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THE COMPARISON OF CLINICAL CHARACTERISTICS OF ACUTE DECOMPENSATED HEART FAILURE PATIENTS BETWEEN JCARE-CARD JAPAN AND DR. KARIADI HOSPITAL REGISTRY

Mochamad Ali Sobirin[1*], Kelly Kuswidiyanto[2], Yan Herry[1], Sodiqur Rifqi[1], Hiroyuki Tsutsui[3,4]
[1]Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[2]Department of Cardiology and Vascular Medicine, Cilacap General Hospital, Cilacap, Indonesia
[3]Department of Cardiovascular Medicine, Faculty of Medical Science, Kyushu University, Japan
[4]School of Medicine and Graduate School, International University of Health and Welfare, Japan
* Corresponding Author : E-mail: dr_alibirin@fk.undip.ac.id

ABSTRACT

Background: Heart failure (HF) is a significant public health issue because of its high prevalence, dismal prognosis, and high financial burden caused by frequent hospitalizations and extensive care. Low socioeconomic status has been linked to an increased incidence of HF, and different regions and races may have varied clinical characteristics of HF patients. Asian nations Indonesia and Japan both have varying socioeconomic conditions that could affect clinical characteristics and outcomes. The differences between HF patients from Indonesia and Japan in terms of clinical characteristics and outcomes have not been previously investigated. **Objective:** To investigate demographic and clinical characteristics of HF patients in Indonesia and compare with Japanese registry. **Methods:** In this retrospective observational study, patients presenting with acute decompensated heart failure (ADHF) at dr. Kariadi Hospital (RSDK) were consecutively recruited during 2014-2015 hospitalization period. Baseline data including demographic, clinical characteristics, laboratory data on admission, medication use before hospitalization, and length of stay during hospitalization were collected from medical record using the form of the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD). The descriptive analysis was performed to compare those HF characteristics. **Results:** A total of 246 ADHF patients in RSDK registry were included with average of age of subjects was 56.4 years-old and 57.3% were male. Etiology was predominantly ischemic heart disease (IHD) in 60.6%, average left ventricular ejection fraction 40.1% and length of hospital stay was 8.8 days. Compared to Japanese registry, the characteristics of clinical status and laboratory data on admission were almost similar between studies except for higher prevalence of ischemic heart disease, renal dysfunction and dyslipidemia but lower prior stroke in RSDK study. The average length of stay at hospital was longer in Japanese registry (8.8 days vs. 33.9 days). **Conclusion:** Ischaemic heart disease and renal dysfunction more prevalent in RSDK registry, but prior stroke and length of stay at hospital higher in Japanese registry of hospitalized ADHF patients.

Keywords: *Acute Decompensated Heart Failure, Clinical Characteristics, Registry, Length of Stay*

INTRODUCTION

Heart failure (HF) is a clinical syndrome as the final stage of a variety of diseases that attack the heart organ. The main manifestations are shortness of breath and fatigue, which limits physical activity, as well as fluid accumulation, leading to pulmonary congestion and peripheral edema. Due to the high frequency, poor prognosis, and significant financial burden associated with healthcare, HF has emerged as a significant health issue in Western countries over the past ten years..[1,2] Indonesia and Japan are demographic Asian countries but have different socioeconomic characteristics which may affect guideline-directed therapy and clinical outcomes. In Indonesia, The Government Basic Health Research (Riskesdas) 2007 with 968,997 respondents in 440 districts of 33 provinces showed that the proportion of patients with HF based on symptoms was 0.31%.[3] Worryingly, Hawkins et reported that low socioeconomic status was linked with increased incidence of HF in both community and hospital settings and due to the increased risk of a significant risk factor for heart diseases like coronary artery disease, hypertension, and diabetes mellitus (DM), the prevalence of HF is anticipated to be equal to the proportion in developed nations.[4] Meanwhile in Japan, a developed nation, as shown in a study by Okura et al. predicted that the number of patients with left ventricular dysfunction (LVD) will increase to 1.3 million in 2030, causing a heart failure pandemic.[5] Moreover, recent reports have shown a dramatic increase in the prevalence of heart failure patients with an ischemic etiology compared to previous studies, it approaches the prevalence observed in Western subjects, accounting for 50–60%.[6] Little is known about the impact of these differences on the

