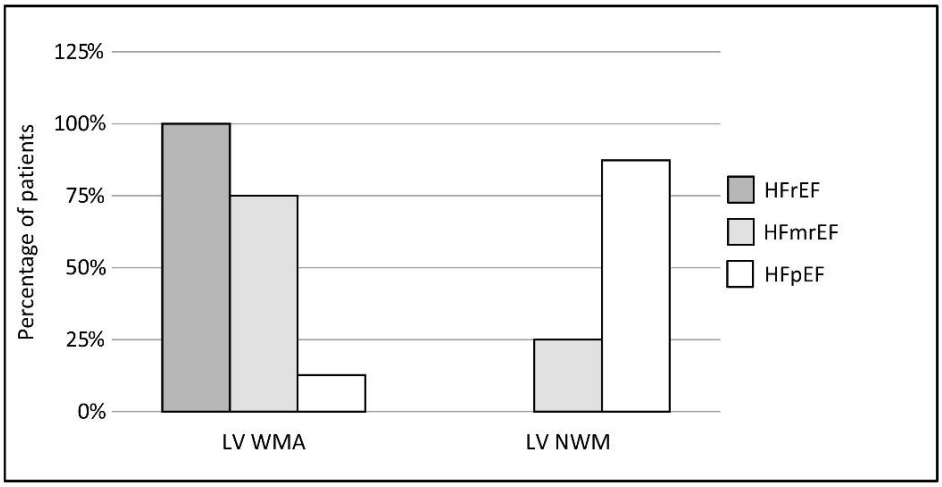

FIGURE 2: Proportion of Patients with Heart Failure subtypes and Left Ventricular Wall Motion by Echocardiography. HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; LV, left ventricular; WMA, wall motion abnormalities; NWM, normal wall motion.

Table No. 1: Characteristics of patients with heart failure by study group of ejection fraction

Clinical characteristics	Total (*n* = 120)	HFrEF (*n* = 18)	HFmrEF (*n* = 16)	HFpEF (*n* = 86)	*p* value
Age (years)	58.8 ± 15.2	57.2 ± 16.3	57.3 ± 16.3	61.8 ± 12.9	0.274
Women, *n* (%)	57 (47.5)	10 (55.5)	4 (25.0)	43 (50.0)	0.14
Men, *n* (%)	63 (52.5)	8 (44.4)	12 (75.0)	43 (50.0)	0.14
Heart rate (beats/min)	93.8 ± 20.0	99.7 ± 21.9	94.1 ± 20.1	87.6 ± 18.2	0.03
Systolic BP (mm Hg)	136.9 ± 31.9	118.5 ± 31.7	146 ± 31.2	146.3 ± 32.7	0.005
Diastolic BP (mm Hg)	81.7 ± 19.2	76.8 ± 21.4	82.8 ± 20.1	85.4 ± 16.1	0.17
Hypertension, *n* (%)	95 (79.2)	7 (38.9)	11 (68.7)	77 (89.5)	<0.001
Diabetes, *n* (%)	58 (48.3)	6 (33.3)	7 (43.7)	45 (52.3)	0.316
CAD, *n* (%)	55 (45.8)	13 (72.2)	9 (56.2)	32 (37.2)	0.015
Atrial Fibrillation, *n* (%)	19 (15.8)	3 (16.7)	5 (31.2)	11 (12.8)	0.177
LVEF, (%)	48.4 ± 5.4	31.6 ± 3.5	47 ± 1.3	65 ± 6.6	<0.001
LVWM abnormalities, *n* (%)	41 (34.2)	18 (100)	12 (75.0)	11 (12.8)	<0.001
Mitral regurgitation, *n* (%)	52 (43.3)	12 (66.7)	11 (68.7)	29 (33.7)	0.003
Mitral stenosis, *n* (%)	8 (6.7)	2 (11.1)	2 (12.5)	4 (4.6)	0.366
LVH, *n* (%)	88 (73.3)	6 (33.3)	10 (62.5)	72 (83.7)	<0.001
DCM, *n* (%)	13 (10.8)	6 (33.3)	4 (25.0)	3 (3.5)	<0.001
Serum creatinine (mg/dL)	3.1 ± 3.8	4.91 ± 6.7	2.67 ± 3.0	1.70 ± 1.8	0.001
Total Cholesterol (mg/dL)	193.9 ± 59.1	157.9 ± 56.3	218.5 ± 48.6	205.3 ± 72.4	0.015
HDL (mg/dL)	37.7 ± 8.9	34 ± 8.7	41.3 ± 8.0	37.8 ± 10.0	0.095
LDL (mg/dL)	127.2 ± 32.5	116 ± 34.2	137.9 ± 26.6	127.6 ± 36.6	0.194

