Acta Cardiologia Indonesiana

pISSN:2460-5700

eISSN:2579-4345

Web page: jurnal.ugm.ac.id/v3/jaci

Epidemiology, Aetiology and Risk Profile of Heart Failure in a Tertiary Referral Hospital: a Report from the Sardjito Heart Failure Registry

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Keywords:
chronic heart failure; epidemiology; aetiology; risk profile;

Manuscript submitted: December 10, 2019
Revised and accepted: March 15, 2020

ABSTRACT

Background: Heart failure (HF) is currently still one of the problems in Indonesia due to the high rate of morbidity, mortality and rehospitalisation. Heart failure is also one of the diseases that use the most health funds. Coronary heart disease is the most common cause of HF. Data on epidemiology of HF is still limited in Indonesia. Understanding the epidemiology of the preclinical and clinical stages of HF may facilitate preventative strategies. This study aims to find out epidemiological data on HF patients in Yogyakarta, starting from the population in the hospital, especially in Dr. Sardjito General Hospital.

Method: This study was a descriptive analytic study with a cross-sectional design conducted at Dr. Sardjito General Hospital, Yogyakarta, Indonesia from February 2016 to February 2018. Patient demographic, clinical signs and echocardiographic data were recorded and analyzed using univariate and bivariate analysis.

Results: Out of a total of 853 patients, the median age of patients was 59 years (19-91 years) with a greater number of male patients (68.2% vs. 31.8%) than women. The most common cause of HF is ischemia heart disease (40.2%), while hypertension is the dominant risk factor found (59.8%). The prevalence of heart failure with preserved ejection fraction (HFpEF), mid-range ejection fraction (HFmrEF) and reduced ejection fraction (HFrEF) were 43%, 20.3% and 36.5% respectively. Diabetes mellitus (DM) was associated with heart failure ejection fraction less than 50% (p<0,001). Both DM and hypertension were significantly associated with IHD (both p<0,001). Hypertension was associated with HHD (p<0,001).

Conclusion: Ischemia heart disease is the most common aetiology of HF in our study. Diabetes mellitus and hypertension are major risk factors leading to IHD. Preventive efforts and risk factor management are the main pillars to reduce the incidence of HF in the future.

INTISARI

Latar Belakang: Gagal jantung masih menjadi salah satu problematika di Indonesia saat ini terkait masih tingginya angka morbiditas, mortalitas serta rehospitalisasinya. Gagal jantung juga menjadi salah satu penyakit yang menggunakan dana kesehatan paling banyak. Penyakit jantung coroner merupakan penyebab gagal jantung yang paling banyak ditemukan. Data mengenai epidemiologi gagal jantung masih terbatas di Indonesia. Memahami epidemiologi gagal jantung dari praklinis hingga klinis dapat meningkatkan upaya strategi pencegahan terhadap kejadian gagal jantung. Studi ini bertujuan untuk mengetahui data epidemiologi pasien gagal jantung di Yogyakarta, dimulai dari populasi di rumah sakit, khususnya di RSUP Dr.Sardjito.

Metode: Penelitian ini merupakan studi deskriptif analitik dengan desain potong lintang yang dilakukan di RSUP Dr. Sardjito dari Februari 2016 sampai dengan Februari 2018. Data demografi, tanda klinis, dan ekokardiografi pasien direkam dan dianalisa dengan menggunakan analisis univariat dan bivariat.

Hasil: Dari total 853 pasien, didapatkan median usia pasien 59 tahun(19-91tahun). Laki- laki lebih banyak ditemukan (68.2% vs 31.8%) dibandingkan wanita. Penyebab yang gagal jantung yang paling banyak ditemukan adalah penyakit jantung iskemia (40.2%), sementara hipertensi menjadi faktor risiko yang dominan ditemukan (59,8%). Gagal jantung dengan fraksi ejeksi yang masih baik ditemukan lebih banyak dibandingkan fraksi ejeksi menengah dan menurun (43% vs 20.3% vs 36.5%; masing-masing). Diabetes mellitus (DM) berhubungan dengan gagal jantung yang memiliki ejeksi fraksi kurang dari 50% (p<0,001). Diabetes mellitus dan hipertensi terkait secara signifikan dengan IHD (keduanya p<0,001). Hipertensi berhubungan dengan HHD (p<0,001).

