Research Article

Atrial Fibrillation as a Predictor of Short-term Rehospitalization in Patients with Heart Failure Reduced Ejection Fraction

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ABSTRACT: Background: Cardiovascular diseases accounted for an estimated 19.8 million deaths globally in 2019, representing 32% of all deaths, with heart failure (HF) contributing to 38% of these deaths.
Aim: This study aims to explore the relationship between atrial fibrillation (AF) and the risk of short-term rehospitalization in patients with heart failure with reduced ejection fraction (HFrEF).
Methods: A prospective cohort study was conducted at the Makassar Cardiac Center of RSUP Dr. Wahidin Sudirohusodo from February 2023 to February 2024. Data were collected from patients diagnosed with HFrEF within the first 24 hours of hospital admission. Follow-up assessments were performed 90 days after discharge to evaluate rehospitalization rates among the participants.
Results: Among 110 patients with HFrEF, the mean age was 56.8 $\pm$ 13.0 years, and 67.3% were male. Patients with AF had an eightfold higher risk of rehospitalization at 30 days ($p = 0.039$) and a 1.4-fold higher risk at 90 days ($p = 0.003$) compared to those without AF. Additionally, for every 1 bpm increase in heart rate, the odds of rehospitalization at 90 days increased by 2.4% ($p = 0.030$). However, the subtype of AF did not significantly affect the likelihood of rehospitalization.
Conclusions: AF was significantly associated with an increased risk of rehospitalization in patients with HFrEF. These findings underscore the importance of early identification and management of AF in this patient population to potentially reduce rehospitalization rates and improve clinical outcomes.

Keywords: atrial fibrillation, rehospitalization, heart failure reduced ejection fraction

I. INTRODUCTION

Cardiovascular disease has remained the leading cause of death worldwide for the past 20 years. Globally, an estimated 19.8 million deaths were attributed to cardiovascular disease in 2019, accounting for approximately 32% of all deaths, with heart failure (HF) contributing to 38% of these cases, representing a substantial proportion [1]. In Indonesia, congestive heart failure is the second leading cause of mortality after stroke [2]. According to data from the Global Health Data Exchange (GHDx), the global prevalence of HF reached approximately 64.34 million cases in 2020, resulting in nearly 9.91 million deaths and imposing an estimated economic burden of 346.17 billion US dollars per patient [3].

As a disease that predominantly affects older adults, HF is rarely present as an independent disease. More than 80% of patients with HF have more than two coexisting chronic conditions [4]. Among these, atrial fibrillation (AF) is particularly significant due to its frequent coexistence with HF. This combination has been described as an emerging cardiovascular epidemic because of its association with increased morbidity, mortality, and healthcare costs. Therefore, the management of AF in the HF population has been the focus of cardiovascular research [5].

In Indonesia, a telemedicine-based study conducted in Makassar reported a prevalence of AF of approximately 0.96%, with a higher frequency in men than in women. A normal ventricular response in AF was more commonly observed than AF with rapid or slow ventricular responses [6]. Evidence from the Framingham Heart Study demonstrated that AF is independently associated with a 1.5- to 1.9-fold increased risk of mortality. Furthermore, a systematic review including 13 studies with a total of 54,587 patients with both AF and HF reported that patients with reduced ejection fraction had higher mortality compared with those with preserved ejection fraction [7].

Previous studies have also demonstrated that uncontrolled AF in patients with HF contributes significantly to rehospitalization. Rehospitalization represents a major clinical and economic challenge, affecting both patients and healthcare systems. In the United States, the cost of a single readmission for HF can exceed 14,000 US dollars [8]. Heart failure with reduced ejection fraction (HFrEF), a severe form of HF, is often associated with high rehospitalization rates and poor clinical outcomes [9]. Among several contributing factors, AF is one of the most common arrhythmias in patients with this condition and may worsen hemodynamic instability and adversely affect clinical outcomes [10, 11].

In addition to the presence of AF, heart rate (HR) is an important clinical parameter in the management of patients with HF [12].

Poorly controlled HR may exacerbate symptoms, impair cardiac function, and increase the likelihood of rehospitalization. Furthermore, variations in the type of AF, such as AF with a rapid ventricular response or AF with a normal ventricular response, may have different implications for the risk of rehospitalization. Understanding whether specific AF subtypes are associated with a higher risk of rehospitalization may help guide more targeted management strategies for patients with HFrEF. However, evidence regarding the influence of AF, HR, and AF subtype on rehospitalization among this population remains limited.

Therefore, this study aimed to explore the relationship between AF, HR, and AF subtype and the risk of short-term rehospitalization among patients with HFrEF. The findings of this study are expected to provide better insights into optimizing clinical management and reducing rehospitalization.

