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# Predicting Outcomes in Patients With Atrial Fibrillation and Acute Mesenteric Ischemia

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| <b>Purpose</b>     | Outcomes in patients with atrial fibrillation who develop acute mesenteric ischemia, and the impact of anticoagulation on complications, are not defined.  |
| <b>Methods</b>     | Patients admitted with acute mesenteric ischemia in the National Inpatient Sample from 2007, with and without atrial fibrillation, were compared for in-hospital outcomes using multivariate regression, and the impact of prior anticoagulation determined.   |
| <b>Results</b>     | Of 48,872 patients with acute mesenteric ischemia, 8,306 had atrial fibrillation, with 680 patients also on anticoagulation. Atrial fibrillation patients were more likely to be older and have hypertension, heart failure, or chronic lung or renal disease. After adjusting for potential confounders, atrial fibrillation remained independently associated with higher mortality ( $P < 0.001$ ). Patients on anticoagulation were less likely to have intestinal resections or shock, less likely to need intubation and had lesser hospital stay and hospital charges compared to those not on anticoagulation. |
| <b>Conclusions</b> | In patients with acute mesenteric ischemia, presence of atrial fibrillation increases mortality, but prior anticoagulation reduces incidence of complications, length of stay and hospital charges. ( <i>J Patient Cent Res Rev.</i> 2016;3:177-186.)  |
| <b>Keywords</b>    | acute mesenteric ischemia; atrial fibrillation; anticoagulation; outcomes  |

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Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting about 5 million patients in the United States.<sup>1-3</sup> It is characterized by disorganized atrial electrical activation causing an irregular heart rate and loss of atrial contractility.<sup>4</sup> In the presence of risk factors, this increases susceptibility for thromboembolic events that can cause ischemic stroke and/or systemic arterial occlusion.<sup>5</sup> Embolic obstruction of the superior mesenteric artery or its

branches results in acute mesenteric ischemia (AMSI), which can lead to intestinal necrosis, peritonitis and death if left untreated.<sup>5</sup> The emboli originate from the heart in more than 75% of cases and preferentially lodge distal to the origin of the middle colic artery from the superior mesenteric artery.<sup>5</sup>

AF is a risk factor for AMSI, with a reported annual incidence of 0.14% in patients with AF and a mortality rate of about 70%.<sup>6</sup> Early diagnosis and prompt surgical intervention are essential to improve survival, and any delay in diagnosis is associated with poor outcomes.<sup>7,8</sup> Despite advancements in management — including endovascular stenting of the mesenteric arterial lesion, thrombolysis of fresh thrombus and exploratory laparotomy with embolectomy followed by resection of necrotic bowel

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— the survival rate remains poor and reflects the low percentage of diagnoses made before the development of intestinal necrosis.<sup>9,10</sup> A significant reduction in the incidence of ischemic stroke in patients with AF has been demonstrated by anticoagulation.<sup>11-15</sup> However, such information is not available for those with AMsI, and the effect of prior anticoagulation on outcomes of AMsI in patients with AF is not known.

In addition to identifying independent predictors of AMsI, we investigated the differences in outcomes of AMsI patients with and without AF as well as the impact of prior anticoagulation on these outcomes.

