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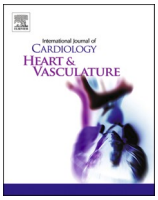

# NSTEMI mortality and hospital outcomes in patients with atrial fibrillation: A propensity score-matched analysis

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ABSTRACT

*Background:* Atrial fibrillation (AF) is associated with increased cardiovascular mortality. Data regarding the relationship between coronary artery disease (CAD) and AF is mixed. It is uncertain if AF directly increases the risk for future coronary events and if such patients are appropriately evaluated for CAD.

*Methods:* This cross-sectional study was performed on hospitalized patients with NSTEMI and concurrent AF in 2019 using the National Inpatient Sample. In-hospital mortality, rates of diagnostic cardiac angiography, percutaneous coronary intervention, ventricular tachycardiac (VT), ventricular fibrillation (VF), cardiogenic shock, cardiac arrest, length of stay (LOS), and total hospitalization charges were studied.

*Results:* A total of 433,965 patients met inclusion criteria (169,725 females [39.1 %], 307,985 Caucasian [71 %], 51,570 African American [11.8 %], 37,265 Hispanic [8.6 %]; mean [SD] age, 67.9 [6.2] years). 86,200 (19.8 %) patients with NSTEMI had AF, including 32,775 (38 %) female patients before propensity matching. Patients with NSTEMI and AF had increased odds of mortality (adjusted Odds ratio, 1.32; CI, 1.21–1.43; $p < 0.001$). AF patients were less likely to undergo diagnostic coronary angiography and PCI and had higher odds of VT, VF, cardiogenic shock, cardiac arrest, tracheal intubation, mechanical ventilation, increased LOS, and higher hospital charges than those without AF.

*Conclusion:* AF was independently associated with increased mortality and serious cardiac complications in patients admitted with NSTEMI.

## 1. Introduction

Atrial fibrillation (AF) is the most common abnormal cardiac rhythm globally [1] The prevalence of AF in the US is at least 3–6 million and is projected to increase to 6–16 million by 2050 [2] The lifetime risk of acquiring AF is estimated to be 33 % [3]. AF is known to increase mortality from sudden cardiac death, congestive heart failure, and stroke [4]; therefore, it is not surprising that healthcare costs associated with AF are significantly higher [5]. Coronary artery disease (CAD), on the other hand, is the most common cardiovascular disease [6]. It is the leading cause of mortality in the US with approximately 610,000 deaths annually [7], and the third leading cause of death worldwide claiming 17.8 million lives annually [8,9]. Healthcare costs related to CAD are estimated to be more than US$200 billion annually [10]. Due to the colossal healthcare burden, considerable efforts have been made to understand the underlying risk factors. These risk factors are segregated into two large categories: modifiable and non-modifiable risk factors. The non-modifiable risk factors include age, gender, family history, and certain ethnicities. The known modifiable risk factors include hypertension, diabetes mellitus, hyperlipidemia, obesity, smoking, sedentary lifestyle, and stress [11]. Significant efforts are made to discover novel risk factors and formulate additional guidelines to alleviate substantial healthcare costs and mortality rates.

While both diseases are known to share a common risk factor profile, the intricate relationship between the two is still largely unclear. It is reported that CAD is a risk factor for AF [12]; however, studies have shown mixed results about AF being an independent risk modifier for CAD, with some proposing direct causality [13], whereas others suggesting no causal relationship between AF and risk of CAD [14]. It is not uncommon in practice for patients to have both AF and CAD. AF is known to have a negative prognostic impact on CAD patients [15]; yet, it remains unclear if the increased mortality is due to increased coronary ischemic events or from unfavorable hemodynamic effects, such as loss of atrial kick, high ventricular rate, and decreased cardiac output [16].

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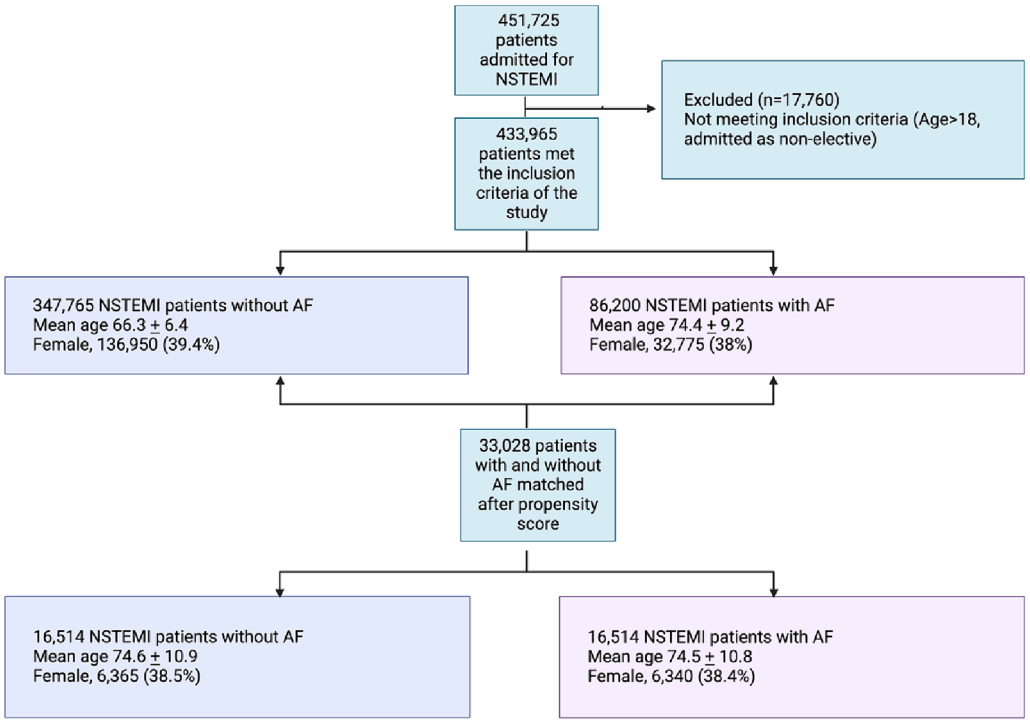