II. METHODS

A. Research design

This study employed a prospective cohort design. Observations were conducted prospectively, with data collected during hospitalization among patients diagnosed with congestive HF. Clinical data were obtained within the first 24 hours of hospitalization. Following discharge, patients were followed for 90 days to evaluate the occurrence of rehospitalization after outpatient treatment.

B. Study setting and period

Sampling was initiated in March 2023 and continued until the required sample size was reached. The study was conducted at the Integrated Heart Center of Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia.

C. Population and sampling

The study population included all patients admitted to the Integrated Heart Center inpatient unit of Dr. Wahidin Sudirohusodo Hospital with a diagnosis of congestive HF who were recorded in the Heart Failure Registry. Study participants were recruited consecutively from the time of hospital admission until discharge using data obtained from medical records and hospital electronic systems. All eligible patients who met the inclusion and exclusion criteria were enrolled until the required sample size was reached.

Participants were eligible for inclusion if they were hospitalized patients diagnosed with AF confirmed by electrocardiography (ECG), had a diagnosis of HF, were 18 years of age or older, and had a left ventricular ejection fraction (LVEF) <50%. Patients were excluded if they had undergone interventional procedures aimed at correcting structural heart disease, such as cardiac resynchronization therapy or valvular replacement; had atrioventricular dyssynchrony, including total atrioventricular block; were unwilling to participate in the study procedures; were lost to follow-up; or died during hospitalization.

D. Follow-up

Follow-up assessments were conducted for 90 days after hospital discharge. Patient follow-up was performed through outpatient clinic visits during routine follow-up appointments in the first and second months after discharge, or through telephone interviews when in-person visits were not possible. Rehospitalization events were further verified by reviewing the hospital inpatient registration database to ensure accurate identification of readmission episodes.

III. RESULTS

A. Subject characteristics

This study analyzed patients recorded in the Heart Failure Registry at our institution. A total of 215 patients with HF were initially identified. After applying the inclusion and exclusion criteria, 110 patients were eligible for analysis. The study population was divided into two groups: patients with AF (n = 36) and those without AF (n = 74).

Among the 110 patients with HFrEF, 74 (67.3%) were male and 36 (32.7%) were female. The mean age of the participants was 56.8 ± 13.0 years. The mean body weight was 61.8 ± 13.0 kg, and the mean height was 160.6 ± 7.2 cm. The average body mass index (BMI) was 23.8 ± 4.0 kg/m^2. The mean HR was 99.1 ± 23.6 bpm. Regarding comorbidities, 60 patients (54.5%) had hypertension and 39 patients (35.5%) had diabetes mellitus. In terms of pharmacological therapy, 26 patients (23.6%) received beta-blockers, while 72 patients (65.5%) were treated with ACE inhibitors. Additionally, 38 patients (34.5%) received digoxin. The mean length of hospital stay was 9.2 ± 4.4 days. Detailed baseline characteristics of the participants are provided in Table 1.

Table 1. Baseline characteristics of research participants

Variables/Categories	Frequency/Mean	Percent/Std. Deviation
Gender		
Woman	36	32.7%
Man	74	67.3%
Age	56.8	± 13.0
Body Weight (Kg)	61.8	± 13.0
Height (Cm)	160.6	± 7.2
BMI (Kg/m^2)	23.8	± 4.0
Heart Rate	99.0	± 23.5
Atrial Fibrillation		
Yes	36	32.7%
No	74	67.3%
Hypertension		
Yes	60	54.5%
No	50	45.5%
Diabetes		
Yes	39	35.5%
No	71	64.5%
Beta Blockers		
Yes	26	23.6%
No	84	76.4%
ACE-I		
Yes	72	65.5%
No	38	34.5%
Digoxin		
Yes	38	34.5%
No	72	65.5%
Length Of Stay	9.2	± 4.4

Table 2 presents the rehospitalization status of the study subjects at 30 and 90 days. Within 30 days, 105 patients (95.5%) were not rehospitalized, while five patients (4.5%) experienced rehospitalization. At 90 days, 81 patients (73.6%) remained free from rehospitalization, whereas 29 patients (26.4%) experienced rehospitalization.

B. Bivariate analysis of AF and Non-AF groups

1) Bivariate analysis of AF and rehospitalization within 30 days. Table 3 presents the bivariate analysis between AF and rehospitalization within 30 and 90 days. Among 36 subjects with AF, 32 (29.1%) did not experience rehospitalization, while four (3.6%) were rehospitalized at 30 days. Overall, 105 subjects (95.5%) were not rehospitalized within 30 days, while five (4.5%) were rehospitalized. The difference between groups was statistically significant (p = 0.039). At 90 days, Among subjects with AF, sixteen (14.5%) were rehospitalized. While among subjects without AF, thirteen (11.8%) were rehospitalized. Overall, 81 subjects (73.6%) were not rehospitalized within 90 days, while 29 (26.4%) experienced rehospitalization. The difference between groups with and without AF was statistically significant (p = 0.003).