## METHODS

### Data Source and Objectives

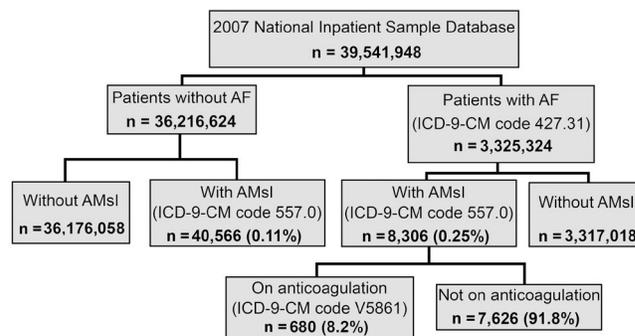
Data were obtained from the National Inpatient Sample (NIS) database for the year 2007. The NIS is sponsored by the Agency for Healthcare Research and Quality as a part of the Healthcare Cost and Utilization Project and is the largest publicly available all-payer database in the United States. The database contains discharge-level data from about 1,000 hospitals designed to approximate a 20% stratified sample of all community hospitals in the United States. Currently, 46 states contribute data to NIS. The database contains more than 100 clinical and nonclinical elements for each hospital stay, including primary and secondary diagnoses and procedures, admission and discharge status, patient demographics, hospital characteristics, payer source, comorbidity measures and length of stay.<sup>16</sup> Discharge weights are provided in each patient discharge record and then used to obtain national estimates. As the data are based on an administrative dataset and de-identified, no informed consent or institutional review board approval was applicable to this study. Our objectives were to determine independent risk factors for AMsI, whether there was a difference in outcome between patients developing AMsI with or without AF, and if being on anticoagulation had an effect on the outcomes of patients with AMsI in the setting of AF.

### Study Population and Outcomes

We used the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 557.0 to identify all patients with a diagnosis of AMsI (n=48,872) and code 427.31 for AF (n=3,325,324).

Of the patients with AMsI, 8,306 had a concomitant diagnosis of AF while 40,566 had no AF. Within the AF plus AMsI group, those on anticoagulation were identified using the ICD-9-CM code V5861 (n=680); the remaining patients (n=7,626) were considered to be not on anticoagulation (Figure 1).

Primary outcome of interest was in-hospital mortality. Secondary outcomes of interest were length of stay longer than 14 days (75% quartile), nonroutine discharges (discharge dispositions other than home or self-care), total hospital charges, endotracheal intubation/mechanical ventilation (ICD-9-CM codes 96.04, 96.70–96.72), small bowel resection (codes 45.61–45.63), colon resection (codes 45.71–45.79, 45.81–45.83), total parenteral nutrition (code 99.15) and shock (codes 785.50–785.52, 785.59, 998.09).



**Figure 1.** Patients with acute mesenteric ischemia in National Inpatient Sample from 2007. Flowchart depicting selection of the study population and number of patients with acute mesenteric ischemia in those with or without history of atrial fibrillation and anticoagulation.

### Statistical Analysis

Multivariable logistic regression was used with AMsI as a binary dependent variable and baseline patient characteristics — including demographics (age, gender, race), primary expected payer, median household income by patient ZIP code, 29 Elixhauser comorbidities (as defined by the Agency for Healthcare Research and Quality)<sup>17,18</sup> and other clinically relevant comorbidities (dyslipidemia, hypertension, congestive heart failure, chronic lung disease, coagulation disorders, diabetes mellitus, liver disorders, neurological disorders, obesity, perivascular disease,

renal failure, tumor, tumor with metastasis, valvular heart disease) — as independent covariates.<sup>19</sup> A list of ICD-9-CM and Clinical Classifications Software codes used to identify comorbidities is provided online in Supplemental Appendix 1.

Data were analyzed using SAS statistical software package Version 9.4 (SAS Institute Inc., Cary, NC). Continuous variables were summarized using means with 95% confidence intervals (CI). Similarly, categorical variables were summarized with the use of frequencies and percentages. Chi-squared test was used to compare categorical variables and the t-test to compare continuous variables. Appropriate survey discharge weights were applied for NIS data, and survey procedure commands were applied for the analysis. A two-sided P-value < 0.05 was used to assess statistical significance. Multivariate logistic regression was used to compare outcomes between the AF versus no AF groups and the AF on anticoagulation versus AF not on anticoagulation groups. The regression model adjusted for demographics, primary expected payer, median household income, all Elixhauser comorbidities, other clinically relevant comorbidities, primary diagnosis of AF and secondary diagnosis of AMsI.

## RESULTS

Baseline characteristics of patients diagnosed with AMsI in 2007 are described in Table 1. In general, patients with AMsI and AF were more likely to be older in age, white and nonsmokers. They also were more likely to have heart failure, chronic lung disease, peripheral vascular disease, renal failure and valvular heart disease (P<0.001).