**Fig. 1.** Flow diagram depicting NSTEMI patient selection for inclusion based on AF status and propensity matched analysis.

Several studies have attempted to understand the impact of both diseases. While previous studies have explored the associated poor outcomes, no study has directly examined the pattern of diagnostic workup, intervention, and cardiac outcomes in this sub-population. This study aims to investigate the effect of AF on non-ST elevation myocardial infarction (NSTEMI) in terms of in-hospital mortality, serious cardiac complications, and resource utilization and explore the trend of ischemic evaluation and treatment in patients with NSTEMI and AF.

## 2. Methods

This is a retrospective cohort study of adult patients hospitalized in the United States with the diagnosis of NSTEMI. The study used the patient cohort from the National Inpatient Sample (NIS) database from January 1, 2019, to December 31, 2019. The NIS is a part of the Healthcare Cost and Utilization Project (HCUP), maintained by the Agency for Healthcare Research and Quality (AHRQ) [17]. NIS is sampled from the State Inpatient Databases (SID), containing information on all hospital stays regardless of the payer source. The NIS 2019 sampling frame included data from 49 statewide organizations, which are estimated to have 97 % of discharges from non-federal short-term US hospitals, covering 98 % of the US population. NIS collects 20 % of the stratified sample of discharge records from all HCUP-participating US community hospitals, excluding long-term acute care facilities and rehabilitation centers. Discharge weights are provided to produce national estimates, approximating 35 million discharges when weights are applied. The data was purchased from a federal institution. The data is de-identified for privacy purposes and, therefore, does not require approval from the ethical committee.

## 3. Study patients

The study included adult (≥18) patients admitted with a primary diagnosis of NSTEMI using the International Classification of Disease (ICD)-10 Clinical Modification (CM) codes. Exclusion criteria included patients who were 1) admitted electively, 2) transferred from another facility, 3) transferred to another facility, 4) patients with missing information, 5) patients with the diagnosis of NSTEMI type II or acute myocardial injury due to secondary causes or a procedural complication and 6) patients who required coronary artery bypass grafts. The ICD-10 codes used are listed in the attached supplemental material.

## 4. Study variables

ICD-10 procedure codes were used to identify patients who underwent diagnostic coronary angiography and percutaneous coronary intervention (PCI). Secondary diagnosis codes were used to identify AF patients. Separate variables were created for all other comorbid conditions. Covariates included in the study were age, gender, race, baseline comorbidity status using the Charlson Comorbidity Index, median annual income in the patient's zip code, geographic region of the United States (Northeast, Midwest, West or South), hospital location (urban vs rural), hospital teaching status, hospital bed size, primary insurance, hypertension, diabetes mellitus, hyperlipidemia, smoking status, obesity, history of coronary artery disease, history of myocardial infarction, history of percutaneous coronary intervention, systolic heart failure, diastolic heart failure, combined systolic and diastolic heart failure, history of peripheral vascular disease, chronic pulmonary disease, pulmonary hypertension, obstructive sleep apnea, acute kidney injury, chronic kidney disease, chronic liver disease, sepsis, septic shock, alcohol use, cocaine, amphetamine use and anemia of chronic disease.

## 5. Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes were rates of in-patient diagnostic coronary angiography, percutaneous ischemic intervention, rates of ventricular tachycardia (VT), ventricular fibrillation (VF), cardiogenic shock, cardiac arrest, tracheal intubation, mechanical ventilation, length of stay (LOS), and total hospitalization charges. NIS provides in-hospital mortality, LOS, and total hospital charges. Separate variables were created for other secondary outcomes.

