

Correlation Between Left Ventricular Ejection Fraction and Anemia in Patients With Congestive Heart Failure in dr. Zainoel Abidin General Hospital Banda Aceh

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Abstrak: Gagal jantung kongestif merupakan kondisi ketika jantung tidak mampu memompa darah secara adekuat untuk memenuhi kebutuhan tubuh. Fraksi ejeksi ventrikel kiri (LVEF) yang diperoleh melalui pemeriksaan ekokardiografi mencerminkan proporsi darah yang dipompa oleh ventrikel kiri pada setiap kontraksi. Anemia didefinisikan sebagai penurunan jumlah sel darah merah atau kapasitas pengangkutan oksigen, sehingga distribusi oksigen ke jaringan menjadi tidak adekuat. Anemia merupakan salah satu komorbid tersering pada pasien gagal jantung dan merupakan prediktor independen terhadap morbiditas dan mortalitas. Penelitian ini bertujuan untuk mengetahui hubungan antara LVEF dan anemia pada pasien gagal jantung kongestif. Penelitian ini merupakan studi analitik observasional dengan desain potong lintang. Sebanyak 137 subjek diperoleh melalui teknik consecutive sampling dari data rekam medis. Dari seluruh subjek, sebanyak 63 pasien (46,0%) termasuk HFrEF, 21 pasien (15,3%) HFmrEF, dan 53 pasien (38,7%) HFpEF. Anemia ditemukan pada 77 pasien (56,2%), yang terdiri dari anemia ringan (57,1%), sedang (33,8%), dan berat (9,1%). Analisis korelasi Spearman menunjukkan adanya hubungan yang bermakna antara LVEF dan anemia ($p = 0,019$). Terdapat hubungan yang signifikan antara fraksi ejeksi ventrikel kiri dan anemia pada pasien gagal jantung kongestif.

Kata kunci: Anemia, Gagal jantung kongestif, Fraksi ejeksi ventrikel kiri

Abstract: Congestive heart failure is a condition in which the heart is unable to pump sufficient blood to meet the body's needs. Left ventricular ejection fraction (LVEF), obtained from echocardiography, reflects the proportion of blood ejected by the left ventricle during each contraction. Anemia is defined as a reduced number of red blood cells or decreased oxygen-carrying capacity, resulting in inadequate oxygen delivery to tissues. It is a common comorbidity in heart failure and an independent predictor of morbidity and mortality. This study aimed to determine the correlation between LVEF and anemia in patients with congestive heart failure. This study employed an observational analytic design with a cross-sectional design. A total of 137 subjects were selected using consecutive sampling from medical records. Among the subjects, 63 (46.0%) had HFrEF, 21 (15.3%) HFmrEF, and 53 (38.7%) HFpEF. Anemia was found in 77 patients (56.2%), consisting of mild (57.1%), moderate (33.8%), and severe anemia (9.1%). Spearman correlation analysis showed a significant association between LVEF and anemia ($p = 0.019$). A significant correlation was found between LVEF and anemia in patients with congestive heart failure.

Keywords: Anemia, Congestive heart failure, Left ventricular ejection fraction

Introduction

Heart failure is a major global health problem and remains one of the leading causes of morbidity and mortality worldwide. It is a clinical syndrome characterized by the inability of the heart to pump sufficient blood to meet the metabolic demands of the body. According to the European Society of Cardiology (ESC), heart failure commonly presents with symptoms such as

dyspnea, fatigue, and peripheral edema (McDonagh et al., 2021). Globally, approximately 64.3 million people are affected by heart failure (Groenewegen et al., 2020). In addition, anemia remains a major public health issue, with the World Health Organization (WHO) reporting that iron deficiency anemia affects approximately 1.5 billion people worldwide (Jansen, 2019). In Indonesia, data from the 2018 Basic Health Research (Riskesdas) reported that the prevalence of heart failure reached 1.5%, equivalent to approximately 1,017,290 individuals (Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan, 2018).

The severity and functional status of heart failure can be evaluated using left ventricular ejection fraction (LVEF). LVEF is an echocardiographic parameter that measures the percentage of blood ejected from the left ventricle during each cardiac contraction (Azam & Muhammad, 2020). A reduction in LVEF reflects impaired ventricular systolic function, which subsequently decreases systemic blood perfusion (Branca et al., 2020). Based on LVEF values, heart failure is classified into heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF), and preserved ejection fraction (HFpEF).

