## *Original Article*
# Atrial fibrillation: a leading cause of heart failure-related hospitalizations; a dual epidemic

Asrar Ahmed[1], Waqas Ullah[1], Ishtiaq Hussain[2], Sohaib Roomi[1], Yasar Sattar[1,3], Faizan Ahmed[1], Rehan Saeed[1], Ammar Ashfaq[1]

[1]Internal Medicine, Abington-Jefferson Health, Abington, USA; [2]Gastroenterology, Cleveland Clinic, Florida, USA; [3]Internal Medicine, Icahn School of Medicine at Mount Sinai-Elmhurst Hospital, New York, USA

**Abstract:** Background: Atrial fibrillation (AF), and heart failure (HF) are a major cardiovascular epidemic over the last decade. The prevalence and rehospitalization of heart failure are on rising edge, and many factors are responsible for these re-exacerbations of heart failure. In this study, we sought to determine an association of a risk factor for frequent rehospitalization of heart failure at our institute. We aimed to find the re-admission rate, heart rate, and rhythm of heart failure exacerbation. Methods: We performed a single-center retrospective study at the Abington Hospital - Jefferson health and 418 patients having a history of heart failure, and AF were selected. The heart failure readmission rate (days), heart rate, and rhythm were analyzed. Results: The mean age of the included population was 82.8 years SD ± 9.2. About 53% had AF with a mean heart rate 90 SD ± 21 bpm, and 47% had normal sinus rhythm (NSR) with a mean heart rate of 78 ± 16 bpm on re-admission. This difference was statistically significant (p=0.02). The mean re-admission rate for atrial fibrillation was 27.49 days SD ± 18.97, compared to 32.68 SD ± 20.26 days for NSR, statistically significant (p=0.007) and the Pearson Chi-square was also significant P = 0.006. Conclusion: There is a significantly increased rate of re-admission in heart failure patients with atrial fibrillation with a rapid ventricular rate. Efforts should be taken to keep the patient in NSR or controlled AF to minimize the rehospitalization rate, and this, in turn, reduces the financial burden on patients and institutes.

**Keywords:** Atrial fibrillation, heart failure, re-hospitalization, exacerbation, treatment

## Introduction

Heart failure affects almost 5 million patients in the United States (US) with a rise of > 550,000 cases/year [1, 2]. It is contributing about 6.5 million hospital days annually and costing about 33-billion-dollar loss to the economy every year [3, 4]. About one-third of heart failure hospitalizations are due to uncontrolled AF, affecting 2.3 million people in the US and this number is rising secondary to increase in the life expectancy of the patients, rising prevalence of chronic heart disease, and more frequent diagnosis as a result of increased monitoring [5]. As a consequence, heart failure and AF carry a significant economic burden on our society.

## Materials and methods

### *Study design*

Patients who had heart failure exacerbation in the setting of atrial fibrillation from year 2016 to 2018 were included. A retrospective chart review at Abington-Jefferson Hospital was conducted to see the association and frequency of exacerbation of heart failure. The heart failure readmission rate (days), heart rate, and rhythm were analyzed.

Patients with re-admission of heart failure within or after 30 days were included. Our included population also had a history of any type of atrial fibrillation. We included any type of heart failure including systolic/diastolic/heart failure with reduced ejection fraction and heart failure with preserved ejection fraction. Our exclusion criteria included patients with no history of heart failure or atrial fibrillation of any type, blood pressure greater than 150/100, and blood glucose greater than 200 mg/dl on admission, fever, infection, and medication non-compliance. A total of 418 patients were selected based on our inclusion and exclusion criteria. All these patients had a history of at least two admissions for heart failure exacerbation within a time frame of 90 days.