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use of evidence-based heart failure treatments and its outcomes in Asian countries with different socioeconomic statuses, such as Indonesia and Japan. Therefore, this study aimed to describe and compare the clinical characteristics of heart failure patients hospitalized with exacerbation of heart failure symptoms in Indonesia and Japan.

METHODS

This descriptive study compared and studied retrospectively the demographic characteristics and treatments in patients hospitalized with worsening HF in dr. Kariadi Hospital (RSDK), Semarang, Indonesia and prospectively in Japan using the same form of the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD).[7] In this study, we analyzed the acute phase data of (1) characteristics (age, sex, cause of HF, and medical history), (2) admission vital signs and laboratory data (blood chemistry and echocardiogram), (3) medical drug use (angiotensin-converting enzyme [ACE] inhibitor, angiotensin II receptor blocker [ARB], β blocker, diuretics, digitalis, calcium channel blocker, aspirin, and statin), (4) length of stay. There were a total of 1677 and 246 patients in Japan and Indonesia, respectively.

RESULTS

Patient characteristics

The average age of the 246 studied patients was 56.4 ± 13.0 years and 57.3% were men (Table 1). The causes of HF were mostly due to ischemic heart disease in 60.6% and or hypertensive heart disease in 37.8%, valvular heart disease in 20.3%, and dilated cardiomyopathy in 8.1%. Risk factors for ischemic heart disease (IHD) included hypertension (61.2%), diabetes mellitus (32.4%), and dyslipidemia (46.8%). Approximately one-thirds of the patients had a history of prior hospitalization due to HF.

Patient characteristics in this study were compared with those in JCARE-CARD Japan (Table 1). The mean age was younger in RSDK 56.3 ± 12.8 years old. Males were predominant sharing 57-60% in both studies. Ischemic heart disease, some with concomitant hypertensive heart disease, was the most predominant cause of HF, but it was higher in RSDK (65.3% vs 34.0%). The prevalence of other causes such as valvular heart disease, and dilated cardiomyopathy was similar between studies.

The comorbidities were also similar between studies such as hypertension (50–60%), diabetes mellitus (25–30%), except prior stroke being lower in RSDK studies (6.0%) than those in Japanese studies 16.3%). However, the prevalence of renal dysfunction (28.4% vs. 11.3%) and dyslipidemia (46.8% vs. 25.8%) were higher in RSDK studies.

Clinical status on admission

The mean heart rate, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were similar between studies. Laboratory data such as sodium electrolyte and hemoglobin were similar between studies except for higher serum creatinine level in RSDK registry. Plasma B-type natriuretic peptide (BNP) was higher on admission in RSDK (collected in small numbers) compared to Japanese studies (data not shown) which also showed more severe heart failure in RSDK registry (Table 2).

Table 1. Patient characteristics COPD, chronic obstructive pulmonary disease; HF, heart failure

Characteristics	RSDK Registry (n= 246)	JCARE-CARD Japan (n= 1677)
Age, yrs (mean ± SD)	56.4 ± 13.0	70.7 ± 13.5
Male, %	57.3	59.4
Causes of HF,%		
Ischemic	60.6	34.0
Valvular	20.3	28.1
Hypertensive	37.8	26.4
Dilated cardiomyopathy	8.1	17.0
Medical history, %		
Hypertension	61.2	52.1
Diabetes mellitus	32.4	29.8
Dyslipidemia	46.8	25.8
Prior stroke	6.0	16.3
Renal dysfunction	36.0	11.3
Anemia	45.6	20.3
COPD	7.2	5.8
Prior hospitalization (HF)	28.4	50.0

Medication use before hospitalization was also compared between studies**.** The use of ACE inhibitors/ARBs (48.4% vs. 55.4%), and β blockers (21.1% vs. 22.3%) was similar between studies, but the choice of using ACE inhibitors was slightly lower in RSDK registry (13.0% vs. 26.5%) (Table 2). The use of calcium channel blockers and aspirin before hospitalization admission was lower in the RSDK registry, but, the use of aldosterone antagonist was

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higher in RSDK study than Japanese study (59.3% and 24.1%).

