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## Impact of atrial fibrillation on outcomes with motor vehicle accidents☆☆☆☆

Kanishk Agnihotri<sup>a</sup>, N.V. Pothineni<sup>b</sup>, Paris Charilaou<sup>a</sup>, Vaibhav R. Vaidya<sup>c</sup>, Badal Thakkar<sup>d</sup>, Vishal Goyal<sup>e</sup>, Sabeeda Kadavath<sup>f</sup>, Nileshkumar Patel<sup>e</sup>, Apurva Badheka<sup>g</sup>, Peter Noseworthy<sup>c</sup>, Suraj Kapa<sup>c</sup>, Paul Friedman<sup>c</sup>, Bernard Gersh<sup>c</sup>, Hakan Paydak<sup>b</sup>, Abhishek Deshmukh<sup>c,\*</sup>

<sup>a</sup> Saint Peters University Hospital, New Brunswick, NJ, United States

<sup>b</sup> University of Arkansas Medical Sciences, Little Rock, AR, United States

<sup>c</sup> Mayo Clinic Division of Cardiovascular Diseases, Rochester, MN, United States

<sup>d</sup> Rutgers New Jersey Medical School, Newark, NJ, United States

<sup>e</sup> University of Miami Miller School of Medicine, Miami, FL, United States

<sup>f</sup> Lincoln Medical and Mental Health Center, Bronx, NY, United States

<sup>g</sup> Everett Clinic, Everett, WA, United States

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### ABSTRACT

**Background:** We examined the effect of AF a commonly encountered arrhythmia with significant morbidity on mortality following a motor vehicle accident (MVA) related hospitalization.

**Methods:** The Nationwide Inpatient Sample (NIS) was queried to identify patients with AF (ICD-9 CM 427.31) and MVA (ICD-9 CM E810.0–E819.9), considered separately and together, from 2003 through 2012. Baseline characteristics were identified and multilevel mixed model multivariate analysis was employed to verify the impact of AF on in-patient mortality in survivors.

**Results:** Of an estimated 2,978,630 MVA admissions reported, 79,687 (2.6%) hospitalizations also had a diagnosis of AF. The in-hospital mortality was 2.6% in MVA alone and 7.6% in MVA and AF. In multivariate analysis, after adjustment for age, gender, Charlson Comorbidity Index (CCI), the Trauma Mortality Prediction Model (TMPM), and hospital characteristics, AF was independently associated with in-hospital mortality [Odds ratio (OR) 1.52, confidence interval (CI) 1.41–1.69,  $P$  value < 0.0001]. In patients with MVA and AF, increasing age, CCI, and TMPM were associated with higher mortality. Female gender is associated with lower mortality (OR 0.84, CI 0.81–0.88,  $P$  = 0.0016). Most patients with MVA and AF had a CHADS2 score of 2 (34.6%). Mortality and transfusion rates were higher in MVA and AF patients compared to patients with MVA alone across all CHADS2 scores.

**Conclusion:** In patients with a MVA, the presence of AF is an independent risk factor for in-hospital mortality.

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### 1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice and has a major impact on the healthcare burden. The prevalence of AF is projected to increase from 5.2 million in 2010 to 12.1 million cases in 2030 [1]. The incidence of AF-related hospitalizations continues to rise [2], and frequently complicates hospitalization for patients admitted for other reasons. Anticoagulation is a standard of care for stroke prevention in patients with AF. As more

patients receive anticoagulation therapy, this translates to a higher bleeding risk in cases of acute blood loss. An emerging body of evidence demonstrates that AF can have an impact on cognition [3], and thus could impact complex tasks such as driving.

In 2013, there were 32,894 deaths in the United States related to motor vehicle accidents (MVAs). Despite a 30% reduction in MVA-related deaths compared to the year 2000, the United States leads a group of 20 high-income countries in MVA related deaths [4]. The clinical course of a MVA patient can be significantly complicated by concomitant AF with regard to bleeding risk and other comorbidities [5]. Based on insurance data in Taiwan, Lai et al. have reported greater in-hospital mortality, worse clinical outcomes, and greater costs and duration of hospitalization in MVA patients with AF, compared to patients without AF [6]. However, there are currently no studies informing in-hospital outcomes in patients with AF admitted for a MVA in the United States.

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\* Corresponding author at: Cardiology, Mayo Clinic, 200 1st St SW, Rochester, MN 55905, United States.

