ORIGINAL RESEARCH PAPER

Cardiology

KEY WORDS: Ejection fraction, Ureum, Creatinine

RELATIONSHIP BETWEEN THE EJECTION FRACTION IN ECHOCARDIOGRAPHY WITH KIDNEY FUNCTION IN HEART FAILURE PATIENTS

Ananda Nikmaturrahmi Lubis — Division Cardiology and Vascular, Department of Internal Medicine, Universitas Sumatera Utara/ Adam Malik Hospital, Jl.Bunga Lau Medan Indonesia

Rahmad Isnanta* — Division Cardiology and Vascular, Department of Internal Medicine, Universitas Sumatera Utara/ Adam Malik Hospital, Jl.Bunga Lau Medan Indonesia *Corresponding Author

Refli Hasan — Division Cardiology and Vascular, Department of Internal Medicine, Universitas Sumatera Utara/ Adam Malik Hospital, Jl.Bunga Lau Medan Indonesia

ABSTRACT

Introduction: Cardiovascular disease is often associated with kidney disease, which increases the mortality rate of individuals with kidney disease (± 50%), and is a higher cause of death than kidney disease itself. In cases of heart failure, kidney dysfunction is often mild and asymptomatic, and is often accidentally detected on routine biochemical examinations. Therefore it is very important to identify from the outset of kidney biochemical abnormalities in patients with heart failure, because the examination is useful in assessing the severity and duration of heart failure. With the identification of early abnormalities and providing adequate therapy for the underlying causes of heart failure, it can restore kidney function and prevent permanent damage. In this study used a cross-sectional study conducted at the Medan General Hospital RSUP starting in June 2017 until the number of samples was fulfilled. An echocardiographic examination is performed to assess the ejection fraction and to examine kidney function. There are 52 patients with a diagnosi of heart failure. Found men who suffer from heart failure (69.2%). With the most age between 46-65 years (61.5%). The ejection fraction in this study was 73.1% were HFrEF. With a higher creatinine average (1.82 ± 0.77) in the ejection fraction ≤ 40%. Based on Chi-Square analysis there was a relationship between ejection fraction and urea (p = 0.003) and there was a relationship between ejection fraction and creatinine (p = 0.04).

1. INTRODUCTION

Heart failure (HF) is a complex clinical syndrome, which is based on the inability of the heart to pump blood throughout the body's tissues adequately, due to structural and functional disorders of the heart. Heart failure is still a major health problem in the world.[1] One of the non-invasive tests performed for heart failure is echocardiography. Through this examination, it can be seen left ventricular function by looking at the left ventricular ejection fraction (EF) and measuring the volume and timing of ventricular filling.[2,3]

The most common cause of heart failure is left ventricular myocardial dysfunction. Left ventricular myocardial dysfunction causes the ability of the left ventricle in terms of blood filling and pumping to be disrupted, therefore heart failure is described using EF measurements of left ventricle (LV) (EF is final diastolic volume reduced by systolic end volume, divided by final diastolic volume).[2] Failure heart with a decrease in ejection fraction (HFrEF) is characterized by the presence of clinical syndrome of heart failure accompanied by LVEF ≤40% or also called systolic heart failure due to a decrease in cardiac contractility; while heart failure with preserved EF (HFpEF) is defined as the presence of clinical syndrome of heart failure accompanied by LVEF ≥50%, and is often referred to as diastolic heart failure.[2,4] Diagnosis is made by doppler-echocardiographic examination of blood flow mitral and pulmonary venous flow.[5]

Cardiovascular disease is often associated with kidney disease, which increases the mortality rate of individuals with kidney disease (± 50%), and is a higher cause of death than kidney disease itself. The prevalence of heart failure is ± 1-2% of the adult population in developing countries, and the number increases 10% in individuals aged 70 years. [4,6]

Forman's study, et al. From 1997 to 1998, reported a worsening of renal function in patients treated for heart failure. The criterion of deteriorating kidney function was an increase in serum creatinine levels 3 0.3 mg / dl when compared with baseline levels.[6]

In the Smith et al. Study, carried out from 1996 to 2005 reported that of the 80,098 patients treated for heart failure 63% experienced deteriorating kidney function, and the rate of deterioration in kidney function was proportional to the increase in mortality. For each increase in serum creatinine level of 0.5 mg / dl there is an increase in mortality by 15%.[7] Impaired renal function occurs in 27% of patients treated and is associated with a worse prognosis.7 The worsening of kidney function is mainly due to congestion chronic vein, hypoperfusion or increased intra-abdominal pressure (≥ 8 mmHg).[8]

