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# Prevalence and Risk Factors of New-Onset Atrial Fibrillation and Its Role in the Prognosis of Critically Ill Patients

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**Abstract**

**Introduction:** Atrial fibrillation (AF) is the most prevalent dysrhythmia in the intensive care unit (ICU). This study aimed to assess the prevalence, clinical outcomes, and risk factors of new-onset AF in patients admitted to ICU, concerning mortality and length of stay.

**Methods:** This cohort study consisted of patients above 18 years old admitted to the ICU of Firoozabadi hospital in 2019_2020. New-onset AF diagnosis was confirmed by ECG electrographic changes watched by cardiologists in 24 hours for each patient. Patients were divided into two groups: without new-onset AF [171 patients, 54.4% men, age: 65.09 (18–97) years] and with new-onset AF [23 patients, 52.2% men, age: 79 (55–95) years]. Clinical and laboratory features, including neutrophil-to-lymphocyte ratio (NLR) and platelet-to- lymphocyte ratio (PLR), were compared between the groups.

**Results:** Among 194 patients, 118 (61%) were survivors, and 76 (39%) were non-survivors. Twenty-three patients (11.9%) developed new-onset AF. The AF group was significantly older than those in the no AF group (AF vs. no AF: 79 ± 11.5 years vs. 65 ± 20 years, P = 0.02). ICU survivors had a significantly shorter ICU stay than non-survivors (6 ± 0.5 days versus 13.6 ± 1.9 days, P < 0.001). Also, patients with new-onset AF had longer ICU stay (AF vs. no AF: 15.5 ± 10.9 days vs. 7.8 ± 10.6 days, P = 0.02). Patients who developed new-onset AF in the ICU had not greater in-hospital mortality (AF vs. no AF: 16.4% vs. 9.6%, P > 0.05). The NLR of AF and no AF subjects were 16.7 ± 12.6 and 11.6. ± 14.9, respectively (P = 0.008). There was no significant difference between the PLR of the AF group (284.6 ± 211.8) and no AF group (264.8 ± 204.8) (P = 0.7).

**Conclusions:** Atrial fibrillation may not be independently associated with hospital mortality. NLR is a predictor of new-onset AF in critically ill patients.

## INTRODUCTION

Atrial fibrillation (AF) is one of the most common heart arrhythmias in the intensive care unit (ICU) that is directly related to age [1, 2]. People under 60 and over 80 years old are affected by atrial fibrillation, which is 1 and 8 percent, respectively [3].

Older age, male sex, electrolyte abnormalities, history of arrhythmias, volume overload, and use of inotropes, cardiac surgery, and mechanical ventilation for more than 24 hours, congestive heart failure, and hypertension are reported as risk factors for developing

AF in the intensive care setting [4]. According to studies, more significant morbidity, higher in-hospital mortality, longer ICU length of stay (LOS), and increased hospital LOS are associated with new-onset arrhythmias. Also, hospitalized patients with sepsis in the ICU may be at risk for AF [1, 2, 5].

Patients with critical illness may be sensitive to new-onset AF because of baseline comorbidity, acute metabolic, ischemic or neuro-hormonal stressors, or other pathophysiological changes during acute illness [6-8]. Studies have shown that newly started arrhythmias are associated with more significant morbidity, higher hospital mortality, longer ICU length of stay (LOS), and increased hospital LOS [1, 4, 5]. Stroke and death in the hospital mostly happen in patients with severe sepsis and new-onset AF. In comparison, septic patients without new-onset AF have a lower risk of death [9].

Although several studies have documented the association between new-onset AF and adverse outcomes, the literature describing the results beyond intensive care is sparse. Our study aimed to assess the prevalence and risk factor of new-onset AF in patients admitted to a medical or surgical ICU and to evaluate clinical outcomes concerning mortality and LOS.

## METHODS

This cohort study consists of 194 patients above 18 years old (105 male and 89 female) admitted to ICU in Firoozabadi hospital in 2019_2020. Patients who had atrial fibrillation, flutter, and heart attack in their past medical history were excluded. New-onset AF diagnosis was confirmed by ECG electrographic changes watched by cardiologists in 24 hours for each patient.

Hematologic factors were measured in patients with new-onset atrial fibrillation. New-onset AF was defined as either (1) AF ≥ 1 h in duration, as noted by bedside telemetry (routinely evaluated in charts where electrocardiograms were not completed); (2) AF < 1 hour, but captured on electrocardiogram; or (3) AF is initiating pharmacologic therapy or electrical cardioversion. The study was approved by the Ethics committee of Iran University of Medical Science.