**Table 1**
Patient characteristics before 1:1 propensity matching.

| Patient characteristics | NSTEMI without AF | NSTEMI with AF | p-value |
|---|---|---|---|
| N = 433,965 | 347,765 | N = 86,200 | |
| Women | 136,950 (39.4) | 32,775 (38) | <0.001 |
| Age, years (SD) | 66.3 (6.4) | 74.4 (9.2) | <0.001 |
| Race/ethnicity, no. (%) | | | |
| Caucasian | 240,415 (71) | 67,570 (80.3) | |
| African American | 44,995 (13.3) | 6,575 (7.8) | |
| Hispanic | 31,735 (9.3) | 5,530 (6.6) | <0.001 |
| Asian or Pacific Islander | 10,030 (3) | 2,240 (2.6) | |
| Native American | 2,250 (0.6) | 365 (0.4) | |
| Other | 9,775 (2.9) | 1,810 (2.1) | |
| Charlson comorbidity index score, no. (%) | | | |
| 1 | 80,395 (23) | 8,635 (10) | |
| 2 | 81,625 (23.4) | 15,195 (17.6) | |
| 3 | 59,750 (17.2) | 15,860 (18.4) | <0.001 |
| >4 | 125,995 (36.2) | 46,510 (54) | |
| Median annual income in patients' zip code, no. (%) | | | |
| $1–45,999 | 109,525 (32) | 24,745 (29.2) | |
| $46,000–58,999 | 90,390 (26.4) | 23,205 (27.4) | |
| $59,000–78,999 | 81,210 (23.7) | 20,865 (24.6) | |
| > $79,000 | 60,345 (17.6) | 15,830 (18.7) | <0.001 |
| Insurance type, no. (%) | | | |
| Medicare | 195,400 (58.2) | 66,880 (79) | |
| Medicaid | 35,165 (10.5 %) | 3,920 (4.7) | |
| Private HMO | 89,030 (26.5) | 11,550 (13.7) | |
| Self-pay | 16,060 (4.8) | 1,600 (1.9) | <0.001 |
| **Hospital characteristics** | | | |
| Hospital region, no. (%) | | | |
| Northeast | 60,170 (17.3) | 14,550 (16.8) | |
| Midwest | 77,020 (22.1) | 20,435 (23.7) | <0.001 |
| South | 145,760 (42) | 34,500 (40) | |
| West | 64,815 (18.6) | 16,715 (19.4) | |
| Hospital bed size, no. (%) | | | |
| Small | 71,145 (20.4) | 16,865 (19.5) | |
| Medium | 105,880 (30.4) | 26,590 (31) | 0.10 |
| Large | 170,740 (49) | 42,745 (49.6) | |
| Urban | 321,155 (92.3) | 79,625 (92.4) | |
| Rural | 26,610 (7.6) | 6,575 (7.6) | 0.92 |
| Hospital teaching status | 253,980 (73) | 63,625 (73.8) | 0.07 |
| Medical Comorbidities | | | |
| Diabetes mellitus | 101,580 (29.2) | 22,955 (26.6) | <0.001 |
| Hypertension | 291,910 (84) | 77,925 (90.4) | <0.001 |
| Hyperlipidemia | 227,850 (65.5) | 56,250 (65.2) | 0.42 |
| Obesity | 75,395 (21.6) | 17,410 (20.2) | <0.001 |
| Smoker | 173,995 (50) | 37,515 (43.5) | <0.001 |
| Chronic kidney disease | 72,840 (21) | 27,925 (32.4) | <0.001 |
| COPD | 61,690 (17.7) | 20,760 (24) | <0.001 |
| AKI | 66,845 (19.2) | 25,735 (29.8) | <0.001 |
| Systolic HF | 54,070 (15.5) | 21,200 (24.6) | <0.001 |
| Diastolic HF | 30,505 (8.7) | 14,300 (16.6) | <0.001 |
| Combine HF | 19,320 (5.5) | 8,580 (9.5) | <0.001 |
| CAD | 270,390 (77.7) | 69,015 (80) | <0.001 |
| History of MI | 61,560 (17.7) | 17,680 (20.5) | <0.001 |
| History of PCI | 65,420 (19) | 18,455 (21.4) | <0.001 |
| PAD | 14,650 (4.2) | 5,505 (6.4) | <0.001 |
| Sepsis | 5,125 (1.4) | 2,260 (2.6) | <0.001 |
| Iron def anemia | 10,915 (3.1) | 3,695 (4.3) | <0.001 |
| ACD | 23,965 (6.9) | 8,395 (9.7) | <0.001 |
| OSA | 36,210 (10.4) | 12,280 (14.2) | <0.001 |
| Alcohol | 8,625 (2.5) | 1,775 (2) | <0.001 |
| Cocaine | 3,445 (0.9) | 330 (0.4) | <0.001 |
| Amphetamine | 2,540 (0.7) | 320 (0.3) | <0.001 |
| CLD | 2,905 (0.8) | 875 (1) | <0.05 |
| Septic shock | 1,945 (0.5) | 885 (1) | <0.001 |

AMI, atrial fibrillation; AF, atrial fibrillation; AKI, acute kidney injury; HF, heart failure; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; PAD, peripheral arterial disease; ACD, anemia of chronic disease; OSA, obstructive sleep apnea; CLD, chronic liver disease.