### Predictors for AMsI

Patients with AF had significantly higher odds of developing AMsI compared to patients without AF (odds ratio [OR]: 1.16, 95% CI: 1.08–1.25, P<0.001). The odds of developing AMsI increased with age. Patients 50 to 74 years of age were at the highest risk (OR: 4.55, 95% CI: 3.88–5.34, P<0.001) of developing AMsI. Further analysis to assess the difference in AMsI risk between elderly (65–74 years) and middle-aged patients (50–64 years) demonstrated a statistically significant greater risk of AMsI in the older patients (OR: 1.24, 95% CI: 1.12–1.36, P<0.001). In addition, female sex (OR: 1.35, 95%

CI: 1.27–1.43, P<0.001), white race (OR: 1.73, 95% CI: 1.53–1.96, P<0.001), emergency admission type (OR: 1.64, 95% CI: 1.42–1.89, P<0.001), peripheral vascular disease (OR: 2.11, 95% CI: 1.93–2.31, P<0.001), chronic blood loss anemia (OR: 1.80, 95% CI: 1.59–2.05, P<0.001), heart failure (OR: 1.31, 95% CI: 1.21–1.41, P<0.001), liver disorders (OR: 1.39, 95% CI: 1.21–1.59, P<0.001), valvular heart disease (OR: 1.24, 95% CI: 1.13–1.37, P<0.001) and renal failure (OR: 1.10, 95% CI: 1.01–1.19, P=0.03) were associated with an increased risk of AMsI (Table 2). A history of anticoagulation use, hyperlipidemia, hypertension, tobacco use, diabetes mellitus, obesity or neurological disorder was associated with a lower risk for AMsI.

### Influence of AF on Outcomes in Patients With AMsI

Patients with AMsI and history of AF were more likely to have adverse outcomes compared to patients with no history of AF (Table 3). A significantly higher percentage of patients with AF and AMsI required colectomy (24% vs 18%, P<0.001) or total parenteral nutrition (17% vs 11%, P<0.001) compared to those without history of AF. There was a statistically significant greater likelihood of shock, intubation or mechanical ventilation as well as greater in-hospital mortality, hospital charges, length of stay and nonroutine discharges (surrogate marker for severity of disease). The unadjusted OR of dying in AF versus non-AF was 2.33 (95% CI: 2.06–2.63). On multivariate logistic regression with adjustment for different confounders, including the comorbidities, the OR of dying still remained significant at 1.59 with 95% CI of 1.3–1.9 (P<0.001).

### Effect of Anticoagulation on Outcomes of AF Patients With AMsI

A lower odds ratio was observed for AMsI in younger (50–64 years) patients with AF on anticoagulation; however, this was not statistically significant (OR: 0.45, 95% CI: 0.19–1.04, P=0.063). On the other hand, elderly patients (65–74 years) with AF on chronic anticoagulation had a lower incidence of AMsI compared with those not on anticoagulation (OR: 0.41, 95% CI: 0.24–0.70, P=0.001). Of the patients diagnosed with AMsI, those with AF but not on anticoagulation had more adverse outcomes (both primary and secondary outcomes) compared to

**Table 1.** Baseline Demographics, Comorbidities, and Hospital Characteristics of Patients With Acute Mesenteric Ischemia