In cases of heart failure, kidney dysfunction is often mild and asymptomatic, and is often accidentally detected during routine biochemical examinations.[9] Therefore, it is very important to identify from the outset of renal biochemical abnormalities in patients with heart failure, because the examination is useful in assessing severity and duration of heart failure. With the identification of early abnormalities and providing adequate therapy for the underlying causes of heart failure, it can restore kidney function and prevent permanent damage.[9]

2. Methods

2.1 Patients Selection

This research was conducted by observational with the method of measuring data by cross section. The study starting in June 2017 until the number of samples was fulfilled. The study was conducted on inpatients of RSUP. H. Adam Malik Medan. Inclusion criteria were Patients with heart failure are enforced based on the Framingham criteria, aged > 18 years old, the subject receives information and gives consent to participate in informed and voluntary research. The exclusion criteria in this study are as follows patients who have a history of kidney disease, pregnant patient, patients receiving nephrotoxic drugs, there are kidney abnormalities in the results of ultrasound, patients who are not willing to take part in the study.

2.2 Definition of heart failure

Definition of Heart failure (HF) according to the current American College of Cardiology Foundation (ACCF) / American Heart Association (AHA) guidelines is a complex clinical syndrome, which is based on the inability of the heart to pump blood throughout the body tissue adequately, due structural and functional disorders of the heart with characteristic symptoms / symptoms (shortness of breath at rest or during activity or feeling tired, not energetic) and signs / signs (fluid retention).[1,11]

2.3. Definition of Ureum and Creatinin

Ureum is the final product of important nitrogen metabolism in humans, which is synthesized from ammonia, carbon dioxide and noted nitrogen amide.Creatinine is metabolic results from creatine and phosphocreatine.

2.4 Statistical Methods

Data were analyzed using SPSS statistics program for Windows, version 23.0; with p value <0.05 considered statistically significant.

3. RESULT

During the study period (June 2017 until the sample is met) in the inpatient ward of RSUP. H. Adam Malik Medan with heart failure in accordance with the inclusion and exclusion criteria in this study. Of the 52 samples in this study, 36 men (69.2%) and 16 women (30.8%) were found. With the most age around 46 years - 65 years as many as 32 people (61.5%).

Tabel 1. Characteristics of research

Variable	Frequency
Gender ; n (%)	
Male	36 (69,2)
Female	16 (30,8)
Age (mean± SD) ; years	52,08 ± 10,52
Age Category ; n (%)	
26-45 years	16 (30,8)
46-65 years	32 (61,5)
>65 years	4 (7,7)
Laboratory (mean±SD)	
Hb gr/dl	12,62 ± 1,97
Leukocytes /mm3	8684,62 ± 2895,46
Platelet /mm3	266346,15 ± 130741,61
Ureum mg/dl	58,27±26,90
Creatinine mg/dl	1,68±0.72
Ejection Fraction (EF) %	36.19±10.43
UA mg/dl	7.62±1.34

In Table 2 it appears the frequency of creatinine increase > 1.3 mg / dl as many as 32 samples (61.5%), with 38 samples (73.1%) with ejection fraction ≤ 40%, whereas urea levels> 55mg / dl are less than normal one.

Tabel 2. Characteristics of kidney function and ejection fraction of the study subjects

Kidney Function	Frequency (n) (%)
UREUM 18 – 55 mg/dl	29 (55,8%)
> 55 mg/dl	23 (44,2%)
CREATININE 0.7 – 1.3 mg/dl	20 (38,5%)
> 1.3 mg/dl	32 (61,5%)
Ejection Fraction ≤ 40 %	38 (73,1%)
> 40 %	14 (26,9%)

Table 3. Characteristics of kidney function based on the Ejection Faction

Kidney Function	Ejection Fraction (mean±SD)	
	EF <= 40 %	EF > 40%
Ureum (mg/dl)	65,26 ± 25,82	39.29 ± 20,21
Creatinine (mg/dl)	1,82 ± 0,77	1,27 ± 0,35

In table 3 it appears that urea and creatinine have a higher mean of ejection fraction ≤ 40% compared to ejection fraction > 40%.