Kesimpulan: Penyakit jantung iskemia menjadi penyebab gagal jantung paling banyak pada studi kami. Diabetes mellitus dan hipertensi merupakan faktor risiko utama terjadinya IHD. Upaya preventif dan manajemen faktor risiko menjadi pilar utama untuk menekan kejadian gagal jantung di kemudian hari.

Introduction

Heart failure (HF) occurs when the heart cannot pump blood throughout the body in sufficient quantities according to the body's metabolic needs (forward failure), or the heart can pump blood only if accompanied by an increase in filling pressure (backward failure), or a combination of both.[1] Heart failure has become a major problem in society where the incidence rate is very high to date and is one of the causes of cardiovascular death in the world today.[2]

The main terminology used to describe HF is based on measurement of the left ventricular ejection fraction (LVEF). The latest study from the European Society Cardiology (ESC) stated that HF is divided into three categories for patient status recognition, ranging from those patients with normal LVEF (≥50%; HF with preserved EF (HFpEF)) to cases with reduced LVEF (<40%; HF with reduced EF (HFrEF)). Patients with an LVEF in the range of 40–49% represent a 'grey area', which we now define as HF with mid-range EF (HFmrEF).[3]

The mortality of HF patients based on various studies is known to be inversely proportional to the left ventricular systolic function. The value of ejection fraction in general has been considered as one of the strongest prognostic factors affecting poor outcomes in patients with HF.[4] Cohn et al. in his study showed that HF patients who had a normal ejection fraction (≥ 45%) tended to have a prognosis which was significantly better than patients with systolic HF (annual mortality rate of 8% vs. 19%; p = 0.0001).[5]

Managing HF in primary care has also becomes a difficult problem in many developing countries, such as Indonesia due to some uncertainty in diagnosis with comorbidities and the difficulty to perform additional examinations still being challenging due to lack of resources.[6] Data on the epidemiology of HF in Indonesia is still limited to date. There are no specific data on the prevalence of HF among patients attending out-patient clinics nor those hospitalized in cardiac wards in Indonesia. The numbers and characteristics are still yet unknown. Studying chronic HF problems must be initiated with the collection of sufficient data from patients. The process begins with data collection and analysis from one area and then extending it to other areas is expected. The aim of this study is to determine the epidemiology and characteristics of HF among patients in our hospital. With this study, it is expected that in the future we can find out more about the characteristics of HF patients in our hospitals so that later we can provide good management in managing these patients. Therefore, we hope that data from this study can contribute to epidemiological data on HF in Indonesia.

Material and Methods

This research is a descriptive study with a cohort research design that conducted at the cardiac clinic and ward of Dr. Sardjito General Hospital, Indonesia. The registry was collected from February 2016 to February 2018. Medical records of 853 patients were selected using consecutive sampling. The demographic, clinical and echocardiographic data of the patients were examined by statistical analysis. Heart failure was diagnosed by using the criteria for the diagnosis of heart failure from the European Society of Cardiology (ESC).[3] Ethical approval was obtained from Medical and Health Research Ethics Committee of Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

For statistics analysis, the patient's demographic characteristics are described in the form of categorical data. Meanwhile, echocardiographic data (ejection fraction values) are described in the form of numerical data. Comparative analysis was carried out between the three heart failure groups (based on the value of ejection

fraction) using the ANOVA test. All data were analyzed and compared using SPSS 18. Software p values <0.05 were considered significant in this study.

Results

There were 853 patients diagnosed with heart failure according to the criteria for diagnosis of HF from the ESC. The median age of patients in this study was 59 years (19-91 years). Male sex was more prevalent in this study than female sex (68.2% vs 31.8%). The most common risk factor found in HF patients in this study was hypertension (59.8%) followed by smoking habits (46.4%), dyslipidemia (35.2%) and diabetes mellitus (21.5%) (Figure 1).