|   | Atrial fibrillation<br>(n=8,306) | No atrial fibrillation<br>(n=40,566) | P      |
|---|----------------------------------|--------------------------------------|--------|
| Mean age, years (95% confidence interval) | 77.45 (76.92–78.98)              | 62.74 (61.78–63.69)                  | <0.001 |
| Age group, n (%)                          |                                  |                                      | <0.001 |
| <35 years                                 | 5 (0.1)                          | 3,762 (9.3)                          |        |
| 35–49 years                               | 114 (1.4)                        | 4,764 (11.7)                         |        |
| 50–74 years                               | 2,662 (32.1)                     | 18,898 (46.6)                        |        |
| 75+ years                                 | 5,526 (66.5)                     | 13,142 (32.4)                        |        |
| Sex,* n (%)                               |                                  |                                      | 0.45   |
| Female                                    | 5,170 (62.2)                     | 24,800 (61.2)                        |        |
| Male                                      | 3,136 (37.8)                     | 15,722 (38.8)                        |        |
| Race, n (%)                               |                                  |                                      | <0.001 |
| White                                     | 5,305 (63.9)                     | 22,596 (55.7)                        |        |
| Black                                     | 370 (4.5)                        | 2,796 (6.9)                          |        |
| Hispanic                                  | 310 (3.7)                        | 2,436 (6.0)                          |        |
| Asian or Pacific Islander                 | 100 (1.2)                        | 780 (1.9)                            |        |
| American Indian                           | 68 (0.8)                         | 248 (0.6)                            |        |
| Other/missing                             | 2,153 (25.9)                     | 11,033 (27.2)                        |        |
| Smoking, n (%)                            | 267 (3.2)                        | 3,703 (9.1)                          | <0.001 |
| Median income by patient ZIP code, n (%)  |                                  |                                      | 0.16   |
| \$1–\$38,999                              | 1,839 (22.6)                     | 9,829 (24.2)                         |        |
| \$39,000–\$47,999                         | 1,987 (23.9)                     | 9,994 (24.6)                         |        |
| \$48,000–\$62,999                         | 2,152 (25.9)                     | 10,116 (24.9)                        |        |
| \$63,000+                                 | 2,158 (26.0)                     | 9,568 (23.6)                         |        |
| Missing                                   | 170 (2.0)                        | 1,059 (2.6)                          |        |
| Payer, n (%)                              |                                  |                                      | <0.001 |
| Medicare                                  | 6,907 (83.2)                     | 22,555 (55.6)                        |        |
| Medicaid                                  | 189 (2.3)                        | 3,257 (8.0)                          |        |
| Private insurance                         | 1,072 (12.9)                     | 11,904 (29.3)                        |        |
| Self-pay                                  | 74 (0.9)                         | 1,494 (3.7)                          |        |
| Other/missing                             | 64 (0.8)                         | 1,356 (3.4)                          |        |
| Admission type, n (%)                     |                                  |                                      | 0.08   |
| Emergency                                 | 5,681 (68.4)                     | 26,344 (64.9)                        |        |
| Urgent                                    | 1,062 (12.8)                     | 5,714 (14.1)                         |        |
| Elective                                  | 699 (8.4)                        | 3,929 (9.7)                          |        |
| Other/missing                             | 864 (10.4)                       | 4,579 (11.3)                         |        |
| Comorbidities, n (%)                      |                                  |                                      |        |
| Hypertension                              | 4,345 (52.3)                     | 19,340 (47.7)                        | 0.001  |
| Hyperlipidemia                            | 996 (12.0)                       | 5,289 (13.0)                         | 0.25   |
| Heart failure                             | 2,881 (34.7)                     | 4,097 (10.1)                         | <0.001 |
| Chronic lung disease                      | 2,572 (31.0)                     | 7,969 (19.6)                         | <0.001 |
| Diabetes mellitus with complications      | 325 (3.9)                        | 1,305 (3.2)                          | 0.18   |
| Liver disorders                           | 185 (2.2)                        | 1,562 (3.9)                          | 0.004  |
| Neurological disorders                    | 621 (7.5)                        | 2,418 (6.0)                          | 0.03   |
| Obesity                                   | 335 (4.0)                        | 2,073 (5.1)                          | 0.06   |
| Peripheral vascular disease               | 1,227 (14.8)                     | 4,353 (10.7)                         | <0.001 |
| Renal failure                             | 1,720 (20.7)                     | 4,510 (11.1)                         | <0.001 |
| Metastatic cancer                         | 178 (2.1)                        | 1,347 (3.3)                          | 0.02   |
| Valvular heart disease                    | 1,141 (13.7)                     | 1,969 (4.9)                          | <0.001 |