E-mail address: [deshmukh.abhishek@mayo.edu](mailto:deshmukh.abhishek@mayo.edu) (A. Deshmukh).

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Using a large nationwide inpatient billing database, we sought to identify the impact of AF on in-hospital mortality for patients admitted.

## 2. Methods

The Nationwide Inpatient Sample (NIS) is a database developed for the Health Care Cost and Utilization Project by the Agency for Healthcare Research and Quality [7]. It is the largest publicly available database in the United States and contains information on all discharges from a 20% stratified-survey complex sample of community, non-federal, hospitals (serving as sampling clusters), yielding national estimates of inpatient hospitalizations, by use of weights. Each individual hospitalization in the NIS is de-identified and contains up to 25 diagnoses and up to 15 procedures during the index hospitalization. The record lists demographic information, insurance status, hospital characteristics, severity and co-morbidity measures, primary and secondary procedures, the outcome of hospitalization, length of stay, and total charges. The NIS has been used extensively to identify national trends in healthcare usage, variations in medical practice, assess the disparity of care, calculate hospitalization rates, quality of care and patient safety, and determine outcomes for various diagnoses and major procedures [2].

The NIS was reviewed using the International Classification of Diseases, 9th Revision Clinical Modification for the years 2003 through 2012. The ICD-9CM diagnostic code E810.0–E819.9 (MVA) [8] for primary diagnosis and ICD-9-CM diagnostic code 427.31 (AF) [9] for secondary diagnoses were analyzed for data elements including demographics, co-morbidities, hospital characteristics in the HCUP registry. The unit of observation was an inpatient stay record. Weighted multivariate regression was performed for all MVA patients, with or without AF. To avoid restricting evaluation to a typical adult population, all observations for the age group < 18 years were excluded. We also excluded patients with missing information regarding age, sex, admission or discharge date, and in-hospital mortality status. The primary outcome measured was in-hospital mortality. Secondary outcomes included the length of stay, and the cost of care. To calculate an estimated cost of hospitalizations, the NIS data was merged with cost-to-charge ratios designed to optimize capacity for national estimates. Costs representing actual expenses incurred with delivery of hospital services including wages, supplies, and utility costs reflect the amount billed by the hospital per admission. For each hospital, a hospital-wide cost-to-charge ratio is then calculated by multiplying the total hospital charge by the cost-to-charge ratio. Adjusted costs for each year were calculated after adjusting for inflation in accordance with the Consumer Price Index data released by the US government in 2015 [10].

NIS variables utilized to identify patients included demographic and location information such as age, sex, and race. The severity of comorbid conditions was identified using the Mayo modification of the Charlson Comorbidity Index (CCI). This index contains 17 comorbid conditions with differential weights. The weight is based on the associated risk of mortality or resource use. The score is based on the sum of all weights and a numeric comorbidity score ranging from 0 to 33 is obtained, with higher scores corresponding to a greater burden of comorbid diseases. These comorbidity measures identify comorbidities and the diagnosis-related group in effect on the date of discharge [11]. These comorbidities are likely present prior to the hospital stay and are not directly linked to the main diagnosis or the principal reason for admission. We also divided patients with MVA alone and those with MVA and AF into subgroups based on CHADS2 score and compared transfusion and mortality rates for these subgroups. Comorbidities such as congestive heart failure, hypertension, diabetes and stroke were identified using appropriate ICD-9 codes and accounted for and combined with the age variable to calculate the CHADS2 score. One of the most reliable injury severity measures was computed [12], which included the minimum independent survival risk ratio (SRRI) [13] of the IC-ISS (ICD-9 Injury Severity Score) [14,15], which most optimally represent the injury severity in administrative databases by utilizing the ICD-9 codes instead of using the Abbreviated Injury Scale (AIS) or even the new Injury Severity Score (NISS) [14,16,17].