**Table 1.** Mean and standard deviation of mean heart rate and readmission days

| Measure | AF HR | NSR HR | Total HR | AF RD | NSR RD | Total RD |
|---|---|---|---|---|---|---|
| Sample | 223 (53%) | 195 (47%) | 418 (100%) | 223 (53%) | 195 (47%) | 418 (100%) |
| Mean | 90.60 | 78.16 | 84.80 | 27.49 | 32.68 | 29.91 |
| SD | 21.71 | 16.24 | 20.31 | 18.97 | 20.26 | 19.73 |
| SE | 1.45 | 1.16 | 157.00 | 1.27 | 1.45 | 97.00 |

Abbreviations: AF: atrial fibrillation; HR: heart rate; NSR: normal sinus rhythm; RD: readmission day; SD: Standard deviation; SE: standard error.

**Table 2.** Pearson Chi-Square analysis of the readmission rate for AF vs. NSR

| Rhythm | Frequency (percentage) | Value | df | Asymp. Sig. (2-sided) | Phi |
|---|---|---|---|---|---|
| AF | 133 (60%) | | | | 012 |
| NSR | 90 (40%) | 7.60 | 1 | .006 | |

*Atrial fibrillation and heart failure*

Echocardiography, rate and rhythm of selected patients from our electronic record at Abington-Jefferson hospital were reviewed. Data include the readmission time frame, rhythm and rate at presentation. The readmission rate and rhythm of patients within 30 days of hospitalization were compared with the rate and rhythm of the patients admitted to the hospital after more than 30 days.

*Data analysis*

The data analysis was carried out using SPSS v22. Initially after data collection based on our eligibility criteria, data was collected into an excel sheet by two independent authors and was cross-checked by third author. Categorical data were reported in proportions and frequencies, and continuous data were reported in means and standard deviations (SD). Inferential statistics of categorical data was done by Pearson Chi-square analysis, and the means of continuous data were compared with independent T-test analysis. The alpha criterion for significance was set at a value of less than 0.05. The analysis was performed using the SPSS v22. The study was conducted in compliance with human/animal study ethical committee. Our study was conducted under the guidelines of the Helsinki declaration, and an Institutional Ethics Board Review approved for informed consent waiver and quality assurance purposes (FWA00004122).

**Results**

A total of 418 patients met a study criterion. The mean age of the study population was 82.8 years SD ± 9.2. In the population of 418 patients who were readmitted to the hospital, 53% (n = 223/418) were having AF on readmission while 47% (n = 195/418) had NSR on readmission. The mean readmission rate for all patients was 29.9 days SD ± 19.7 while the mean heart rate was 84 beats per minute (bpm) with an SD ± 20, range 157. The mean heart rate for patients readmitted with AF was 90 SD ± 21 bpm compared with NSR, which was 78 ± 16 bpm. The mean readmission rate for atrial fibrillation was 27.49 days SD ± 18.97, while it was 32.68 days for NSR with a standard deviation of ± 20.26. This is shown in **Table 1**.

The readmission rate for all patients showed that 60% (n = 133/223) of patients were having AF while 40% (n = 90/195) were having NSR on the 30 days readmission of previous hospitalization. The readmission rate within 30 days for uncontrolled AF was significantly higher than patients with NSR with a Pearson Chi-Square value of 7.6, degree of freedom (df) 1 and $p$-value 0.006 (< 0.05). The measured, estimated size was assessed using the phi test was 0.12 signifying a weak association (< 0.3). This is summarized in **Table 2** and **Figure 1**.