\*There were nine observations for the sex category missing from the group without atrial fibrillation (weighted number: 44).

those with AF who were on anticoagulation (Table 4). Patients with AF who were not on anticoagulation were more likely to have small bowel resections (25% vs 16%,  $P=0.03$ ) and colectomy (25% vs 11%,  $P<0.001$ ). There were significantly greater numbers of cases of shock and those requiring total parenteral nutrition and intubation/mechanical ventilation (all acting as surrogate markers of severity) in groups not on anticoagulation compared to those on anticoagulation. Furthermore, hospital charges, length of stay, in-hospital mortality and nonroutine discharges also were greater in the group not on anticoagulation. The unadjusted odds of in-hospital death in those with AMsI with AF who were not on anticoagulation versus those with AMsI with AF who were on anticoagulation was 2.09 with a 95% CI of 1.37–3.20 ( $P=0.006$ ). After multivariate analysis, however, this difference in mortality between the two groups became statistically nonsignificant (OR: 1.85, 95% CI: 0.86–3.98,  $P=0.12$ ).

## DISCUSSION

The main findings of this study in a large number of patients hospitalized with AMsI are that: 1) this complication is more often present in patients with AF than those without, and 2) patients with AF are more likely to have worse outcomes, including higher

**Table 2.** Significant Predictors for Acute Mesenteric Ischemia

| Covariates                          | Odds ratio | 95% CI    | P      |
|-------------------------------------|------------|-----------|--------|
| Atrial fibrillation                 | 1.16       | 1.08–1.25 | <0.001 |
| Age category                        |            |           |        |
| <35 years (reference)*              | –          | –         | –      |
| 35–49 years                         | 2.24       | 1.90–2.65 | <0.001 |
| 50–74 years                         | 4.55       | 3.88–5.34 | <0.001 |
| ≥75 years                           | 4.39       | 3.72–5.17 | <0.001 |
| Sex: female vs male                 | 1.35       | 1.27–1.43 | <0.001 |
| Race: white vs black                | 1.73       | 1.53–1.96 | <0.001 |
| Admission type: emergency vs urgent | 1.64       | 1.42–1.89 | <0.001 |
| Hyperlipidemia                      | 0.69       | 0.63–0.75 | <0.001 |
| Use of anticoagulation              | 0.70       | 0.59–0.83 | <0.001 |
| Tobacco use                         | 0.77       | 0.69–0.86 | <0.001 |
| Chronic blood loss anemia           | 1.80       | 1.59–2.05 | <0.001 |
| Heart failure                       | 1.31       | 1.21–1.41 | <0.001 |
| Diabetes mellitus                   | 0.74       | 0.69–0.79 | <0.001 |
| Hypertension                        | 0.93       | 0.87–0.99 | 0.04   |
| Liver disorder                      | 1.39       | 1.21–1.59 | <0.001 |
| Neurological disorder               | 0.73       | 0.66–0.81 | <0.001 |
| Obesity                             | 0.76       | 0.66–0.86 | <0.001 |
| Peripheral vascular disease         | 2.11       | 1.93–2.31 | <0.001 |
| Renal failure                       | 1.10       | 1.01–1.19 | 0.03   |
| Valvular heart disease              | 1.24       | 1.13–1.37 | <0.001 |

\*Reference group = all other age groups were compared to this age group.

CI, confidence interval.