**Table 2**
Patient characteristics after 1:1 propensity matching.

| **Demographics** | **NSTEMI without AF** | **NSTEMI with AF** | **P value** |
|---|---|---|---|
| N = 33,028 | N = 16,514 | N = 16,514 | |
| Women, no. (%) | 6,365 (38.5) | 6,340 (38.4) | 0.77 |
| Age, mean (SD) | 74.6 (10.8) | 74.5 (10.9) | <0.001 |
| Race/ethnicity, no. (%) | | | |
| Caucasian | 12,804 (77.53) | 13,289 (80.47) | |
| African American | 1,876 (11.3) | 1,287 (7.8) | |
| Hispanic | 1,188 (7.2) | 1,087 (6.6) | |
| Asian or Pacific Islander | 366 (2.2) | 442 (2.7) | <0.001 |
| Native American | 50 (0.3) | 65 (0.4) | |
| Other | 230 (1.4) | 344 (2) | |
| Charlson comorbidity index score, no. (%) | | | |
| 1 | 1,972 (12) | 1,657 (10) | |
| 2 | 2,915 (17.6) | 2,889 (17.5) | |
| 3 | 2,856 (17.3) | 3,033 (18.4) | <0.001 |
| >4 | 8,771 (53.1) | 8,935 (54) | |
| Median annual income in patients' zip code, no. (%) | | | |
| $1–45,999 | 5,047 (30.5) | 4,819 (29) | |
| $46,000–58,999 | 4,398 (26.6) | 4,506 (27.3) | 0.05 |
| $59,000–78,999 | 4,023 (24.3) | 4,087 (24.7) | |
| >78,999 | 3,046 (18.4) | 3,102 (18.8) | |
| Insurance type, no. (%) | | | |
| Medicare | 12,782 (79.6) | 12,876 (80) | 0.41 |
| Medicaid | 768 (4.8) | 726 (4.5) | |
| Private HMO | 2,178 (13.5) | 2,191 (13.6) | |
| Self-pay | 330 (2) | 301 (1.9) | |
| Hospital region, no. (%) | | | |
| Northeast | 2,823 (17) | 2,833 (17) | |
| Midwest | 3,690 (22.3) | 3,869 (23.4) | 0.07 |
| South | 6,826 (41.3) | 6,635 (40.2) | |
| West | 3,175 (19.2) | 3,177 (19.2) | |
| Hospital bed size, no. (%) | | | |
| Small | 3,259 (19.7) | 3,211 (19.4) | |
| Medium | 5,024 (30.4) | 5,116 (31) | 0.52 |
| Large | 8,231 (49.8) | 8,187 (49.6) | |
| Urban | 15,261 (92.4) | 15,273 (92.5) | 0.80 |
| Rural | 1,253 (7.6) | 1,241 (7.5) | |
| Teaching hospital | 12,255 (74.2) | 12,210 (74) | 0.57 |
| **Medical Comorbidities, no. (%)** | | | |
| Diabetes mellitus | 4,443 (27) | 4,394 (26.6) | 0.54 |
| Hypertension | 14,973 (90.6) | 14,937 (90.4) | 0.41 |
| CAD | 13,300 (80.5) | 13,246 (80.2) | 0.45 |
| History of MI | 3,390 (20.5) | 3,419 (20.7) | 0.69 |
| History of PCI | 3,583 (21.7) | 3,554 (21.5) | 0.7 |
| Hyperlipidemia | 5,563 (33.7) | 5,700 (34.5) | 0.11 |
| Systolic heart failure | 4,035 (24.4) | 4,038 (24.4) | 0.96 |
| Diastolic heart failure | 2,592 (15.7) | 2,758 (16.7) | 0.01 |
| Combine heart failure | 1,619 (10) | 1,643 (10) | 0.65 |
| AKI | 4,881 (29.5) | 4,936 (30) | 0.50 |
| Chronic Kidney disease | 5,309 (32) | 5,371 (32.5) | 0.46 |
| Obesity | 3,410 (20.6) | 3,348 (20.3) | 0.39 |
| OSA | 2,336 (14) | 2,355 (14.3) | 0.76 |
| Smoking | 7,171 (43.4) | 7,173 (43.4) | 0.98 |
| COPD | 4,049 (24.5) | 3,971 (24) | 0.31 |
| Alcohol | 335 (2) | 343 (2) | 0.75 |
| ACD | 1,573 (9.5) | 1,605 (9.7) | 0.55 |
| Sepsis | 368 (2.23) | 428 (2.6) | 0.03 |

AMI, acute myocardial infarction; HF, heart failure; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; OSA, obstructive sleep apnea.

### 5.1. Statistical Analysis

STATA Statistical Software: Release 18 was used to analyze the results. Continuous variables were reported as weighted means with standard deviation (SD) and categorical data as numbers and percentages. Univariable linear and logistic regression analyses were used to calculate means and unadjusted odds ratios (ORs) for continuous and categorical variables. Variables with $p < 0.05$ were included in the multivariable linear and logistic regression analyses to measure weighted means for continuous and adjusted odds ratios for categorical and dichotomous variables. As the control group (NSTEMI without concurrent AF) was larger than the test group (NSTEMI with concurrent AF), a secondary analysis was performed after propensity score matching (PSM) to confirm the results. Variables included in multivariable analysis were used for propensity matching using a 1:1 nearest neighbor propensity score with a 0.05 caliper width. A secondary multivariable regression model was built on the matched cohort, as described above.