The analysis of the differences in the heart rates of AF and NSR on readmission was done. Comparison between the two groups showed a significant variance having a Levene's test value (F) of 12.2 and $p$-value 0.001; therefore, the modified independent t-test for equality of means was calculated. The t value was 6.67, df 406 and $p$-value 0.02. The Levene's test for a variance for readmission rate showed F 0.62. P = 0.43 (not significant), so equal variance between the two groups was safely assumed.
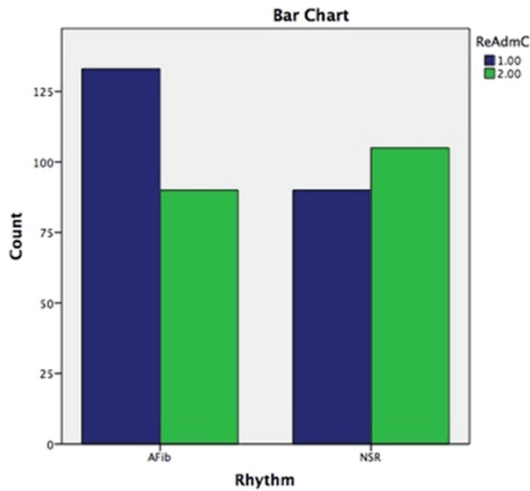
Figure 1. Readmission rate in AF within the 30 days is higher than patients having NSR.

The t-value was 2.70, df 416, and the *p*-value was 0.007 (significantly low). These values are shown in **Table 3**.

## Discussion

Heart failure is a significant health problem and is the most common cause of hospitalization among patients over 65 years of age [6, 7]. It accounts for about 2% of the total healthcare budget spent, and this number is growing exponentially due to an increase in the life expectancy and a high proportion of the old aged population in the western world [8]. Moreover, heart failure hospitalization signifies poor prognosis, further putting the patient at a higher risk for recurrent hospitalization (50% every 6 monthly). In addition to the financial burden, heart failure carries a higher 1-year mortality rate of about 30% [9, 10]. Many factors contribute towards the high rehospitalization and mortality rate of the heart failure patient, AF is the most common.

AF is associated with an increase in the prevalence and adverse outcomes of Heart failure [11]. Inversely, heart failure patients are at a higher risk to develop AF than the general population [12]. Prevalence of AF directly increases with an increase in the class of heart failure New York Heart Association (NYHA). The AF prevalence is low (4%) in NYHA class I, increased to 40% in NYHA class VI [13]. Some of the proposed mechanisms for worsening heart failure with AF are atrioventricular dys-synchrony,

impaired diastolic filling, atrial systolic dysfunction and rapid ventricular response [13]. Atrial fibrillation is also associated with an increased risk of readmission for heart failure exacerbation [14-17]. This can explain the findings of our study, where most of the patients readmitted with the heart failure exacerbation had uncontrolled AF. The mean 30 days readmission rate for patients with AF was significantly higher than the patients with the regular heart rate on readmission. This underscores the fact that controlling the heart rate of known AF patients is of paramount importance to decrease the heart failure readmissions and to reduce the associated financial burden on the healthcare budget, AF was also shown to be a predictor of adverse cardiovascular outcomes in the CHARM study [10, 18]. Atrial fibrillation was identified as one of the 11 predictors of death and readmission in a retrospective study of 189 African American and Hispanic patients hospitalized for heart failure [19]. ACCF/AHA guidelines prefer a rate control strategy over rhythm control for AF in heart failure. This recommendation is based on the results from several studies showing a higher incidence of adverse events, including higher mortality with antiarrhythmic medications [20-22]. Maintaining sinus rhythm in heart failure has been shown to reduce the heart failure readmission rate and adverse outcomes. A study by Fung et al. [15] demonstrated that Atrial fibrillation is a significant predictor of death and readmission in 238 heart failure with Normal EF patients. The atrial fibrillation group had a higher admission rate than the patients with sinus rhythm (28.6% vs. 10.6%, P < 0.01) [23]. The findings in our study were more robust than the previous studies; 60% of the patients had AF on presentation in the 30 days readmission group. These findings are shown in **Table 4**.