Anemia is defined as a reduction in the number of red blood cells or a decrease in oxygen-carrying capacity, resulting in inadequate oxygen delivery to tissues (Chaparro & Suchdev, 2019). Anemia is frequently identified as a comorbidity in patients with heart failure and has been recognized as an independent predictor of hospitalization, morbidity, and mortality (Beladan & Botezatu, 2021). In patients with heart failure, reduced hemoglobin levels may contribute to impaired tissue oxygenation, neurohormonal activation, and cardiovascular remodeling, including an increase in left ventricular muscle hypertrophy (Sutil-Vega et al., 2019). Consequently, the coexistence of anemia may aggravate the clinical condition and worsen the prognosis of patients with heart failure.

Several previous studies have demonstrated an association between anemia and the severity of heart failure. Study reported that anemia was positively correlated with both mortality and severity of heart failure (Yazdanfar et al., 2022). Other study also found that anemia was common among patients with heart failure, particularly in patients with more severe clinical manifestations (Nathaniel et al., 2020). Furthermore, studies suggested that variations in LVEF categories may influence the prevalence of anemia, with HFpEF patients showing a higher incidence of anemia compared with other heart failure phenotypes (Savarese et al., 2019).

Despite these findings, evidence regarding the relationship between LVEF and anemia remains inconsistent, particularly in developing countries and local hospital-based populations. In addition, limited data are available regarding the correlation between LVEF categories and anemia among patients with congestive heart failure in Indonesia, especially in Aceh. Therefore, further

investigation is necessary to clarify the relationship between cardiac systolic function and anemia in this population. This study aimed to determine the correlation between LVEF and the incidence of anemia among patients with congestive heart failure treated at Dr. Zainoel Abidin General Hospital Banda Aceh.

Method

This study employed an observational analytic method with a cross-sectional approach. The study was conducted at Dr. Zainoel Abidin General Hospital, Banda Aceh, using medical record data from 2020. The study population included all hospitalized patients diagnosed with congestive heart failure who met the inclusion and exclusion criteria. Inclusion criteria were patients with complete medical records, including age, sex, New York Heart Association (NYHA) classification, and LVEF. Patients with hematological disorders, malignancy, acute hemorrhage, hereditary diseases, or chronic renal failure were excluded. Samples were obtained using a consecutive sampling technique. Data were analyzed using univariate and bivariate methods. The relationship between LVEF and anemia was assessed using the Spearman rank correlation test with a significance level of $p < 0.05$. This study was approved by the Health Research Ethics Commission of Faculty of Medicine, Universitas Syiah Kuala – Dr. Zainoel Abidin Hospital (No: 270/EA/FK-RSUDZA/2021).

Result and Discussion

Respondents in this study were patients with congestive heart failure at Dr. Zainoel Abidin General Hospital Banda Aceh in 2020. A total of 137 cases met the inclusion and exclusion criteria. The baseline characteristics of the study population are presented in Table 1. The majority of patients were male (73%), aged 56–65 years (29.9%), and classified as NYHA functional class II (43.8%). Most patients were categorized as HFrEF (46.0%). Anemia was found in 56.2% of patients, with mild anemia being the most common degree (57.1%). Table 1 shows that the majority of patients with congestive heart failure in this study are male as many as 100 respondents (73%), the age group 56-65 years as many as 41 respondents (29.9%) and the NYHA II functional class as many as 60 respondents (43.8%). The majority of patients with congestive heart failure in this study were in Heart Failure with reduced Ejection Fraction (HFrEF) as many as 63 respondents (46.0%). Congestive heart failure patients who had anemia in this study were 77 respondents (56.2%) and 60 respondents (43.8%) who had not anemia. Patients with congestive heart failure who experienced anemia in this study were mostly mild anemia degrees as many as 44 respondents (57.1%).

Table 1. Baseline characteristics of patients

Variable	Cases (n)	Percentage (%)
Gender		
Male	100	73.0
Female	37	27.0
Age Group		
16 – 25	5	3.6
26 – 35	7	5.1
36 – 45	11	8.0
46 – 55	33	24.1
56 – 65	41	29.9
> 65	40	29.1
NYHA Functional Class		
I	5	3.6
II	60	43.8
III	58	42.3
IV	14	10.2
LVEF		
HFrEF	63	46.0
HFmrEF	21	15.3
HFpEF	53	38.7
Incidence of Anemia*		
Anemia	77	56.2
No Anemia	60	43.8
Degree of Anemia**		
Mild Anemia	44	57.1
Moderate Anemia	26	33.8
Severe Anemia	7	9.1