Data analysis was performed by SPSS software for windows (statistical product and service solutions, version 20.0. SPSS Inc., Chicago, IL, USA). Statistical analysis is present by mean ± SD. The $\chi^2$ test was used for the study of categorical data, and the Student t-test or Mann-Whitney U test was used for continuous data. A P-value of less than 0.05 was defined as statistically significant.

## RESULTS

In this study, a total of 194 patients admitted to the medical and surgical ICU at the time of emergency admission were evaluated. Among them, 118 (61%) were survivors, and 76 (39%) were non-survivors. The mean age of the survived group was 63.8 ± 21.3 years, and 71.3 ± 17.5 in the un-survived group.

Twenty-three patients (11.9%) developed new-onset AF. The AF group was significantly older than those in the no AF group (AF vs. no AF: 79 ± 11.5 years vs. 65 ± 20 years, P = 0.02). There were 11 women and 12 men in the AF group and 78 women and 93 men in the no AF. Gender was not significantly different between the survived and non-survivors groups (P = 0.84). ICU survivors had a significantly shorter ICU stay than non-survivors (6 ± 0.5 versus 13.6 ± 1.9 days, P < 0.001). Other demographic information by the cohort of AF compared with no AF can be found in Table 1.

We also carried out a subgroup analysis based on the type of ICUs, including medical (MICU) and surgical (SICU) ICUs. We found that there was no statistically significant difference in the incidence of new-onset AF between the two groups (P > 0.05).

The most prevalent underlying diseases were hypertension, anemia, diabetes, cerebrovascular accident, and end-stage renal disease (ESRD) with a rate of 37.8%, 30.9%, 28.4%, 18.4%, and 14.4%, respectively. Moreover, 36.1% of all patients experienced sepsis. There was no significant difference in the comorbidity of AF and no AF group (P > 0.05) (Table 1) Hemoglobin, RDW, PDW, troponin, and plasma glucose levels of the patients in the AF group were not significantly different from no AF group (P > 0.05 for all).

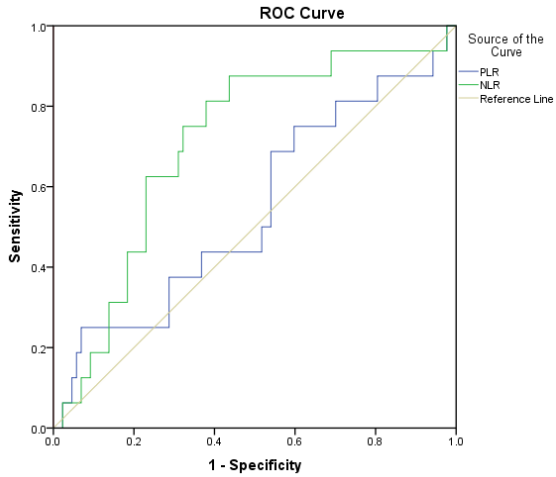


**Figure 1**. ROC curve analysis for predictive values of NLR and PLR for incidence of new onset atrial fibrillation. The area under the ROC curve, 95% confidence interval (CI), and P values are as follows, respectively: 0.71, 0.068 to 0.760, and .008 for NLR, 0.544, 0.384 to 0.704, and .579 for PLR. PLR: platelet to Lymphocyte ratio; NLR: neutrophil to lymphocyte ratio.

The NLR of AF and no AF subjects were 16.7 ± 12.6 and 11.6. ± 14.9, respectively. NLR was significantly higher in the AF group compared with no AF (P = 0.008). There was no significant difference between the PLR of the AF group (284.6 ± 211.8) and no AF group (264.8 ± 204.8) (P = 0.7). Neutrophil count and PDW were as

significantly higher in the AF group compared with no AF (P = 0.02 and P = 0.03, respectively). Table 2 indicates the other serum biomarker characteristics between AF and no AF.

ROC curve analysis was performed comparing the abilities of NLR and PLR as predictors of AF (Fig 1). The ROC analysis revealed that NLR higher than 9.2 had 81% sensitivity and 62% specificity in predicting AF (AUC: 0.71, P = 0.008). The cutoff value for PLR as a predictor of AF with 75% sensitivity, and 40% specificity was 185 (AUC = 0.544, P = 0.579) (Fig 1).