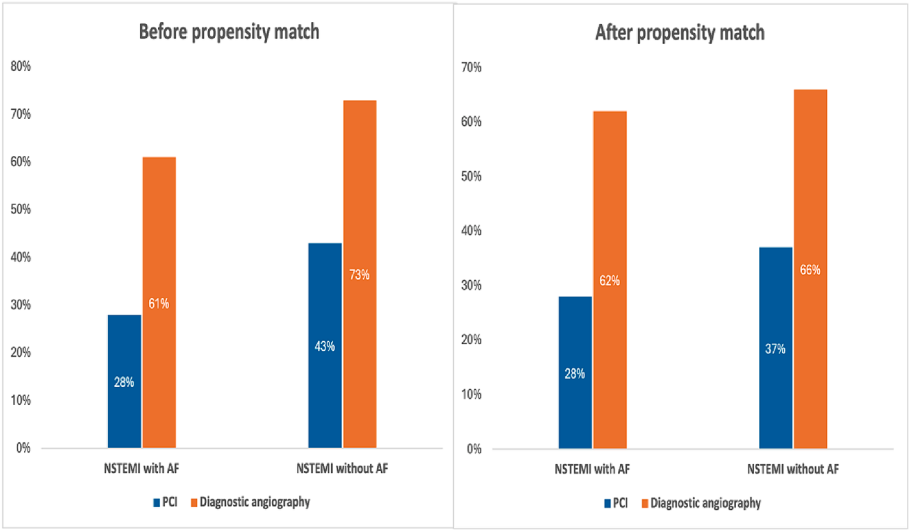


**Fig. 2.** Bar graph comparing the rates of diagnostic angiography and PCI before and after propensity. NSTEMI: Non-ST elevation myocardial infarction, AF: Atrial fibrillation, PCI: Percutaneous coronary intervention.

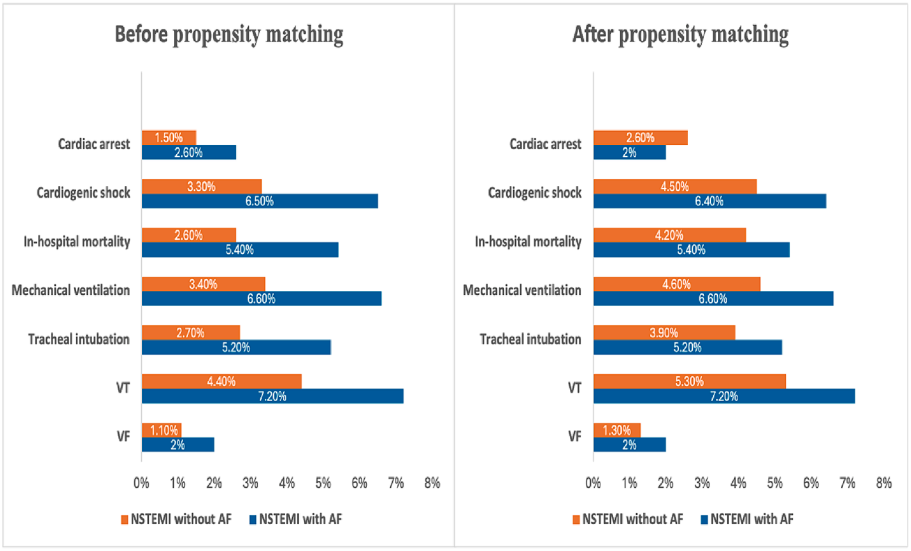


**Fig. 3.** Bar graphs comparing the rates of hospital outcomes before and after propensity matching. NSTEMI: Non-ST elevation myocardial infarction, AF: Atrial fibrillation, VT: Ventricular tachycardia, VF: Ventricular fibrillation.

All p-values obtained were two-sided, and 0.05 was used as the threshold for statistical significance.

## 6. Results

### 6.1. Patient characteristics

A total of 35 million weighted discharges were included in the NIS 2019, of which 433,965 met the inclusion criteria of our study. Fig. 1 shows the flow diagram of patient selection based on AF status and propensity matched analysis. Table 1 summarizes the baseline characteristics before propensity matching. The prematch analysis included 169,725 (39 %) female patients, and the predominant race was Caucasian (71 %). There were 86,200 (19.8 %) patients with a secondary AF diagnosis. In the prematch comparison, patients with a history of AF were more likely older (74.4 vs. 66.3), Caucasian (80.3 vs. 71 %), had higher Charlson comorbidity score (54 vs. 36.2 %), and insured by Medicare (79 vs. 58.2 %). In terms of medical comorbidities, patients with AF had a higher prevalence of heart failure with reduced ejection fracture (24.6 vs. 15.5 %), hypertension (90 vs. 84 %), and COPD (24 vs. 17.7 %).

Variables from Table 1 were used to generate a propensity score and matched 16,514 patients in each cohort of NSTEMI (with and without AF). The baseline characteristics of the matched cohort are presented in Table 2. Both groups' demographic and medical comorbid differences were neutralized after propensity matching.

### 6.2. The prematch and post-match comparisons of hospital outcomes

Fig. 2 compares the rates of diagnostic coronary angiography and PCI in patients with and without AF before and after propensity matching. Fig. 3 and Table 3 summarize the comparison of hospital outcomes in pre and post-match cohorts. In the prematch analysis, patients with AF had increased odds of mortality (adjusted OR, 1.32; CI, 1.21–1.45; $p < 0.001$) and decreased odds of diagnostic coronary angiography and PCI. In terms of hospital complications, AF patients had increased odds of VT,