Table 2. Rehospitalization status of research participants

Variable	Frequency/Mean	Percent/Std. Deviation
30 Days Rehospitalization		
No Rehospitalization	105	95.5%
Rehospitalization	5	4.5%
90 Days Rehospitalization		
No Rehospitalization	81	73.6%
Rehospitalization	29	26.4%

Table 3. Bivariate analysis of atrial fibrillation and rehospitalization events within 30 and 90 days

30 days	Rehospitalization	No Rehospitalization	p-value
Atrial Fibrillation (n=36)	4 (3.6%)	32 (29.1%)	0.039*
No AF (n=74)	1 (0.9%)	73 (66.4%)	
Total (n=110)	5 (4.5%)	105 (95.5%)	
90 days	Rehospitalization	No Rehospitalization	p-value
Atrial Fibrillation (n=36)	16 (14.5%)	20 (18.2%)	0.003*
No AF (n=74)	13 (11.8%)	61 (55.5%)	
Total (n=110)	29 (26.4%)	81 (73.6%)	

Table 4 illustrates the distribution of AF types based on 30-day and 90-day rehospitalization status. At 30 days, of the 36 patients with AF, the majority did not experience rehospitalization (88.9%). Rapid AF was the most common type (47.2%), followed by Normo AF (41.7%). No significant association was observed between AF type and rehospitalization within 30 days (p = 0.747). At 90 days, rehospitalization occurred in 10 patients (27.8%) with Rapid AF and six patients (16.7%) with Normo AF. However, the association between AF type and 90-day rehospitalization was not statistically significant (p = 0.093).

C. Multivariate analysis of 90-day rehospitalization incidence

Variables remained in the final multivariable logistic regression model: atrial fibrillation and heart rate. AF was significantly associated with 90-day rehospitalization (p = 0.029), with an odds ratio (OR) of 1.41 (95%CI 1.16 – 2.11). Heart rate was also significantly associated with the outcome (p = 0.036), with an OR of 1.02 (95% CI 1.01–1.046), with each increase of 1 time per minute in HR was associated with a 2.4% increase in the odds of rehospitalization at 90 days (Table 5).

Table 4. The distribution of AF types based on 30-day and 90-day rehospitalization status

AF types	30-Day Rehospitalization Status		Total (n=36)	p-value
	Rehospitalization	No Rehospitalization		
Rapid AF	2 (5.6%)	15 (41.7%)	17 (47.2%)	0.747
Normo AF	2 (5.6%)	13 (36.1%)	15 (41.7%)	
Paroxysmal AF	0 (0.0%)	4 (11.1%)	4 (11.1%)	
Total	4 (11.1%)	32 (88.9%)	36 (100.0%)	
Rapid AF	10 (27.8%)	7 (19.4%)	17 (47.2%)	0.093
Normo AF	6 (16.7%)	9 (25.0%)	15 (41.7%)	
Paroxysmal AF	0 (0.0%)	4 (11.1%)	4 (11.1%)	
Total	16 (44.4%)	20 (55.6%)	36 (100.0%)	

Table 5. Multivariable analysis analysis of 90 day rehospitalization events

Variable	Odds ratio	95%CI Lower	95%CI Upper	p-value
Sex	1.586	0.553	4.551	0.391
Age	1.002	0.965	1.039	0.931
BMI	0.892	0.782	1.018	0.091
Heart rate	1.024	1.002	1.046	0.030*
Hypertension	1.620	0.627	4.189	0.319
Atrial Fibrillation	1.412	1.153	2.109	0.029*
Type 2 DM	1.017	0.327	3.160	0.977
Beta Blockers	1.253	0.370	4.242	0.717
ACEi	1.617	0.620	4.222	0.326
Digoxin	0.652	0.160	2.654	0.550

IV. DISCUSSION

The management of HF requires a comprehensive and sustainable approach due to the chronic nature of the disease. One of the major challenges in HF management is hospital readmission. Readmissions have a substantial impact not only on patients but also on healthcare systems, as they increase the economic burden associated with HF treatment. The EVEREST study reported that the readmission rate among patients with systolic HF reached 24% within 30 days after discharge and increased to 46% within 60 days [13]. These findings are consistent with our study, which showed an increase in rehospitalization rates at the 90-day follow-up.