Length of stay

The average length of stay was 8.8 ± 6.7 days in the present study. It was much longer in Japanese study (33.9 ± 34.9 days). Median length of stay reported in JCARE-CARD RSDK and Japan is shown in Fig. 1. The most striking difference was longer length of stay in Japanese study (15 days vs. 7 days).

Table 2. Vital signs, laboratory data and medication use on admission

Characteristics	RSDK Registry (n= 246)	JCARE-CARD Japan (n= 1677)
Vital signs		
Heart rate, bpm	91.1 ± 19.0	87.8 ± 24.4
SBP, mmHg	125.3 ± 23.3	134.3 ± 30.3
DBP, mmHg	79.4 ± 15.3	75.4 ± 18.2
Laboratory Data		
Serum creatinine, mg/dl	1.81 ± 1.56	1.28 ± 1.03
BUN, mg/dl	26.5 ± 19.1	26.2 ± 16.7
Na, mequiv/L	139.9 ± 4.8	139.7 ± 4.6
Hemoglobin, g/dL	12.7 ± 2.1	12.4 ± 4.5
LVEF, %	40.1 ± 19.2	42.5 ± 17.9
Medication Use		
ACE inhibitor, %	13.0	26.5
ARB, %	35.4	28.9
Beta blocker, %	21.1	22.3
Diuretics,		
Loop diuretics,%	54.9	54.4
Aldosterone antagonist, %	59.3	24.1
Digitalis, %	34.1	26.6
CCB, %	6.5	24.2
Aspirin, %	22.8	34.5
Statin, %	23.6	16.2

SBP, systolic blod pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction;

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blockers

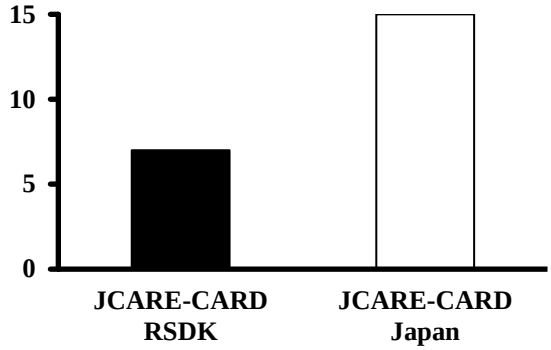

Figure 1. Median Length of Stay (days)

DISCUSSION

In the present study, using the JCARE-CARD database, the characteristics, clinical status, and laboratory data at the admission of patients hospitalized with acute decompensated heart failure were almost the same between studies, except for a higher prevalence of ischemic heart disease, renal dysfunction, and dyslipidemia but lower prior stroke in RSDK study. Management was also similar except for the higher use of ACE inhibitors and lower use of aldosterone antagonists in the Japanese study. The most surprising difference between RSDK and the Japanese study was the longer length of stay in Japan.

The clinical characteristics of patients hospitalized due to HF were almost similar between RSDK and Japan study, even with previous large studies such as ATTEND (acute decompensated heart failure syndromes) registry,[8] ADHERE (Acute Decompensated Heart Failure National *Registry*),[9] OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure),[10] EHFS-II (Euro Heart Failure Survey II).[11] This patient similarity may be due to the inclusion of only hospitalized patients with exacerbated heart failure, which may also include patients with somewhat uniform conditions on admission. However, the prevalence of ischemic heart disease (IHD) in JCARE-CARD Japan (34%) was lower than that in the RSDK study (approximately 60%), and the prevalence was similar in Western countries. Interestingly, Shiba et al reported a trend of westernization from CHART-2 study that showed IHD was the most prevalent cause of HF reaching 53%, this has led many experts to speculate that the apparent trend toward increasing prevalence of CAD