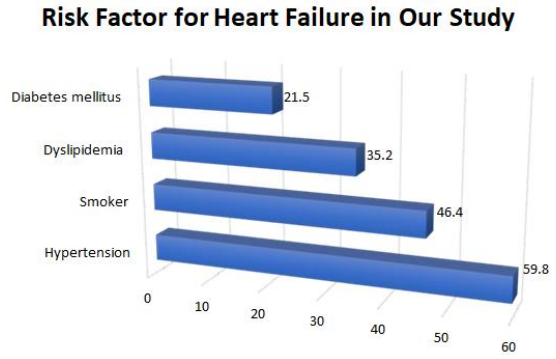

Figure 1. Hypertension (59.8%) is the most common risk factor causing heart failure followed by smoker (46.4%), dyslipidemia (35.2%), and diabetes mellitus (21.5%).

The etiology of HF varies among regions of the world. Ischemic heart disease (IHD) (40.2%) is a major cause of HF in our study followed by other causes such as valvular heart disease (VHD) (17%) and hypertensive heart disease (HHD) (10.2%). In addition, there were also patients with HF caused by more than 1 etiology such as VHD accompanied by hypertension or ischemia (27.5%) (Figure 2).

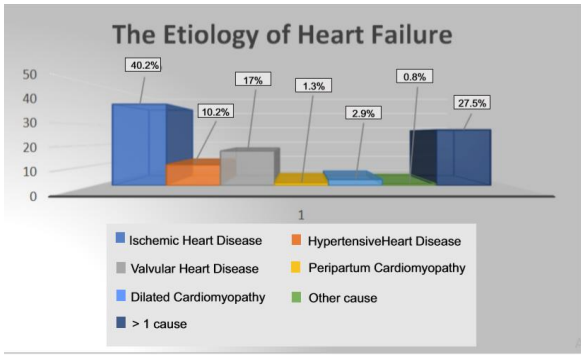

Figure 2. Etiology of HF in our study. It seen that ischemic heart disease is the most common cause that contributes to the incidence of heart failure.

Then if HF patients in this study were classified based on the value of the ejection fraction, 312 patients (36.5%) were included in the HFrEF group, 367 patients (43%) were included in the HFpEF group and 174 patients (20.3%) found in the HFmrEF group. Male sex is more prevalent in the HFrEF and HFmrEF groups, whereas in the HFpEF group, male and female sexes have the same proportion (Table 1).

Hypertension is the most common risk factor in all three groups of HF. Meanwhile, when viewed from the cause of HF itself, IHD is a major cause of HF in the HFrEF and HFmREF groups. This is different from the HFpEF group, where VHD is the most common cause of heart failure (Table 1).

Table 1.
Demographic characteristics of HF patients based on new HF classification

Variables	HFrEF (n=312)	HFmrEF (n=174)	HFpEF (n=367)
Age, years, mean±SD	57±12	61±12	58±14
Gender			
Male, n (%)	239 (74)	117 (69.2)	226 (62.6)
Female, n (%)	84 (26)	52 (30.8)	135 (37.4)
Risk Factors			
Hypertension, n (%)	185 (57.3)	110 (65.1)	215 (59.6)
DM, n (%)	89 (27.6)	41 (24.3)	53 (14.7)
Smoker, n (%)	186 (57.6)	89 (52.7)	121 (33.5)
Aetiology			
IHD, n (%)	174 (53.9)	92 (54.4)	77 (21.3)
VHD, n (%)	6 (1.9)	16 (9.5)	123 (34.1)
HHD, n (%)	8 (2.5)	7 (4.1)	72 (19.9)
DCM, n (%)	19 (5.9)	3 (1.8)	3 (0.8)
>1 aetiologies, n (%)	113 (35)	50 (29.6)	72 (19.9)

HFrEF: heart failure with reduce ejection fraction, HFmEF: heart failure with mid-range ejection fraction, HfpEF: heart failure with preserved ejection fraction, IHD: ischemic heart disease; VHD: valvular heart disease; HHD: hypertensive heart disease; DCM: dilated cardiomyopathy; DM: diabetes mellitus

We analyzed the association between diabetes mellitus (DM) and the heart failure sub-group (HFpEF and non-HFpEF) as described by ESC criteria using ejection fraction. It showed that 125 patients (70,5%) with DM versus 357 patients (53,3%) without DM had ejection fraction less than 50% with p<0,001 (RR 1,32 and 95% CI 1,17 – 1,48). We did the same analysis to the hypertension group. Similar proportion of patients with hypertension and without hypertension (56,8% versus 57,3% respectively) had ejection fraction less than 50% with p=0,92 (RR 0,99 and 95% CI 0,88-1,11).