**Table 3.** Adverse Outcomes in Acute Mesenteric Ischemia: With AF vs Without AF

| Outcomes  | Acute mesenteric ischemia with AF (n=8,306) | Acute mesenteric ischemia without AF (n=40,566) | P      |
|---|---|---|--------|
| Small bowel resection, n (%)                      | 1,992 (24)                                  | 9,035 (22)                                      | 0.14   |
| Colectomy, n (%)                                  | 1,955 (24)                                  | 7,128 (18)                                      | <0.001 |
| Shock, n (%)                                      | 1,418 (17)                                  | 5,157 (13)                                      | <0.001 |
| Total parenteral nutrition, n (%)                 | 1,430 (17)                                  | 4,346 (11)                                      | <0.001 |
| Intubation and/or mechanical ventilation, n (%)   | 2,701 (33)                                  | 8,287 (20)                                      | <0.001 |
| Mean hospital charges in U.S. dollars, n (95% CI) | 110,802 (101,378–120,226)                   | 87,114 (80,840–93,388)                          | <0.001 |
| Length of stay > 14 days (>75% quartile), n (%)   | 1,884* (35)                                 | 6,870* (21)                                     | <0.001 |
| In-hospital mortality, n (%)                      | 2,946 (35.5)                                | 7,756 (19)                                      | <0.001 |
| Nonroutine discharges, n (%)                      | 6,553 (79)                                  | 20,842 (51)                                     | <0.001 |

\*Patients who died prior to discharge were excluded.

AF, atrial fibrillation; CI, confidence interval.

**Table 4.** Adverse Outcomes in Acute Mesenteric Ischemia: AF on Anticoagulation vs AF Not on Anticoagulation

| Outcomes   | AF on anticoagulation<br>(n=680) | AF no anticoagulation<br>(n=7,626) | P      |
|--|----------------------------------|------------------------------------|--------|
| Small bowel resection, n (%)                         | 111 (16)                         | 1,881 (25)                         | 0.03   |
| Colectomy, n (%)                                     | 76 (11)                          | 1,880 (25)                         | <0.001 |
| Shock, n (%)   | 68.41 (10)                       | 1,350 (18)                         | 0.02   |
| Total parenteral nutrition, n (%)                    | 27 (4)                           | 1,403 (18)                         | <0.001 |
| Intubation and/or mechanical ventilation, n (%)      | 68 (10)                          | 2,633 (35)                         | <0.001 |
| Mean hospital charges in U.S. dollars,<br>n (95% CI) | 42,426<br>(34,701–50,150)        | 116,931<br>(106,854–127,009)       | <0.001 |
| Length of stay > 14 days (>75% quartile), n (%)      | 43* (6)                          | 1,068* (14)                        | <0.001 |
| In-hospital mortality, n (%)                         | 148 (22)                         | 2,798 (37)                         | <0.001 |
| Nonroutine discharges, n (%)                         | 378 (56)                         | 6,175 (81)                         | <0.001 |

\*Patients who died prior to discharge were excluded.

AF, atrial fibrillation; CI, confidence interval.

in-hospital mortality and greater likelihood of small bowel resection, colectomy and shock. Moreover, elderly patients with AF who were on anticoagulation were less likely to be admitted with AMsI than those not on anticoagulation, and patients with AF on anticoagulation had fewer complications, including hemodynamic compromise with shock, small bowel resection, colectomy and need for intubation or mechanical ventilation. Length of stay and hospital charges also were significantly less in the anticoagulation group.

AMsI is a serious medical condition with high mortality and morbidity.<sup>6</sup> Therefore, it is necessary to define factors affecting poor outcomes in order to reduce complications associated with AMsI and improve health outcomes. Due to its low incidence, knowledge about reported outcomes and mortality predictors has been obtained from retrospective studies involving a limited number of patients. Although AF is a known risk factor due to the potential for thromboembolism, the incidence of AMsI as a complication and the impact of anticoagulation in patients with AF on outcomes have not been fully defined. Our study, which used a national database comprised of a large number of patients, helps fill some of these knowledge gaps.

AMsI results from perfusion impairment mainly due to vascular occlusion (arterial thrombus/embolus or venous thrombus) or nonocclusive low-flow state (vasospasm or decreased cardiac output) with

decreased perfusion to the small bowel and colon.<sup>20</sup> Since AMsI results from circulatory insufficiency in the mesenteric arteries, it is logical to expect that most of the risk factors would be vascular in nature. In our study, age 65–74 years, peripheral vascular disease, chronic blood loss anemia, liver disorders and valvular heart disease were all associated with increased risk of AMsI.