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as a cause of heart failure is due to: (1) the number of CAD patients is increasing due to the accelerating westernization of Japanese lifestyles. (2) recent therapeutic advances have dramatically increased the number of survivors of acute coronary events.[5] Meanwhile, the prevalence of stroke was higher in Japan than in the RSDK study. These differences, therefore, suggest that there are still clinical features of heart failure patients that may vary by region and race.

HF patients in the RSDK study had a similarly low rate of beta-blocker usage before hospitalization compared to the Japan study (21.1% vs. 22.8%) despite the beneficial effect of beta-blockers on heart failure patients. Angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs) and beta-blockers are known to improve outcomes in patients with chronic heart failure secondary to left ventricular systolic dysfunction, and recent European Society of Cardiology (ESC) guidelines for the treatment of HF stated that both beta-blockers and ACE inhibitors should be started as soon as possible after diagnosis of heart failure with reduced ejection fraction (HFrEF).[12] ACE inhibitors have moderate effects on left ventricular remodeling, whereas β-blockers often lead to marked improvements in EF. In addition, beta-blockers have antiischemic effects and are probably more effective in reducing the risk of sudden cardiac death, leading to a significant and earlier reduction in all-cause mortality. The Euro Heart Failure Study also found that heart failure medications, especially beta-blockers, were underused and inappropriately low when prescribed.[13] This may be a throwback to the past, when beta-blockers were considered contraindicated in patients with left ventricular dysfunction.[14] This study also revealed that patients in RSDK had a lower rate of ACE inhibitor use and higher use of ARBs, similar to the Japan study.

Regarding the association between heart failure and stroke, a population-based cohort study by Adelborg et al. reported that heart failure patients had a higher risk of not only ischemic stroke, but also all stroke subtypes, than the general population.[15] After a first stroke, women were 25 times more likely to have a major adverse cardiac event, including heart attack, heart failure, and cardiovascular death, and men without apparent heart disease were 23 times more likely to have MACE 30 days later.[16] Ultimately, concomitant patients with stroke and HF have higher mortality rates, more severe neurological deficits, and longer hospital stays than those without HF.[17] The study found that the higher rate of experiencing stroke in Japan may be due to the higher proportion of older people, and the rate of hemorrhagic stroke is thought to be twice as high in Japan as in Western countries.[18]

The longer stay in Japan compared to the RSDK study may be due to differences in the medical system, continued management of comorbidities, and intensive management of risk factors during hospitalization due to worsening heart failure. Longer hospital stays may increase opportunities for optimizing management and are known to improve outcomes in HF patients.[19] Unfortunately, as the nature of HF patients, it is known for the high rates for hospitalization, recurrence and treatment that in the United States (U.S.) the expenses reaching 39 billion dollars per year.[20] In the other hand, despite fewer length of stay in RSDK patients, there was low usage of standard medication i.e. beta blocker that could affect the recurrence rate for admission and survival which is worse in low socioeconomic status as concluded by Hawkins et al.[4] Therefore, it is extremely important to move forward so that patients receive the best possible care (including education) and access to multidisciplinary HF teams.

CONCLUSION

The characteristics, clinical status, and laboratory data on admission in patients hospitalized with ADHF were similar between dr. Kariadi Hospital (RSDK) and Japan registry, except for higher ischemic etiology, renal dysfunction and dyslipidemia in RSDK, but higher prior stroke in Japan which might contribute to the longer length of stay in Japan.

ETHICAL APPROVAL

This study was reviewed and approved by The Ethics Commission of the Faculty of Medicine, Universitas Diponegoro, and dr. Kariadi Hospital Semarang, Indonesia, with approval number: 909/EC/FK-RSDK/IX/2016.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

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