### Clinical Outcomes

The mortality of MICU patients was significantly higher than that of SICU patients (OR = 11.6; 95%CI 1.5-89.7). Patients who developed new-onset AF in the ICU had not more significant in-hospital mortality (AF vs. no AF: 16.4% vs. 9.6%, P > 0.05). However, patients with new-onset AF had more extended ICU stay (AF vs. no AF: 15.5±10.9 days vs. 7.8±10.6 days, P = 0.02)

**Table 1.** Demographic Data of the Study Participants (n = 194).

| Characteristic | AF, N = 23 | No AF , N = 171 | P Value |
|---|---|---|---|
| **Age, year** | 79.04 ± 11.5 | 65.09 ± 20.5 | 0.02 |
| **Male sex** | 12 (52.2%) | 93 (54.4%) | 0.842 |
| **Admission Cause** | | | |
| IHD | 1 (4.3%) | 10 (5.8%) | 0.770 |
| Sepsis | 9 (39.1%) | 61 (35.7%) | 0.746 |
| GIB | 1(4.3%) | 20 (11.7%) | 0.287 |
| **Comorbidity** | | | |
| Anemia | 9(39.1) | 51(29.8) | 0.365 |
| CKD/ESRD | 2(8.7.) | 26(15.2) | 0.37 |
| HTN | 10(43.5) | 63(36.8) | 0.433 |
| DM | 7( 30.4) | 48(28.1) | 0.818 |
| **ICU stay ,days** | 15.5 ±10.9 | 7.8 ±10.6 | < 0.00 |

Variables are expressed as mean ± standard deviation and categorical data are expressed as number (percentage). IHD: ischemic heart disease; GIB: gastro intestinal bleeding; CKD: chronic kidney disease; ESRD: end stage renal disease; and HTN: hypertension

**Table 2.** Serum Biomarkers Characteristics between AF and No AF Group.

| Characteristic | AF, N = 23 | No AF, N = 171 | P Value |
|---|---|---|---|
| **WBC count ,u/mm$^3$** | 12.4 ± 5.1 | 10.7 ± 5.4 | 0.07 |
| **Hb, g/dl** | 11.8 ± 2.7 | 12 ± 3.3 | 0.45 |
| **RDW** | 15.4 ± 1.4 | 15.9 ± 3.2 | 0.59 |
| **Plt, u/mm$^3$** | 213.1 ± 76.6 | 326.2 ± 115.1 | 0.036 |
| **Neutrophil count ,u/mm$^3$** | 12 ± 4.5 | 9.6 ± 5.6 | 0.022 |
| **Lymphocyte count ,u/mm$^3$** | 1.2 ± 1.2 | 1.4 ± 0.9 | 0.015 |
| **PDW** | 12.2± 2.2 | 10.8 ± 1.6 | 0.029 |
| **PLR** | 284.6 ± 211.8 | 264.8 ± 204.8 | 0.7 |
| **NLR** | 56.47 ± 16.7 | 11.6 ± 14.9 | 0.008 |
| **Troponin, ng/ml** | 134.6 ± 276.7 | 133.8 ± 468.2 | 0.1 |

Variables are expressed as mean ± standard deviation. ICU: intensive care unit; WBC: white blood cell; Hb: hemoglobin; RDW: red cell distribution width; Plt: platelet, PDW: platelet cell distribution width; PLR: platelet to Lymphocyte ratio; NLR: neutrophil to lymphocyte ratio.

## DISCUSSIONS

The present study shows that new-onset AF is not an independent predictor of in-hospital mortality in the ICU population. The management of critically ill patients developing AF is challenging. Indeed, AF may impair the ventricular filling and precipitate acute heart failure [10-12]. On the other hand, there are contraindication and reduction in the efficacy of antiarrhythmic treatments. Therefore it is hard to manage ICU patients with AF, and also it can predispose to early relapses [13-15].

New-onset AF frequently occurred in critically ill patients. A high prevalence of AF has been shown in medical, surgical, and cardio-surgical ICU settings, which were confirmed in our study in critically ill patients [16-19]. According to Meierhenrich's study, septic shock patients had a high rate of new-onset AF (46.0%) [16]. Also, Echahidi's study even found that the incidence of AF was as high as 50% [20]. Our research has shown that the prevalence of new-onset AF is 11.9%, which is consistent with the 9 to 11% rates in mixed ICU populations [21, 22] but far lower than the 23 to 46% rates in sepsis patients detected in some of the previous studies [16, 23, 24].