AF can potentially be confounded by other risk factors of heart failure exacerbation, including hypertension, obesity, diabetes, chronic kidney disease (CKD). Hypertension can directly precipitate heart failure exacerbation and subsequent readmission due to high systolic and diastolic pressures or can indirectly through causing coronary artery disease and chronic kidney disease [24, 25]. Obesity and insulin resistance, on the other hand, accelerates the atherosclerosis process resulting in a higher incidence of cardiovascular events leading to he-

**Table 3.** Independent samples test comparing the means of Heart rate and number of days of readmission between AF and NSR

| Variables | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tests | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | 95% Confidence Interval | |
| HR | 12.23 | 0.001 | 6.67 | 406.54 | 0.02 | 12.43 | 8.7 | 16.09 |
| RD | .62 | 0.43 | -2.70 | 416 | .007 | -5.18 | -8.9 | -1.40 |

**Table 4.** Frequency of AF and NSR in patients with re-admission within 30-days and more than 30-days

| | AF | NSR HR |
| --- | --- | --- |
| Total Patients | 223 (53%) | 195 (47%) |
| Readmission < 30 days | 133 (60%) | 90 (40%) |
| Readmission > 30 days | 90 (40%) | 105 (60%) |

art failure exacerbation and the associated increase in readmission rates [26-28]. Heart failure is one of the major cardiovascular complication in CKD patients, and its prevalence increases proportionally with a declining kidney function [29]. Renal failure is reported to be associated with an increase in the readmission rate in heart failure [30-34]. Similarly, COPD and anxiety are associated with a higher risk of heart failure readmission [19, 23, 35-39]. We, therefore, further studied the included population to avoid any confounding effect due to baseline characteristics and comorbidities. Both the groups had heart failure, and atrial fibrillation as a baseline diagnosis, and the two groups were further matched based on their demographics and clinical characteristics. In our study, 56% of the AF and 54% of the NSR were hypertensive. The proportion of other risk factors were also almost the same, diabetes prevalence was 49% and 53% in the AF and NSR groups respectively, CKD was 1% in both groups. Only 3% of AF and 4% of NSR patients had COPD. Prevalence of anxiety in our population was 2% in both groups. Our exclusion criteria were stringent to exclude all patients who might have other explanation for heart failure exacerbation.

The primary endpoint in our study was readmission of heart failure exacerbation within 30-90 days of the previous hospitalization. The rate of within 30-day readmission and more than 30-day readmission were compared in all patients with AF and heart failure. Our study showed that the mean readmission days for AF were 27.49 (± 18.97) days while it was 32.68 (± 20.26) days for NSR (statistically significant). This shows that the odds of having uncontrolled AF in heart failure patients readmitted within 30 days of the previous hospitalization were higher than the odds of having NSR. This difference of 5 days has a significant detrimental effect not only on patient's mortality but also on the healthcare budget.

Previously conducted studies on AF related heart failure readmissions rates showed conflicting and variable results. Some small sample studies performed previously had similar studies. A restrospective study by Fung et al. [15] evaluated only 146 patients with heart failure over a median duration of 10.5 months and found that the rate of recurrent hospitalization in AF group was significantly higher than the NSR group (28.6% vs. 10.6%; P < 0.01). Another study by Whellan et al. [40] evaluated the predictability of diagnostic data obtained from CRT-D (Cardiac resynchronization therapy- defibrillator) devices in 166 heart failure patients at hospitalization for early readmission within 30 days. In 34 early readmissions within 30 days; poor rate control (HR > 90 bpm) was attributed to early rehospitalizations. [40] Our study was different from these previously done studies as we included a significantly larger population, and the patients in two groups were matched, we also endured to exclude the patients having the possible confounders.

### Limitations

We could not do randomization as it is a retrospectively performed study, but the patients in both groups were matched appropriately as evident by the Levene's test of variability. We looked at the temporal relationship between AF and heart failure exacerbation related readmissions and did not analyze the causation.

## Conclusion

Uncontrolled AF has a significantly higher re-admission rate in patients with heart failure. Re-hospitalization of heart failure leads to an increase in the financial burden on the health-care economy. Efforts should be made to keep patients in NSR and to control the heart rate.

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## Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Waqas Ullah, Internal Medicine, Abington-Jefferson Health, Abington, USA. Tel: +12673775410; E-mail: waqasullah.dr@gmail.com

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