Advanced age is a known risk factor for vascular disease and mesenteric ischemia. The presence of peripheral arterial disease, which reflects overall atherosclerotic burden<sup>21</sup> and is therefore a surrogate for mesenteric atherosclerosis, also was predictive of AMsI regardless of the presence of AF. Valvular heart diseases increase the risk for AF and thromboembolism, and thereby for AMsI.<sup>22,23</sup> Chronic blood loss anemia also was associated with increased risk for AMsI. Although the precise mechanism behind this is not clear, a secondary hypercoagulable state due to thrombocytosis associated with iron deficiency, microcytosis or reduction in red blood cell deformability<sup>24–26</sup> could be responsible, especially when combined with the diminished oxygen-carrying capacity of reduced hemoglobin levels precipitating hypoxia in hypoperfused areas with preexisting atherosclerotic disease.<sup>27</sup> This could be further exaggerated by hemodynamic stress imposed by cardiac arrhythmias, such as AF, which by itself is associated with increased risk of thromboembolism.<sup>28</sup> This may explain the 127% greater risk for AMsI

among patients with AF (0.25%) when compared to non-AF patients (0.11%).

Another important finding of our study is the reduced risk of AMsI in patients with diabetes, hyperlipidemia, hypertension, tobacco use or obesity. This is in contrast to the greater risk of ischemic stroke/transient ischemic attack in patients with AF with a history of hypertension and diabetes. The reason for this discrepancy is not known but could be related to the previously described paradoxical effect of hyperlipidemia or obesity as protective against mortality in high-risk patients (i.e. those with advanced heart diseases such as myocardial infarction, heart failure, AF, etc.)<sup>29-34</sup> This paradoxical effect has been attributed to better care received by patients with risk factors or coronary artery disease, as they are more likely to receive beta blockers, statins, angiotensin-converting enzyme (ACE) inhibitors or antiplatelet agents, which improve survival and thus contribute to the paradoxically lower risk of cardiovascular events. A subanalysis of patients on cardioprotective medications (beta blocker, ACE inhibitor, antiplatelet) would be interesting. However, information regarding these medications cannot be obtained using the NIS database due to the lack of associated ICD codes.

The overall prognosis of patients with AMsI is poor, and our results indicate that patients with AF do worse than those without AF. In-hospital mortality in patients with AMsI was 22%, but in AF patients the in-hospital mortality was 85% higher (35.5%) than in non-AF patients (19.1%). The higher in-hospital mortality in AF when compared with non-AF patients could be partly explained by the older age of the AMsI patients, a known risk factor for increased mortality<sup>35,36</sup> and higher prevalence of comorbidities. About two-thirds of the patients in the AF group were older than 75 years of age compared to only one-third in the non-AF group. AF patients also were more likely to have valvular heart disease (13.7% vs 4.8% in patients without AF), a known risk factor for atrial enlargement and systemic embolization,<sup>22,23,37</sup> coagulation disorder or liver disease. Previous studies have shown that the time lapse between the onset of symptoms and surgical intervention for AMsI, extent of tissue damage,<sup>35</sup> and presence of shock, acidosis,

previous cardiac illness, acute renal failure and colon involvement were predictors of higher in-hospital mortality and perioperative death.<sup>38</sup> Early diagnosis of AMsI, especially before the onset of intestinal necrosis and peritonitis, is critical to the patient's survival,<sup>35</sup> with the survival rate decreasing from 50% among patients diagnosed less than 24 hours after the onset of symptoms to 30% among those diagnosed more than 24 hours after onset of symptoms.<sup>39</sup>