Tabel 4. Relationship of Ejection Fraction to kidney function (Chi-Square analysis)

Kidney Function	Ejection Fraction (n)		p
	EF ≤ 40 %	EF > 40%	
UREUM18 – 55 mg/dl	16	13	0,003
> 55 mg/dl	22	1	
CREATININE 0.7-1.3 mg/dl	11	9	0,045
> 1.3 mg/dl	27	5	

In the table above, based on the Chi-Square analysis, the value of p <0.05 for the relationship between urea Ejection Fraction (p = 0.003) and creatinine (p = 0.045). The analysis concluded that there was a relationship between the Ejection fraction of urea and creatinine.

4. DISSCUSSION

In this study, found 52 heart failure patients who had met the inclusion criteria, which showed that 36 men (69.2%). This is in line with Aronow's research in 2006 in America which stated that the prevalence of heart failure in men was higher than that of women, namely 4.5% for men, with a risk ratio of 1.4.33

Research conducted by Mehta and colleagues in the United States concluded that the incidence of heart failure was 0.3% in men and 0.2% in women, with the incidence of men being greater than women at all ages with a ratio of 1.67.[10,11]

In this study, it was found that the majority of people who experienced heart failure were aged 46-65 years as many as 32 people (61.5%). It will still be the role of age risk factors to be reviewed in terms of gender factors. This is because in terms of sex, a person's vulnerability to heart failure is influenced by the role of female hormones, namely estrogen, which protects women from various cardiovascular diseases. Therefore men are susceptible to heart failure at the age of 50 while women are at the age of 65 or after menopause. [10]

In a study in the United States by the Framinghaim Study it was reported that the prevalence of heart failure sufferers was 0.8% in both sexes at the age of 50-59 years. And the prevalence increased with age, increasing to 6.6% and 7.9%. in men and women aged 80-89 years. [11]

Of the total sample, there were 38 people with EF values ≤ 40 as many as 38 people (73.1%), while EF> 40 were 14 people (26.9%). Creatinine and urea levels in this study increased in the ejection fraction ≤40%. This is in accordance with the 2012 ESC guidline, that more than 50% of heart failure patients were found with EF values ≤ 40.4 Research conducted by Forman et al. In 2004 found 21% of patients with HFpEF, which means that patients with HFrEF were more than HFpEF .[6]

Research conducted by Ronco, et al. States that worsening renal function that is more severe occurs in patients with ejection fraction% 40%, 70% of heart failure patients who experience deteriorating kidney function are patients with HFrEF. [12,13]

Research conducted by Forman et al. In 2004, in which the study found deterioration of renal function in 27% of patients treated for heart failure with an ejection fraction of ≤40%, which was associated with a poor prognosis.[6] Beldhuis dkk in a meta-analysis study in 29,000 people, it was also found that there was an increase in creatinine level pada 0.3 in patients with heart failure which would increase the risk of death (RR: 1.35; 95% CI: 1.25 - 1.46) .[14]

Research conducted by Gottlieb, et al. Found that an increase in creatinine level of 0.2 mg / dl was associated with a worse prognosis in patients with heart failure.[7] However, the large increase in creatinine levels that can worsen the prognosis in heart failure is also debated by researchers.[15]

Research conducted by Sheerin, et al. Found that increasing creatinine levels that were mild to severe together could worsen the prognosis of patients with heart failure.[16]

In heart failure, a decrease in left ventricular systolic or diastolic function results in a number of hemodynamic changes including decreased cardiac output, stroke volume, and arterial filling. This arterial blood pressure reduction is noted by arterial baroreceptors and neurohormonal release occurs as a compensation mechanism aimed at correcting and improving organ perfusion . Activation of RAAS, the sympathetic nervous system, endothelin, and arganin vasopressin promotes fluid retention. If it continues it can cause kidney dysfunction which activates pathological RAAS which will activate the nicotinamide adenine dinucleotide phosphate-oxidase pathway (NADPH-oxidase), causing excessive ROS

formation. Excessive ROS causes an imbalance of NO-ROS which decreases antioxidants and NO, increases oxidative stress in the kidneys and heart, which ultimately activates proinflammatory cytokines such as interleukin-1 (IL-1), IL-6, reactive C protein, and tumor necrosis factor- α (TNF-α) which affects the structure and function of the heart and kidneys.[17,18,19]

In this study, the value of $p < 0.05$ was obtained for the relationship between urea Ejection Fraction ($p = 0.003$) and creatinine ($p = 0.045$). The analysis concluded that there was a relationship between the Ejection fraction of urea and creatinine. This study is consistent with a study conducted by Ronco et al. In 2008 which concluded that deterioration of kidney function was more common in patients with EF ≤ 40, ie 70% of heart failure patients who had worsened renal function were patients with HFrEF.[12,13]

5. CONCLUSION

Based on the results and discussion in this study, it can be concluded:

1. Found men who suffer from heart failure (69.2%). With the most age between 46-65 years (61.5%). The ejection fraction in this study was 73.1% were HFrEF. With a higher creatinine average (1.82 ± 0.77) in the ejection fraction ≤ 40%.
2. Based on Chi-Square analysis, there is a relationship between ejection fraction and urea ($p = 0.003$) and there is a relationship between ejection fraction and creatinine ($p = 0.04$). The analysis concluded that there was a relationship between ejection fraction and kidney function.