**Table 3**
Uni- and multivariate analysis of in-hospital outcomes before and after propensity matching.

| | Before propensity matching | | | | After propensity matching | | | |
|---|---|---|---|---|---|---|---|---|
| | Univariate, OR (95 % CI) | P value | Multivariate, OR (95 % CI) | P value | Univariate, OR (95 % CI) | P value | Multivariate, OR (95 % CI) | P value |
| In-hospital mortality | 2.11 (1.95–2.28) | <0.001 | 1.32 (1.21–1.43) | <0.001 | 1.32 (1.19–1.46) | <0.001 | 1.36 (1.23–1.52) | <0.001 |
| Diagnostic angiography | 0.59 (0.57–0.62) | <0.001 | 0.79 (0.75–0.82) | <0.001 | 0.84 (0.80–0.88) | <0.001 | 0.82 (0.78–0.86) | <0.001 |
| PCI | 0.52 (0.50–0.54) | <0.001 | 0.62 (0.59–0.65) | <0.001 | 0.67 (0.63–0.70) | <0.001 | 0.65 (0.62–0.69) | <0.001 |
| VT | 1.68 (1.57–1.80) | <0.001 | 1.43 (1.32–1.54) | <0.001 | 1.38 (1.26–1.51) | <0.001 | 1.37 (1.25–1.50) | <0.001 |
| VF | 1.74 (1.52–1.98) | <0.001 | 1.59 (1.38–1.84) | <0.001 | 1.47 (1.24–1.75) | <0.001 | 1.46 (1.22–1.73) | <0.001 |
| Cardiogenic shock | 2.05 (1.89–2.22) | <0.001 | 1.48 (1.36–1.61) | <0.001 | 1.44 (1.30–1.58) | <0.001 | 1.48 (1.34–1.64) | <0.001 |
| Cardiac arrest | 1.73 (1.55–1.94) | <0.001 | 1.45 (1.27–1.64) | <0.001 | 1.30 (1.13–1.50) | <0.001 | 1.30 (1.13–1.51) | <0.001 |
| Intubation | 1.96 (1.81–2.12) | <0.001 | 1.50 (1.36–1.64) | <0.001 | 1.37 (1.23–1.52) | <0.001 | 1.40 (1.26–1.56) | <0.001 |
| Mechanical ventilation | 2.00 (1.86–2.15) | <0.001 | 1.59 (1.46–1.73) | <0.001 | 1.46 (1.33–1.60) | <0.001 | 1.50 (1.36–1.66) | <0.001 |
| LOS | 2.11 (2.00–2.25) | <0.001 | 1.34 (1.24–1.44) | <0.001 | 2.11 (2.02–2.20) | <0.001 | 1.32 (1.21–1.44) | <0.001 |
| Total charges | 27,098 (23,821–20,375) | <0.001 | 22,071 (19,033–25,109) | <0.001 | 27,098 (24917–29279) | <0.001 | 21,510 (18,492–24,528) | <0.001 |

PCI, percutaneous coronary intervention; VT, ventricular tachycardia; VF, ventricular fibrillation; LOS. Length of stay.

VF cardiogenic shock, cardiac arrest, tracheal intubation, and mechanical ventilation. AF patients exhibited longer lengths of stay and higher total hospitalization charges.

After propensity matching, the results were identical with increased mortality, hospital complications, extended hospital stays, and lower diagnostic angiography and PCI utilization in patients with AF on univariate and multivariate regression analyses.

## 7. Discussion

This study demonstrates that patients with NSTEMI and concomitant AF had poorer outcomes than those without AF. This subpopulation was not only found to have increased mortality, but they were also less likely to undergo ischemic evaluation and treatment and had higher rates of cardiac complications, increased length of stay, and higher total hospitalization charges.

The interaction and causality relationship between CAD and AF is complex, and many studies in the past have shown varied results. The prevalence of CAD in AF was previously estimated to be between 18 and 46.5 %, whereas the prevalence of AF in CAD was low, from 0.5 to 5 % [12,18]. Previous research identified CAD as an independent risk factor for the development of AF [19], and early onset AF post-AMI is linked with a dismal prognosis [20]. Studies have demonstrated poor short and long-term outcomes in patients with NSTEMI and AF [21]. The large Global Registry of Acute Coronary Events (GRACE) showed a three-fold increased risk of death for patients with new-onset AF during index hospitalization for acute coronary syndrome [22]. This presenting study concurs with previous findings and found AF as an independent predictor for increased odds of mortality while controlling for other known variables associated with increased mortality after propensity matching.

Several mechanisms are considered as possible etiologies behind increased mortality in this sub-population. One theory suggested that due to shared risk factors between the two conditions, AF and CAD are both the products of these underlying risk factors that promote atrial ischemia, induce AF, and encourage obstructive coronary artery disease [23]. Another hypothesis suggests reentry pathways with different refractory times create reentry circuits and, along with the structural remodeling of the left atrium, increase vulnerability to AF [24,25]. Very few cases of thromboembolic AMI have been reported with AF due to the associated systemic inflammatory state promoting prothrombotic environment [26,27]. Lastly, the increased ventricular rate can induce subendocardial ischemic and cause NSTEMI [28].

Interestingly, one study found that most deaths in anticoagulated AF patients were from cardiac causes (37 %) rather than stroke (9.8 %) [29]. Another prospective cohort study demonstrated an association between AF and NSTEMI and not with STEMI [30] Pooled data from a 2016 *meta*-analysis showed a 39 % elevated risk of NSTEMI in AF patients and a two-fold increased likelihood of cardiovascular events or death compared to patients without AF [31]. Finally, a single-center retrospective analysis showed no association between anatomical characteristics of CAD and AF; however, it found more severe CAD in patients with AF [32].