NYHA, New York Heart Association; LVEF, Left Ventricular Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HFmrEF, Heart Failure with mildly reduced Ejection Fraction; HFpEF, Heart Failure with preserved Ejection Fraction; *Classification of anemia based on European Society of Cardiology/ESC; **Classification of anemia based on WHO Cut-offs Point Anemia

Left Ventricular Ejection Fraction (LVEF)

The results indicate that most respondents in this study are HFrEF, as many as 63 respondents (46.0%). The results of this study are in line with the study of Savarese et al who stated that the LVEF of patients with congestive heart failure was most commonly found in HFrEF, which is 55%. The incidence of heart failure was more in HFrEF than HfpEF (Savarese et al., 2019). Other studies that support this research are the Cui et al study was showed distribution of heart failure most commonly found in HFrEF (53.0%) compared HFpEF (26,6%) and HFmrEF (10,4%). Increase HFrEF associated with highest cardiovascular and heart failure readmission rate, cardiovascular therapy (ACEIs, ARBs, aldosterone antagonists, statins, and platelet inhibitors), and history of revascularization therapy (Cui et al., 2020).

Anemia

The results of this study indicate that most patients with congestive heart failure who experienced anemia in this study were at a mild degree of anemia as many as 44 respondents (32.1%). The results of this study are in line with study from Chairat et al, which stated that heart failure patients who experienced anemia found to be 62,6% (Chairat et al., 2020). The incidence

of anemia can be explained by the higher age and the number of comorbidities experienced by the patient. Patients with anemia also had characteristics reflecting more severe heart failure in a higher NYHA functional class and lower systolic blood pressure (Savarese et al., 2019).

Severity of Anemia

The study showed that the patients with congestive heart failure who had anemia in this study were 77 respondents (56.2%). The results of this study in line with the study by Pintér et al stated that heart failure patients who had mild anemia predominated in heart failure patients as many as 52,4% (Pinter et al., 2022). Nathaniel et al study supported this study which stated that most patients with heart failure experienced mild anemia as many as 50.6% of respondents (Nathaniel et al., 2020).

Table 2. Relationship Between LVEF and Anemia

LVEF	No Anemia		Anemia						Total	P-value		
			Mild Anemia		Moderate Anemia		Severe Anemia					
	n	%	n	%	n	%	n	%				
HFrEF	35	25.5	17	12.4	11	8.0	0	0.0	63	46.0	0.019*	0.201
HFmrEF	7	5.1	6	4.4	5	3.6	3	2.2	21	15.3		
HFpEF	18	13.1	21	15.3	10	7.3	4	2.9	53	38.7		
Total	60	43.8	44	32.1	26	19.0	7	5.1	137	100.0		

HFrEF, Heart Failure with reduced Ejection Fraction; HFmrEF, Heart Failure with mildly reduced Ejection Fraction; HFpEF, Heart Failure with preserved Ejection Fraction; *r*, coefficient correlation; *Statistically significant if p-value less than 0.05

The relationship between LVEF and anemia is presented in Table 2. The results showed that anemia was more prevalent than non-anemia across all LVEF categories. HFpEF patients had the highest proportion of anemia, particularly mild anemia. Spearman correlation analysis demonstrated a significant relationship between LVEF and anemia ($p = 0.019$) with a weak positive correlation ($r = 0.201$). This indicates that higher LVEF was associated with a higher incidence of anemia. This finding suggests that patients with higher LVEF, particularly those with HFpEF, may have a greater burden of comorbidities contributing to the higher prevalence of anemia.

Relationship between LVEF and Anemia

This study is in line with Savarese et al, which stated that patients with heart failure experienced anemia as many as 34%. The highest incidence of anemia occurred in HFpEF as many as 41%. There was show LVEF correlated with incidence of anemia ($p\text{-value} < 0,01$). A LVEF was independently associated with a higher probability of anemia. This result can be explained by older age and the number of comorbidities associated with anemia in patients with a higher LVEF (Savarese et al., 2019). The study Ambrosy et al. was showed correlation between the incident of anemia and the spectrum of LVEF with $d\text{-value} = 0,11$ ($d\text{-value} \geq 0,10$ was considered a meaningful

difference). The crude rate of anemia incident was higher for HFpEF compared with HFmrEF or HFrEF (Ambrosy et al., 2019).

The study of Gupta et al showed different results, the LVEF was not significantly different with $p\text{-value} = 0,750$ between anemia and non-anemia in heart failure patients. The main difference between the study of Savarese et al, Ambrosy et al, and Gupta et al, is the study sample. The sample in the study of Savarese et al and Ambrosy et al was taken from various levels of LVEF including HFrEF, HFmrEF, and HFpEF, while the sample in the study of Gupta et al, was only taken from patients with HFpEF (Gupta et al., 2023). Study by Kurz et al, stated that more than half of patients with heart failure experience anemia from time to time with $p\text{-value} \leq 0,001$ which indicates a significant relationship between LVEF and the incidence of anemia (Kurz et al., 2020).