Values are shown as *n* (%) or mean±SD. HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; ECG, electrocardiogram; LVEF, left ventricular ejection fraction; LVWM, left ventricular wall motion; LVH, left ventricular hypertrophy; 2D, two-dimensional; Echo, echocardiography; DCM, dilated cardiomyopathy; HDL, high-density lipoproteins; LDL, low-density lipoproteins.

4. TREATMENT

Table 2. shows that ACEi/ARB (51.7%) were the most common essential medication used to treat HF. The percentage of patients with HFrEF who were given ACEi/ARB (44.4%, P = 0.324) was lower than those with HFpEF (55.8%, P = 0.324). Oral beta-blockers were commonly used in HFrEF (44.4%, P <0.175). Spironolactone was prescribed more in HFmrEF (56.2%, P <0.001) patients than in those with HFrEF (44.4%, P <0.001). HFmrEF was more frequently treated with furosemide (62.5%, P = 0.008) and digoxin (43.7%, P <0.001). Furthermore, calcium channel blockers (CCB), lipid-lowering drugs, and anti-coagulants were more frequently prescribed in patients with HFpEF. The percentages of patients with HFrEF who were given guideline recommended HF medication (ACEi/ARB, beta blocker or aldosterone antagonist) was only 44%.

Table No. 2: Drug used in patients with heart failure by study group

Medication	Total (*n* = 120)	HFrEF (*n* = 18)	HFmrEF (*n* = 16)	HFpEF (*n* = 86)	*p* value
Beta-blockers, *n* (%)	33 (27.5)	8 (44.4)	5 (31.2)	20 (23.2)	0.175
ACEi / ARB, *n* (%)	62 (51.7)	8 (44.4)	6 (37.5)	48 (55.8)	0.324
Calcium Channel Blocker, *n* (%)	47 (39.2)	3 (16.7)	8 (50.0)	36 (41.8)	0.087
Furosemide, *n* (%)	42 (35.0)	9 (50.0)	10 (62.5)	23 (26.7)	0.008
Spironolactone, *n* (%)	31 (25.8)	8 (44.4)	9 (56.2)	14 (16.2)	0.001
Digoxin, *n* (%)	15 (12.5)	4 (22.2)	7 (43.7)	4 (4.6)	<0.001
Aspirin, *n* (%)	57 (47.5)	10 (55.5)	6 (37.5)	41 (47.7)	0.574
PY12 receptor inhibitor, *n* (%)	42 (35.0)	4 (22.2)	6 (37.5)	32 (37.2)	0.468
Isosorbide dinitrate, *n* (%)	20 (16.7)	4 (22.2)	6 (37.5)	10 (11.6)	0.031
Lipid-lowering drugs, *n* (%)	58 (48.3)	5 (28.8)	6 (37.5)	47 (54.6)	0.075
Sublingual Nitroglycerin, *n* (%)	12 (10.0)	5 (28.8)	3 (18.7)	4 (4.6)	0.005

Values are shown as *n* (%). HF*r*EF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HF*p*EF, heart failure with preserved ejection fraction; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker, PY12 receptor inhibitor, antiplatelet agent.

5. DISCUSSION

The prevalence of HF in our patients was 2.8% which is similar to published studies from Asian countries (1%–3%) [4], the United States (2%) [15] and Europe (1–2%) [16]. More of our patients had HFpEF vs HFrEF or HFmrEF. The percentage of patients with HFpEF (71.6%) is similar to the one reported by Kaneko et al in Japan [17]. The I PREFER study undertaken in Latin America, Middle East and North African regions found a 65% prevalence of HFpEF [18]. The Atherosclerosis Risk in Communities (ARIC), a multi-center study across 25 countries found that HFpEF represented 65%–75% of prevalent cases, the percentage being fairly similar in women and men [8–13]. In our Cambodian patients, the mean age was much lower than in other studies, and the proportion of patients with HFpEF was substantially higher than in other countries.