REFERENCES

1. Manurung D, Muhadi. Gagal jantung akut. In: Setiati S, Alwi I, Sudoyo AW, K MS, Setiyohadi B, Syam AF, eds. Buku Ajar Ilmu Penyakit Dalam. VI ed. Jakarta – Indonesia: InternaPublishing; 2014:1136-1147.
2. Cagli K, Basar FN, Tok D, Turak O, Basar O. How to interpret liver function test in heart failure patients?.Turk J Gastroenterol. 2015;26:197-203.
3. Hunt SA, Abraham WT, Chin MH, et al. Focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults: A report of the American College of cardiology Foundation/ AHA task force on practise guidelines developed in collaboration with the International Society for Heart and Lung Transplantation. J. Am. Coll. Card. 2009;53:el-e90.
4. European Society of Cardiology (ESC). Esc guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur Heart J. 2012;33:1787-847.
5. Pangabean MM. Gagal jantung. In: Setiati S, Alwi I, Sudoyo AW, K MS, Setiyohadi B, Syam AF, eds.Buku Ajar Penyakit Dalam. VI ed. 2014:1132-1135.
6. Forman DE, Javed B, Wang Y. Incidence, predictors at admission, and impact of worsening renal function among patients hospitalized with heart failure. J. Am. Coll. Cardiol. 2004;43:61-67.
7. Smith LG,Litchtman HJ,Braken BM. Renal impairment and outcomes in heart failure: systematic review and meta-analysis. J Am Coll Cardiol. 2006;47:127-36.
8. Sankar K, Kumar GR, Anandan H. Correlation between ejection fraction and hepatic and renal functions in heart failure patients. International Journal of Scientitic Study. 2016;4:164-167.
9. Mann DL, Chakinala M. Heart failure: pathophysiology and diagnosis. In : Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. Harrison's Principles of Internal medicine. 19th ed. Mc Graw Hill; 2015:1500-1505.
10. Regitz-Zagrosek V, Broket S, Tschope C. Role of Gender in Heart Failure with Normal Left Ventricular Ejection Fraction. Prog Cardiovasc Dis. 2007;49:241–251.
11. Mehta PA, Cowie MR. Gender and heart failure: a population prospctive: Heart jnl.2006;92(3): iii14-iii18.
12. Ronco C, House AA, Haapio M. Cardiorenal syndrome. J Am Coll Cardiol.2008;52:1257-1339
13. Ronco C, Cicoira M, McCullough PA. Cardiorenal syndrome type 1: Pathophysiological crosstalk leading to combined heart and kidney dysfunction in the setting of acutely decompensated heart failure.J Am Coll Cardiol.2012;60(12): 1031-1042.
14. Beldhuis IE, Streng KW, Ter Maaten JM, et al. Renin-angiotensin system inhibition, worsening renal function, and outcome in heart failure patients with reduced and preserved ejection fraction: a meta-analysis of published study data. Circ Heart Fail. 2017;10:e003588.
15. Damman K, Tang WH, Testani JM, McMurray JJ. Terminology and definition of changes renal function in heart failure.Eur Heart J. 2014;35:3413-3416.
16. Sheerin NJ, Newton PJ, Macdonald PS,et al. Worsening renal function in heart failure: the need for a consensus definition.Int J Cardiol. 2014;174:484-491.
17. Liang KV, William AW, Greene EL, Redfield MM. Acute decompensated heart failure and the cardiorenal syndrome. Crit Care Med. 2008;36:S75-88.
18. Adam KF, Fonarow GC, Merman CL. Characteristics and outcomes of patients hospitalized for heart failure in the United States.Am Heart J.2005;149(2):209-216.
19. Hadjiphilippou S, Kon SP. Cardiorenal syndrome: Review of our current understanding. J Roy Soc Med. 2016;109(1):12-17.