Anemia is an important prognostic factor in heart failure patients and is a common comorbidity in heart failure patients (Ezekowitz et al., 2021). The study of Bryan Nathaniel et al. supports this study which states that increasing NYHA functional class is associated with a decrease in LVEF percentage. Decreased LVEF will activate the body's compensatory mechanisms for the heart to function normally. The body's compensatory mechanism results in mild to moderate anemia (Nathaniel et al., 2020). The body's activated compensatory mechanisms are the renin-angiotensin-aldosterone system/RAAS and the sympathetic nervous system/SNS, increasing plasma volume and causing hemodilution. Hemodilution as a causative factor in almost half of all patients with heart failure (Scicchitano et al., 2023). Patients with anemia in congestive heart failure due to hemodilution only need to adjust the diuretic dose to reduce plasma volume and effectively treat anemia in heart failure. The difference between anemia due to hemodilution and true anemia is the results of the red blood cell count/RBC examination. True anemia indicates a decrease in hemoglobin, hematocrit, and red blood cell count/RBC. Anemia due to hemodilution shows an increase in plasma volume which causes the hemoglobin concentration to decrease. It shows a picture of anemia and a normal red blood cell count/RBC (Kittipibul et al., 2023).

The results of the study conducted by Migone et al strengthen the results of this study by stating that mild anemia is most common in heart failure patients compared to moderate and severe anemia (Pinter et al., 2022). The results of this study indicate that mild anemia is more common in heart failure patients, especially at higher LVEF. These results are also associated with a high mortality rate in heart failure patients, which makes severe anemia difficult or undiagnosed before the patient dies, so severe anemia is rarely found in heart failure patients (Nathaniel et al., 2020). Decreased hemoglobin in heart failure patients is associated with sodium and water retention reduced renal blood flow, and neurohormonal activation (Magri & Martino, 2019).

Patients with severe anemia and normal left ventricular function will experience decrease

oxygen-carrying capacity so that non-hemodynamic and hemodynamic compensation mechanisms will occur. Non-hemodynamic responses to hypoxia include increased erythropoiesis to increase oxygen transport capacity, such as changes in the Hgb-oxygen dissociation curve that show decreased hemoglobin binding for greater oxygen distribution to peripheral tissues (Bianchi & von Haehling, 2023; Min et al., 2020). The main hemodynamic factors are increased cardiac output mediated by lower afterload, increased preload, and positive inotropic and chronotropic effects. Decreased afterload is due to vasodilation and decreased vascular resistance resulting from lower blood viscosity, hypoxia-induced vasodilation, and increased nitric oxide activity. These hemodynamic changes will progress to cardiac enlargement and left ventricular hypertrophy in the long term (Kurbonova & Lapašova, 2022).

The treatment of erythropoietin-stimulating agent in symptomatic heart failure patients with mild anemia could improve exercise tolerance and show improvement in clinical symptoms. Improvements in clinical symptoms due to the administration of erythropoietin-stimulating agents showed that the complaints of shortness of breath and fatigue decreased, LVEF increased, and the length of stay/LOS in heart failure patients decreased (Anand & Gupta, 2021). Management of anemia in congestive heart failure is adjusted to the cause of anemia. Erythropoietin-stimulating agent therapy is considered as a therapy to increase hemoglobin and treat anemia in heart failure patients. Treatment of anemia with such therapy can reduce oxidative stress (Siddiqui et al., 2022).

The consequences of treating anemia in heart failure with erythropoietin-stimulating agents have both beneficial and detrimental effects. Beneficial effects include increased oxygen delivery and cardioprotective effects. Adverse effects are increased viscosity, vascular resistance, hypercoagulability, increased blood pressure, and affect the effectiveness of treatment on heart failure.¹⁰ The administration of erythropoietin-stimulating agent therapy does not improve the prognosis and has a worse risk of complications so that erythropoietin-stimulating agent therapy is not indicated for the treatment of anemia in heart failure (Sharma et al., 2021).

Conclusion

Patients with congestive heart failure at Dr. Zainoel Abidin General Hospital were predominantly classified as HFrEF, while anemia was more frequently observed in HFpEF patients. More than half of the patients experienced anemia, with mild anemia being the most common degree. A statistically significant correlation was found between LVEF and anemia, although the strength of the correlation was low.

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