Furthermore, we also analyzed diabetes mellitus and hypertension as risk factor to the heart failure etiology especially ischemic heart disease (IHD) and hypertensive heart disease (HHD). Both diabetes mellitus and hypertension were significantly associated with IHD. There were 149 (81,4%) diabetic patients and 389 (58,2%) non-diabetic patients who had IHD (p<0,001; RR 1,39 and 95% CI 1,27 – 1,53). Meanwhile, there were 351

(68,8%) hypertensive patients and 187 (54,8%) non-hypertensive patients experienced IHD (p<0,001; RR 1,25 and 95% CI 1,12 – 1,40).

Moreover, only hypertension was associated with HHD with p<0,001 whereas diabetes mellitus exhibited non-significant result with p=0,99. The analysis showed that 234 (46,2%) hypertensive patients and 82 (24,2%) non-hypertensive patients had IHD (RR 1,90 and 95% CI 1,54 – 2,35). In contrast, there were similar proportion of patients in the diabetic group vs non-diabetic group (37,4% vs 37,3%) who had HHD (RR 1,00 and 95% CI 0,80 – 1,23).

Discussion

Our study shows that HF is more common in men than women with a median age of patients who have heart failure is 59 years. In our study also showed the incidence of HF increased with increasing age of patients, ie 15.7% in the age group <45 years, 40.2% in the age group 46-60 years and 44.1% in the age group >60 years. This was also found in the Rotterdam and Hillingdon studies where HF was found to be more prevalent in men than women (15 vs 12 per 1000 people per year). The Hillingdon study showed that the incidence of heart failure increased by 0.2 / 1000 people per year in the age group 45-55 to 12.4/1000 people per year in the age group >85 years. While in the Rotterdam study, the incidence of heart failure increased from 2.5 / 1000 people per year (age group 55-64 years) to 44/1000 people per year (age group> 85 years).[7, 8]

The HF registry compares the population in Western countries, namely the ADHERE9 registry in the United States and EHFS II/UKNHFA10 in Europe with heart failure registry in the Asia-Pacific (registry ASIAN-HF11 and INTER-CHF12) shows that the age of patients with HF younger in the Asia-Pacific than in the West, with an average age of 60 years with the majority of patients being male. These results are also parallel to those found in our study where the average age of patients was 58.28 ± 13.08 years. Our study shows that 68.2% of patients who experience HF are men. This result is similar to the findings of the Framingham study where the incidence of HF was more common among men than women at all ages.[13] In our study HF patients were predominantly male because male patients in our study had more risk factors for HF than women like hypertension (70.8% vs 29.2%; p <0.05) and smoking habits (79.6% vs 20.4%; p <0.05).

Hypertension is the risk factor most often associated with the incidence of HF, as in our study where the incidence of hypertension was found to be 59.8% associated with HF. Longstanding hypertension ultimately leads to HF. Cardiac remodeling to a predominant pressure overload consists of diastolic dysfunction and concentric LV hypertrophy. When pressure overload is sustained, diastolic dysfunction progresses, filling of the concentric remodeled LV decreases, and HF with preserved ejection fraction ensues. Diastolic dysfunction and HF with preserved ejection fraction are the most common cardiac complications of hypertension. The end stage of HHD results from pressure and volume overload and consists of dilated cardiomyopathy with both diastolic dysfunction and reduced ejection fraction.[14]

The Framingham study showed the potential contribution of hypertension to the incidence of HF.[15] Another study also demonstrated that hypertensive men had a nearly 8-fold risk of developing chronic HF compared with normotensive men. Similarly, hypertensive women had a 4-fold risk compared with normotensive women.[16]

The utmost etiology of HF in our study was ischemic heart disease (IHD), followed by VHD and HHD. Traditional risk factors for instance hypertension, diabetes mellitus and smoking are contribute to the onset of the atherosclerosis process which will later develop into coronary heart disease or IHD. This manifestation of coronary heart disease can be a stable chest pain (or angina pectoris) or a heart attack commonly known as acute coronary syndrome. Patients with coronary heart disease will be at risk for HF in the future if they do not get the right treatment. From a study involving 1.537 patients who had myocardial infarction and then followed up for an average of 7.6 years, 36% of patients had HF. Reperfusion therapy carried out in patients with myocardial infarction is associated with a lower risk of HF after myocardial infarction.[17]