This study showed lower rates of diagnostic coronary angiography and PCI in patients with AF. This finding could be explained by higher rates of anticoagulation therapy in AF patients, potentially delaying the diagnostic work. Also, patients with NSTEMI and AF commonly present with rapid ventricular rate, and this can mislead the treating physician to diagnose type II NSTEMI more commonly in this subpopulation. The lower utilization of diagnostic evaluation is alarming, as the presenting study showed increased mortality in NSTEMI patients with concurrent AF. Finally, the study indicated an increased propensity for cardiac complications and elevated resource utilization, underscoring the crucial importance of treating AF as a distinct risk factor for CAD and advocating for early ischemic evaluation.

**Limitations:** Our study had the following limitations. Like other retrospective studies, the patients were not randomized, and only hospitalized patients were included. The anticoagulation status was unknown, which may explain the lower rate of diagnostic workups during index hospitalization. The ICD-10 coding methodology within the NIS contains some inherent limitations. NIS provides all-cause mortality as the outcome instead of cardiovascular-specific mortality. There is a potential for coding error as the accuracy of the ICD-10 codes depends on the treating physician. The patients with missing information were excluded from the analysis, which may infer selection bias.

## 8. Conclusion

This study examined the impact of AF on NSTEMI mortality, cardiac complications, length of stay, and total hospital charges. NSTEMI patients with AF had higher odds of mortality. They were less likely to undergo ischemic workup or intervention, more likely to suffer serious cardiac complications, and, on average, had longer lengths of hospital stay and higher hospital charges. AF should be considered as an independent marker for CAD. More research is required to understand the challenges of obtaining ischemic workup in AF patients. More education is needed to promote early consideration of ischemic evaluation in patients with AF.

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## CRediT authorship contribution statement

**Mirza Faris Ali Baig:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Formal analysis, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References


[1] J. Andrade, P. Khairy, D. Dobrev, S. Nattel, The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms, Circ. Res. 114 (9) (2014) 1453–1468, https://doi.org/10.1161/CIRCRESAHA.114.303211.

[2] J. Kornej, C.S. Börschel, E.J. Benjamin, R.B. Schnabel, Epidemiology of atrial fibrillation in the 21st century: novel methods and new insights, Circ. Res. 127 (1) (2020) 4–20, https://doi.org/10.1161/CIRCRESAHA.120.316340.

[3] A.D. Elliott, M.E. Middeldorp, I.C. Van Gelder, C.M. Albert, P. Sanders, Epidemiology and modifiable risk factors for atrial fibrillation, Nat. Rev. Cardiol. 20 (6) (2023) 404–417, https://doi.org/10.1038/s41569-022-00820-8.

[4] S.S. Virani, A. Alonso, E.J. Benjamin, et al., Heart disease and stroke Statistics-2020 update: a report from the American Heart Association, Circulation 141 (9) (2020) e139–e596, https://doi.org/10.1161/CIR.0000000000000757.

[5] A. Deshmukh, M. Iglesias, R. Khanna, T. Beaulieu, Healthcare utilization and costs associated with a diagnosis of incident atrial fibrillation, Heart Rhythm O2. 3 (5) (2022) 577–586, https://doi.org/10.1016/j.hroo.2022.07.010.

[6] E. Olvera Lopez, B.D. Ballard, A. Jan, Cardiovascular Disease. StatPearls, StatPearls Publishing, Treasure Island (FL), 2023..

[7] J.C. Brown, T.E. Gerhardt, E. Kwon, Risk Factors for Coronary Artery Disease. StatPearls, StatPearls Publishing, Treasure Island (FL), 2023..

[8] U. Ralapanawa, R. Sivakanesan, Epidemiology and the magnitude of Coronary artery disease and acute Coronary syndrome: a Narrative review, J. Epidemiol. Glob. Health. 11 (2) (2021) 169–177, https://doi.org/10.2991/jegh.k.201217.001.

[9] GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1736-1788. https://doi.org/10.1016/S0140-6736(18)32203-7.

[10] M.M. Murphy, J.K. Schmier, Cardiovascular Healthcare cost savings associated with increased whole grains consumption among adults in the United States, Nutrients 12 (8) (2020) 2323, https://doi.org/10.3390/nu12082323.

[11] R. Hajar, Risk factors for Coronary artery disease: historical perspectives, Heart Views. 18 (3) (2017) 109–114, https://doi.org/10.4103/HEARTVIEWS.HEARTVIEWS_106_17.

[12] E. Michniewicz, E. Mlodawska, P. Lopatowska, A. Tomaszuk-Kazberuk, J. Malyszko, Patients with atrial fibrillation and coronary artery disease - double trouble, Adv. Med. Sci. 63 (1) (2018) 30–35, https://doi.org/10.1016/j.advms.2017.06.005.

[13] E.Z. Soliman, M.M. Safford, P. Muntner, et al., Atrial fibrillation and the risk of Myocardial Infarction, JAMA Intern. Med. 174 (1) (2014) 107–114, https://doi.org/10.1001/jamainternmed.2013.11912.

[14] T. Yan, S. Zhu, C. Xie, et al., Coronary artery disease and atrial fibrillation: a bidirectional mendelian randomization study, J Cardiovasc Dev Dis. 9 (3) (2022) 69, https://doi.org/10.3390/jcdd9030069.