Complications of AMsI, such as ileus, peritonitis, pancreatitis and gastrointestinal bleed, may mask AMsI symptoms, delay diagnosis and contribute to higher mortality.<sup>35,40</sup> In our study, more AF than non-AF patients had emergency admissions and were sicker, with greater incidence of shock and intestinal damage requiring colectomy, total parenteral nutrition, intubation and mechanical ventilation; this prolonged the hospital stay and resulted in significantly higher hospital charges and in-hospital mortality (Table 3). This might be related to the sudden embolic occlusion of the mesenteric artery in AF, without time for the bowel to develop sufficient collaterals or activate compensatory responses, contributing to graver outcomes resulting from bowel infarction, systemic inflammatory response syndrome, sepsis, respiratory failure (intubation/mechanical ventilation), multiple organ dysfunction and death.<sup>41</sup>

In AF patients on chronic anticoagulation, these complications were significantly reduced when compared to AF patients not on anticoagulation (Table 4), suggesting that patients with AF who are not on anticoagulation are more likely to have thromboembolic events, including AMsI, and ultimately worse outcomes. This provides support for the recommendation for chronic anticoagulation for protection against AMsI, similar to what has been endorsed to reduce risk of stroke in AF.<sup>3,12,42-44</sup>

### Limitations

The main limitation of our study is that it is a retrospective analysis of an administrative database with the potential for selection bias in a hospitalized population with mesenteric ischemia. The NIS database, due to its administrative nature, largely relies on ICD codes; thus, factors that do not have an ICD code cannot be studied using this database.

The patients were gravely ill and had complex disease processes occurring that could have impacted outcomes, including hemodynamic stress in sicker patients that could have aggravated rhythm and rate control. Information on such processes could not be obtained. Multivariate analysis was performed to account for known baseline differences; however, the impact of undocumented confounding factors could not be completely dissected in this retrospective analysis.

The type of AF (persistent vs paroxysmal) could have had an impact on patient outcomes. However, this effect could not be studied using this administrative database as the types of AF cannot be differentiated using ICD codes. Prior studies suggest that thromboembolic outcomes do not differ based on the type of AF.<sup>45,46</sup> The individual risk of thromboembolism based on an individual's CHADS<sub>2</sub>VASc score and the resultant outcomes in the same patient could not be calculated using this administrative database. Based on the current data, we do not know if the patients with a high CHADS<sub>2</sub>VASc score were anticoagulated, whether patients with AMsI had high thromboembolic risk and were not anticoagulated for other reasons, or whether patients were at low risk of thromboembolism. Short of a randomized controlled study, use of an institutional database with patient-level information could help further clarify this question. Despite these limitations, our study, one of the largest assessing the relationship between AF and AMsI, identifies important differences in outcomes in patients with and without AF and provides data in support of the protective role of anticoagulation in reducing complications of AMsI.

## CONCLUSIONS

In this largest cohort of patients with acute mesenteric ischemia, patients with atrial fibrillation had significantly higher in-hospital mortality and poorer outcomes when compared to patients without AF. Since AF is a common arrhythmia observed in the community and after surgery, it is critical to manage the risk of thromboembolism appropriately.<sup>2-4,44</sup> Our results emphasize the need for aggressive management in this high-risk subgroup. Among patients with AF, those who were not on anticoagulation had worse outcomes than those on anticoagulation, and therefore anticoagulation should be considered in patients with thromboembolic risk factors.

## Patient-Friendly Recap

- Acute mesenteric ischemia results in restricted blood flow to vital organs and can be deadly if left untreated.
- After identifying which clinical factors increased the risk for developing this syndrome, the authors zeroed in on the finding that patients who also had a history of the heart rhythm disorder atrial fibrillation fared significantly worse.
- On further analysis, they discovered that patients who had been taking anticoagulation medication for their atrial fibrillation not only developed mesenteric ischemia less often but that the ones who did develop the syndrome experienced fewer complications.
- Study results led the authors to encourage anticoagulant use for atrial fibrillation and other high-risk clotting conditions, especially in patients aged 65–74 years, to prevent acute mesenteric ischemia.

## Conflicts of Interest

None.

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