AF has previously been identified as a risk factor for reduced exercise capacity, stroke, and mortality in patients with HF. However, limited evidence is available regarding the impact of AF on the response to inpatient therapy for worsening HF and the subsequent risk of hospitalization. In the present study, patients with HF and AF had a significantly higher risk of rehospitalization, supporting the growing body of evidence on the interaction between AF and HF [14].

Our study demonstrates that AF is strongly associated with an increased risk of rehospitalization among patients with HF, both within 30 days and 90 days after discharge. These results are consistent with previous studies identifying AF as an important factor associated with increased hospital readmission in HF patients, such as the study by Sadiq et al., which states that AF is one of the conditions associated with readmission in HF patients [15]. In our study, the risk of rehospitalization was significantly higher in patients with AF, with statistically significant results for both the 30- and 90-day periods. These findings underline the importance

of effective rate control in patients with AF as a strategy to reduce the frequency of rehospitalization and the financial burden on the health system [15].

HR data in our study also showed that patients with AF had a significantly higher mean HR compared with those without AF. Elevated HR may exacerbate HF by increasing myocardial oxygen demand and reducing diastolic filling time, thereby contributing to a higher risk of rehospitalization. These findings emphasize the importance of effective HR control in patients with AF and are consistent with current management recommendations for HF patients with AF, which include both rhythm and rate control strategies [16].

Our results are also in line with previous studies showing that patients with uncontrolled AF experienced higher 30-day readmission rates for HF exacerbations compared with patients with normal heart rhythm at readmission [10]. AF has also been identified as a predictor of adverse cardiovascular outcomes in the CHARM study and was included among the predictors of mortality and readmission in a retrospective analysis of African-American and Hispanic patients hospitalized for HF. Maintaining sinus rhythm in patients with HF has been associated with lower readmission rates and poorer outcomes [17].

Previous studies further support our findings by demonstrating that the prevalence of AF increases with the severity of HF according to the New York Heart Association (NYHA) classification. For example, the prevalence of AF increases from relatively low levels in NYHA class I to approximately 40% in NYHA class IV. Pathophysiological mechanisms such as atrial systolic dysfunction, impaired diastolic filling, and rapid ventricular response associated with AF may contribute to worsening HF and an increased risk of rehospitalization. Our findings strengthen these observations and highlight the need for improved management strategies for AF in this condition [10].

In addition, our results align with previous studies that recommend an HR control strategy rather than rhythm control for HF patients with AF [10]. Effective rate control has been associated with reduced hospitalization rates and a lower healthcare cost burden [5].

However, our study also found that AF subtype, including Rapid, Normo, or Paroxysmal, was not significantly associated with the risk of rehospitalization. This finding differs from some studies suggesting that AF subtypes may influence clinical outcomes. Our results indicate that the presence of AF itself, rather than its specific subtype, may play a more important role in increasing the risk of rehospitalization.

Our findings provide additional context when compared with international data. Gangu et al. reported that the 30-day rehospitalization rate in the United States (16.7%) was higher than that observed in Australia (9.9%) and similar to the national rehospitalization rate in the United States (18.2%). In our study, the 30-day rehospitalization rate was lower (4.5%); however, AF remained a significant risk factor for rehospitalization, highlighting the importance of appropriate management strategies for patients with AF [18].

This study has several limitations. First, this study was conducted at a single tertiary referral center, which may limit the generalizability of the findings. Second, the relatively small sample size may have limited the statistical power to detect associations in certain subgroup analyses, particularly for different AF subtypes. Third, the follow-up period was limited to 90 days and may not fully reflect long-term rehospitalization patterns in patients with HF. In addition, several potential confounding factors, including medication adherence, post-discharge management, and clinical biomarkers, were not evaluated. Future multicenter studies with larger sample sizes and longer follow-up periods are needed to confirm these findings and better assess the long-term relationship between atrial fibrillation and rehospitalization in patients with HF.

V. CONCLUSIONS

AF was significantly associated with an increased risk of rehospitalization, showing an eightfold higher risk at 30 days and a 2.5-fold higher risk at 90 days compared with patients without AF. HR was also significantly related to the risk of rehospitalization in patients with HFrEF. However, the type of AF was not significantly associated with the risk of rehospitalization.

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CONFLICT OF INTEREST

The authors declare no competing interests.

ETHICAL APPROVAL AND INFORMED CONSENT

Ethical approval was obtained from the Research Ethics Committee Board, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia. Written informed consent was obtained from all participants. All procedures involving human subjects were performed in accordance with the ethical standards of the institutional and/or national research committee and with the principles of the 1964 Declaration of Helsinki and its subsequent amendments.

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