Moreover, Zesheng Wu et al. [25], in their systematic review, found that the incidence of new-onset AF in critically ill patients varies in a wide range from 4.1% to 46% between studies. This variation is maybe due to the sample sizes of included studies, a difference in patient populations, the severity of illness, and the study design. According to several studies, critically ill patients have a lot of risk factors that can develop AF. Age is an essential factor for developing and rising AF, and it can increase the incidence and prevalence of this disease (> 60 years: 1%; > 80 years: 5-15%) [8, 26-28]. Similarly, in this study, older age was a predictive factor for the incidence of AF.

Issac's study found systemic inflammatory response syndrome (SIRS) associated with the occurrence of AF [29], and they suggest that SIRS might be a significant predictor of AF occurrence. Recently, inflammatory

markers derived from a complete blood count (CBC), especially NLR, have attracted attention in the prediction of new-onset AF various conditions. Ulus T et al. [30] reported that using a cut point of > 4.41, NLR predicted new-onset AF in elderly patients with ACS undergoing PCI. Similarly, Wagdy S et al. [31] stated that older patient age, higher NLR, and MPV on admission are good predictive factors for the occurrence of new-onset AF in STEMI revascularized patients. Yet no study has not evaluated the role of NLR in the prediction of new-onset AF in critically ill patients. Our study showed that using a cut point of > 9.26, NLR predicted new-onset AF in critically ill patients with a sensitivity of 81.3% and specificity of 62.1%.

Previous studies have shown that critically ill patients with new-onset AF have higher mortality [6, 32, 33]. However, there is a retrospective, large cohort study that revealed that new-onset AF was not an independent predictor for hospital mortality of cardiac surgery patients [34].

Two systematic reviews by Yoshida et al. and Kuipers et al. [35, 36] reported higher mortality in critically ill patients with new-onset AF. Still, the pooled analysis was not performed in the two studies. Gandhi et al. found another point about new-onset AF. They revealed that hospital mortality of critically ill patients with sepsis had significantly increased because of this problem [37]. The latest meta-analysis by Kanjanahattakij et al. [38] reported that there had been a significant association between new-onset AF and in-hospital mortality. Liu et al. [39] found that the new-onset AF group has a higher in-hospital mortality rate (61.3%) compared with no new-onset AF groups (17.5%) in critically ill patients with sepsis.

Our study found new-onset AF is not an independent predictor factor in-hospital mortality, and it was not significantly higher in critically ill patients with new-onset AF compared with patients without AF. This observation is consistent with data from a retrospective single-center study by Gupta et al. and a prospective multi-center study by Annaneet et al., which both showed there was no association between AF and increased in-hospital mortality [1, 40] These results are in contrast with previous data, with Kanjanahattakij's result and prior studies that mentioned.

All of the previous studies showed that critically ill patients with new-onset AF had longer lengths of stay in ICU and hospital in comparison. Chen et al. conducted a retrospective single-center study on the medical ICU population. They identified that new-onset AF as an independent predictor of 60-day mortality [33]. Prior studies in the ICU population [8, 9, 16, 36, 38] have found a 1.8 fold increase in the mean ICU lengths of stay in patients with new-onset AF, similar to our observed 1.97 fold increase in the ICU lengths of stay, respectively. Our study is the first of its kind in general ICU patients that introduced NLR as a predictive factor of new-onset AF in critically ill patients.

There are some limitations to our study. First, it was a single center-study, possibly limiting the external validity of our results. Like any observational study, the potential for residual confounding remains. Also, as we were unable to document patients' home regimens, we were unable to determine the effect of home medications on the development of new-onset AF. Finally, the ability to capture 60-day mortality is limited by documentation with actuarial records and database documentation.

## CONCLUSION

Atrial fibrillation may not be independently associated with hospital mortality. NLR is a predictor of new-onset AF in critically ill patients. Given the poor prognosis of new-onset AF, early identification of such patients through the variables mentioned above may help to prevent poor outcomes. However, our results should be further confirmed in multi-center, more extensive studies.

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**Ethics Approval and Consent to Participate**

This study was approved under the registration number: IR IUMS.REC 1398-093, by the Ethics committee of Iran University of Medical Sciences. All patients filled an informed written consent form.

**Availability of Data and Material**

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request

**Competing Interests**

The authors declare that they have no competing interests.

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Not applicable

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