The findings of our study differ from those in the USA and Europe where the frequency of HFrEF and HFpEF are similar. A Mayo Clinic study [21] reported that 47% of patients hospitalized for heart failure in Olmsted County, Minnesota between 1987-2001 had HFpEF. A follow-up, prospective cohort study by the Mayo Clinic found that 55% of patients in Olmsted County who underwent echocardiogram for evaluation of HF between 2000-2005 had preserved LV function with EF>50% [22]. In the Framingham Heart study, 51% of cases presenting with HF between 1983-1991 had EF>50% [23]. The percentage of HF patients with HFpEF seems to be higher in Asia than in the USA and Europe and suggest that Cambodian patients are in the upper range of those numbers.

Similarly, to our study, HFrEF in most countries is largely due to CAD [9–13; 18–20]. In Japan, patients with HFrEF were more likely to have ischemic heart disease as an etiology compared to those with HFpEF. On echocardiography, HFrEF was likely to have eccentric hypertrophy, whereas HFpEF was likely to have concentric hypertrophy [24]. We found that global wall abnormalities were most common in HFrEF due to the increased incidence of CAD in these patients. Wall motion abnormalities occurring in patients with HFmrEF were less severe. It is not clear if these mild regional motion abnormalities are due to subclinical CAD or other types of myocardial injury.

Systemic HTN contributes to the pathophysiology of HFpEF [25] by causing increased afterload on LV, leading to LVH and subsequent LV diastolic dysfunction [26–29]. HFpEF is

recognized as a multifactorial syndrome with hypertension and diabetes as major contributing risk factors. Thus, the management of HTN and diabetes are the cornerstone of HFpEF management for improving outcomes in patients with HFpEF [25].

In our study, ACEi/ARB were less frequently prescribed in HFrEF than in patients with HFpEF. To date, trials with ACEi/ARB have not shown a mortality benefit in patients with HFpEF [30, 31], but a significant benefit has been shown in preventing HF hospitalization [20] and decreasing mortality and morbidity with HFrEF [32]. ACEi with a beta blocker can slow and, in some cases, even reverse certain parameters of cardiac remodeling leading to improved EF [33–37]. Additionally, in our study, spironolactone was more frequently prescribed in patients with HFrEF and HFmrEF than that in HFpEF. Spironolactone appears to improve diastolic function, induce reverse LV remodeling, and even reduce cardiac hospitalizations and improve quality of life in subjects with HFrEF in some studies. On the other hand, there is no demonstrable beneficial effect of spironolactone on all-cause and cardiac mortality in patients with HFpEF [38].

5.1 Limitations

There are important limitations to acknowledge in our study. The sample size is small. The data, while carefully collected, were based on information in the medical record, some being self-reported. The presence of inaccurate information cannot be excluded. Only patients admitted to the ICU were eligible to be included in the study, as their evaluation enabled an accurate assessment of the type of HF present. Patients admitted to non-ICU wards were not included in the study and it is unknown if they had the same or different distribution of HF. A strength of the study is that the criteria for diagnosis and treatment strictly followed internationally accepted guidelines.

6. CONCLUSIONS

Our data suggest that HFpEF is more common in Cambodian patients admitted to a referral hospital ICU than HFrEF or HFmrEF. This is likely due to the high rate of hypertension and diabetes vs CAD in this population. Preventing and treating the risk factors, especially hypertension and diabetes, are important to reduce the incidence of HFpEF. The use of guideline recommended therapy for patients with HFrEF was lower than desired. This provides the opportunity to reduce mortality and morbidity in these patients by encouraging the use of this therapy in patients with HFrEF. This study provides important information on the types and therapy of HF observed in a small number of patients in the ICU of a single hospital in Phnom Penh. Similar data needs to be collected in a larger cohort of HF patients in Cambodia. Ideally a national registry of HF patients should be implemented with the goal of improving quality of life and survival in these patients.

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8. FUNDING STATEMENT

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9. ETHICAL APPROVAL

The study was approved by the Research Committee of the University of Puthisastra and the Technical Bureau of Preah Ket Mealea Hospital. The data were retrospectively collected from all discharged patients' medical records, without patient interaction or consent form. The data were recorded without using the patient's name or other identifying information to protect patient confidentiality.

10. DISCLOSURES

The author declare that has no any conflicts of interest.

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