One previous study of the etiology of heart failure carried out by Lee et al. in 534 patients with HF revealed that IHD occurred in 278 participants (52%), VHD in 42 participants (8%), hypertension in 140 participants (26%), and other etiologies/ unknown in 74 participants (14%).[18] Similar findings were also found in our study that IHD due to heart disease was still the most common etiology of HF (40.2%) followed by VHD (17%) and HHD (10.2%).

When we did subgroup analysis, we found that 43% of our patients are HFpEF patients. This finding is similar to a study by Hogg et al.[19], in which HFpEF comprise between 44% and 72% of all cases of HF. In our study, valvular heart disease is the most common etiology in HFpEF group. This finding is relevant with the review from Ziaeian and Fonarow[20], as VHD, especially secondary to rheumatic heart disease, is commonly found in developing countries and contributes substantially to morbidity and mortality. But in developed countries, HFpEF is commonly caused by hypertension.[20]

Patients with HFrEF (36.5%) became the second largest population in our study after HFpEF. IHD is the most common cause in this group of patients. This shows that many of these patients are likely to experience myocardial infarction in the past who did not get optimal therapy so that now the patient has fallen into a condition of HF. From these findings indicate the importance of prevention strategies from the beginning (primary prevention) in patients who have risk factors such as hypertension and diabetes mellitus which in fact these risk factors are very closely related to the incidence of IHD. In addition secondary prevention also needs to be done in patients who have had IHD so as not to fall into conditions of HF,

such as through a strategy of revascularization of the coronary arteries (if indicated) or with optimal drugs.

In 2016, the ESC issued a new guideline to the classification of HF based on LV function wherein HFpEF and HFrEF, HFmrEF was also introduced with the function of ejection fraction between 40-49%.[3] Some studies discuss specifically about this latest classification where some opinions suggest that HFmREF is a transition from patients who initially HFpEF then experience progressive decrease in LV function (for example because of IHD) or vice versa patients who initially HFrEF have improved ventricular function because of optimal treatment.[21]

Limitation

In our study the basic aetiology of the HFmrEF group resembled those in the HFrEF group where IHD was the most common cause (54.4%). But our limitation is that we did not know the clinical course of the disease from the HFmREF group whether initially it was the HFrEF group that improved treatment or initially the HFpEF group who later experienced the incidence of coronary heart disease and decreased LV function. This is an interesting matter for us to examine further in the future regarding the course of the disease in this HFmrEF group. Furthermore, the study population was limited only from one referral hospital in Yogyakarta, there should be more data to be collected from other hospitals to provide better analysis. Moreover, the classification of the heart failure group is merely based on the ejection fraction defined by echocardiography.

Conclusions

Our study shows IHD is the most common aetiology of HF among patients. Diabetes mellitus and hypertension are major risk factors leading to IHD. Knowing the epidemiology of HF will help us clinicians in dealing with the problems of HF, especially in terms of early prevention of existing risk factors in patients so that the incidence of HF can be reduced.

Acknowledgment

The authors acknowledged and appreciated the support of the heart failure registry research assistant teams in the Cardiology Research Office (CRO): Ferdinandus Bayu Satria, Muhammad Aprianto Ramadhan, Daria Ilmasari, Yuwinda Prima Ardelia, Guntur Marganing Adi Nugroho, Rufita Ismu Astania, Luthfina Mufidati, Annisa Laksmi Wardani, Septiana Rizki Fauziah, Laras Prasasti, Karina Kristanti and Amri Adhyatma.

Funding Sources

This work was supported by the 2017 Faculty of Medicine, Universitas Gadjah Mada Community Grant Fund for Hasanah Mumpuni as the principal investigator. Grant number: UPPM/220/M/05/04/05.17.

Disclosures and Ethics

Authors whose names appear on submission have contributed sufficiently to design the study and acquired, analyzed, and interpreted data. The authors declare that there are no conflicts of interest.

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