The analytical software used was the SAS 9.2 (SAS Institute Inc., Cary, NC), which accounts for the complexity of the survey design and the clustering. As mentioned earlier, the NIS is stratified complex-survey and all analyses are advised to account for these features for accurate estimation of standard errors and confidence intervals, as advised by HCUP [18]. Analyses were performed using hospital-level discharge weights provided by the NIS and national estimates of AF hospitalizations were obtained [7]. In the multi-level mixed-model, the hospital ID-year was random intercepts, representing every hospital on a different year of sampling. In the mixed-model multivariate analysis for in-hospital mortality, we included variables that were significant at  $P < 0.20$  in the univariate analysis, and which had clinical significance. Adjustment for potential differences in injury severity, was achieved by including the injury severity index, IC-ISS, after logit transformation, since it represents the probability of in-hospital survival/death. Care was taken to avoid multicollinearity and overfitting (Mean Variance Inflation Factor = 3.70). Even though the Hosmer-Lemeshow test is the traditional test for goodness-of-fit in logistic models, it has been described to be inappropriate (due to over-powering) for sample sizes  $n > 25,000$  [19], which is the case in our analysis ( $n = 469,046$ ). Therefore, the area under the curve (AUC) was used to assess the accuracy of this model (AUC = 0.92; Supplementary Fig. 1).

Propensity score matching was used to isolate the independent effect of AKI on mortality, hospitalization costs and LOS. We used a non-weighted mixed model logistic regression model for predicting AF, which included other baseline AHRQ comorbidity variables as well as SSRi, CCI, age, gender and hospital level variables as confounders for AF and hospital mortality, LOS and cost. The regression models were visually tested for confounder balance between the matched groups (AF vs. non-AF, see Supplementary Figs. 2–4). Furthermore, all three logistic regression models for predicting AKI had a good discrimination (AUC = 0.90 for inpatient mortality, AUC = 0.90 for LOS and AUC = 0.90 for cost). Among the matched

pairs used in the final logistic regression (adjusting for matched pairs/clusters), AKI was univariately regressed against inpatient mortality, hospitalization costs and LOS, in order to estimate a propensity-matched odds ratio (pmOR) for each of these outcomes.

## 3. Results

We identified 2,978,630 MVA related hospitalizations between 2003 and 2012. Of these, 79,687 (2.6%) also had AF. Patient characteristics are summarized in Table 1. In the MVA alone group, 53.7% of patients

**Table 1**  
Baseline patient characteristics with a MVA.

Baseline characteristics	MVA alone	MVA and AF
Total no. of weighted observations - n (% of N)	2,898,943	79,687
Age - Mean (SE), years		
Age (%)		
18–34 years	34.8	2.5
35–49 years	22.7	5.2
50–64 years	17.8	17.8
65–79 years	9.3	38.6
>80 years	4.2	35.9
Sex (%)		
Male	61.0	59.8
Female	38.5	40.2
Race (%)		
Whites	53.7	71.8
Blacks	10.6	4.3
Hispanics	11.3	4.1
Others	2.3	1.6
Missing	22.2	18.3
Comorbidities (%)		
Obesity	3.5	6.2
Hypertension	18.5	54.9
Diabetes mellitus	7.7	20.8
Congestive heart failure	1.2	18.0
History of chronic pulmonary disease	7.0	17.3
Median household income category by zip code (%)		
1. 0–25th percentile	26.5	22.6
2. 26–50th percentile	24.9	24.6
3. 51–75th percentile	23.8	25.3
4. 76–100th percentile	21.5	24.9
Primary payer (%)		
Medicare	7.6	32.5
Medicaid	11.7	2.8
Private including HMOs & PPOs	56.4	53.7
Other/self-pay/no charge	23.6	10.4
Hospital characteristics		
Bed size of hospital depending on location & teaching status (%)		
Small	6.0	7.2
Medium	20.9	21.2
Large	72.1	70.5
Hospital location & teaching status (%)		
Rural	7.8	9.4
Urban non-teaching	26.0	32.5
Urban teaching	65.2	57.1
Hospital region		
Northeast	18.8	23.0
Midwest	18.6	19.2
South	41.5	38.4
West	21.1	19.4
Admission day (%)		
Weekdays	67.6	74.9
Weekends	32.4	25.1
Disposition (%)		
Home	71.4	38.1
Transfer to short-term hospital/other facilities/home health care	28.6	61.9
Died in hospital	76,339.0	6083.0
In-hospital mortality (%)	2.6	7.8
Length of hospital-stay - Means (std. error), days	5.9	9.1
Adjusted cost (\$)	19,615.0	28,217.0

Abbreviations: AF, atrial fibrillation; HMO, health management organization; MVA, motor vehicle accident; PPO, Preferred Provider Organization; SE, standard error.

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