[15] G. Batra, B. Svennblad, C. Held, et al., All types of atrial fibrillation in the setting of myocardial infarction are associated with impaired outcomes, Heart 102 (12) (2016) 926–933, https://doi.org/10.1136/heartjnl-2015-308678.

[16] P. Stojadinović, A. Deshraju, D. Wichterle, et al., The hemodynamic effect of simulated atrial fibrillation on left ventricular function, J. *Cardiovasc. Electrophysiol.* 33 (12) (2022) 2569–2577, https://doi.org/10.1111/jce.15669.

[17] HCUP National Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2019. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/nisoverview.jsp.

[18] Y.P. Sharma, A. Batta, K. Makkar, et al., Angiographic profile and outcomes in persistent non-valvular atrial fibrillation: a study from tertiary care center in North India, Indian Heart J. 74 (1) (2022) 7–12, https://doi.org/10.1016/j.ihj.2021.12.010.

[19] A. Brandes, M.D. Smit, B.O. Nguyen, M. Rienstra, I.C. Van Gelder, Risk factor Management in Atrial Fibrillation, Arrhythm. Electrophysiol. Rev. 7 (2) (2018) 118–127, https://doi.org/10.15420/aer.2018.18.2.

[20] P. Jabre, V.L. Roger, M.H. Murad, et al., Mortality associated with atrial fibrillation in patients with myocardial infarction: a systematic review and meta-analysis, Circulation 123 (15) (2011) 1587–1593, https://doi.org/10.1161/CIRCULATIONAHA.110.986661.

[21] G. Tsigkas, G. Kopsida, I. Xanthopoulou, et al., Diagnostic accuracy of electrocardiographic ST-segment depression in patients with rapid atrial fibrillation for the prediction of coronary artery disease, Can. J. Cardiol. 30 (8) (2014) 920–924, https://doi.org/10.1016/j.cjca.2014.03.023.

[22] R.H. Mehta, O.H. Dabbous, C.B. Granger, et al., Comparison of outcomes of patients with acute coronary syndromes with and without atrial fibrillation, Am. J. Cardiol. 92 (9) (2003) 1031–1036, https://doi.org/10.1016/j.amjcard.2003.06.001.

[23] L. Polimeni, L. Perri, M. Saliola, S. Basili, F. Violi, The risk of myocardial infarction in patients with atrial fibrillation: an unresolved issue, Intern. Emerg. Med. 5 (2) (2010) 91–94, https://doi.org/10.1007/s11739-010-0352-2.

[24] D.H. Lau, S. Nattel, J.M. Kalman, P. Sanders, Modifiable risk factors and atrial fibrillation, Circulation 136 (6) (2017) 583–596, https://doi.org/10.1161/CIRCULATIONAHA.116.023163.

[25] J. Heijman, N. Voigt, S. Nattel, D. Dobrev, Cellular and molecular electrophysiology of atrial fibrillation initiation, maintenance, and progression, Circ. Res. 114 (9) (2014) 1483–1499, https://doi.org/10.1161/CIRCRESAHA.114.302226.

[26] R.K. Garg, N. Jolly, Acute myocardial infarction secondary to thromboembolism in a patient with atrial fibrillation, Int. J. Cardiol. 123 (1) (2007) e18–e20, https://doi.org/10.1016/j.ijcard.2006.11.095.

[27] J. Tomcsányi, K. Takó, B. Sármán, [Recurrent acute myocardial infarction as a thromboembolic complication of atrial fibrillation], Orv Hetil. 157 (5) (2016) 191–193, https://doi.org/10.1556/650.2016.30349.

[28] B. Kea, T. Alligood, V. Manning, M. Raitt, A review of the relationship of atrial fibrillation and acute Coronary syndrome, Curr. Emerg. Hosp. Med. Rep. 4 (3) (2016) 107–118, https://doi.org/10.1007/s40138-016-0105-2.

[29] E. Marijon, J.Y. Le Heuzey, S. Connolly, et al., Causes of death and influencing factors in patients with atrial fibrillation: a competing-risk analysis from the randomized evaluation of long-term anticoagulant therapy study, Circulation 128 (20) (2013) 2192–2201, https://doi.org/10.1161/CIRCULATIONAHA.112.000491.

[30] E.Z. Soliman, F. Lopez, W.T. O'Neal, et al., Atrial fibrillation and risk of ST-segment-elevation versus non-ST-segment-elevation Myocardial Infarction: the atherosclerosis risk in communities (ARIC) study, Circulation 131 (21) (2015) 1843–1850, https://doi.org/10.1161/CIRCULATIONAHA.114.014145.

[31] W. He, Y. Chu, Atrial fibrillation as a prognostic indicator of myocardial infarction and cardiovascular death: a systematic review and meta-analysis, Sci. Rep. 7 (1) (2017) 3360, https://doi.org/10.1038/s41598-017-03653-5.

[32] L.J. Motloch, S. Reda, R. Larbig, et al., Characteristics of coronary artery disease among patients with atrial fibrillation compared to patients with sinus rhythm, Hellenic J. Cardiol. 58 (3) (2017) 204–212, https://doi.org/10.1016/j.hjc.2017.03.001.