Diabetes and atrial fibrillation in hospitalized patients in the United States

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Abstract

Background: Data on the burden of atrial fibrillation (AF) associated with diabetes among hospitalized patients are scarce. We assessed the AF-related hospitalizations trends in patients with diabetes, and compared AF outcomes in patients with diabetes to those without diabetes.

Hypothesis: AF-related health outcomes differ between patient with diabetes and without diabetes.

Methods: Using the National Inpatient Sample (NIS) 2004–2014, we studied trends in AF hospitalization rate among diabetic patients, and compared in-hospital case fatality rate, length of stay (LOS), cost and utilization of rhythm control therapies, and 30-day readmission rate between patients with and without diabetes. Logistic or Cox regression models were used to assess the differences in AF outcomes by diabetes status.

Results: Over the study period, there were 4 325 522 AF-related hospitalizations, of which 1 075 770 (24.9%) had a diagnosis of diabetes. There was a temporal increase in AF hospitalization rate among diabetic patients (10.4 to 14.4 per 1000 hospitalizations among patients with diabetes; +4.4% yearly change, p-trend <.0001). Among AF patients, those with diabetes had a lower in-hospital mortality (adjusted odds ratio [aOR]: 0.68; 95% CI: 0.65–0.72) and LOS (aOR: 0.95; 95% CI: 0.94–0.96), but no difference in costs (aOR: 0.95; 95% CI: 0.94–0.96) and a higher 30-day readmission rate compared with no diabetes (aHR 1.05; 95% CI: 1.01–1.08), compared to individuals without diabetes.

Conclusion: AF and diabetes coexist among hospitalized patients, with rising trends over the last decade. Diabetes is associated with lower rates in-hospital adverse AF outcomes, but a higher 30-day readmission risk.

KEYWORDS
atrial fibrillation, diabetes mellitus, trends
Atrial fibrillation (AF) is the most common arrhythmia in the United States, with AF cases projected to increase to 15.9 million by the year 2050. The US burden of diabetes has also been growing, with a projected 30% or more increase by 2050. Diabetes increases the risk of AF by ~40%. Diabetes and AF often coexist, posing unique clinical challenges. There is a paucity of US national data on the patterns and time trends of coexisting AF and diabetes. Insights into the burden of coexisting diabetes and AF may help in improving outcomes, as diabetes may adversely influence AF outcomes. The link between diabetes and AF also has potential implications for diabetes screening among those with AF patients and vice versa, and a potential therapeutic implication. Emerging trial data suggests that sodium glucose cotransporter (SGLT)-2 inhibitors may have beneficial effects on AF outcomes among individuals with diabetes.

Using the Nationwide Inpatient Sample (NIS) registry data, we investigated: (1) the trends in AF hospitalization rate, in-hospital case fatality rate, average length of stay (LOS), cost and utilization of rhythm control therapies among patients with diabetes; and (2) the potential differences in in-hospital mortality, LOS, cost, utilization of rhythm control therapies, and 30-day readmission rates between hospitalized AF patients with and without diabetes.

2 | METHODS

2.1 | Data sources and study population

Our study was based on data from the National Inpatient Sample (NIS) covering the 2004–2014 period. The NIS is the largest all-payer database of inpatient hospital stays in the United States with approximately 35 million weighted hospitalization records per year. The NIS is developed by the Agency for Healthcare Research and Quality (AHRQ) as part of its Healthcare Cost and Utilization Project (HCUP). Briefly, the NIS is a 20% stratified sample of inpatient hospitalizations from participating states. It is representative of >95% of all inpatient hospitalizations in the United States. Prior to 2012, the NIS comprised all hospitalizations from a 20% stratified sample of community hospitals (defined as all non-federal hospitals with the exception of rehabilitation facilities). In 2012, the NIS underwent a redesign and is now comprised of a 20% stratified systemic sample of discharges from all community hospitals from participating states. This design has been shown to decrease SE estimates while calculating variances at the national level and make these estimates more generalizable to the target universe. To facilitate multi-year trend analysis and ensure comparability of estimates, the AHRQ has published trend weights using the 2012 methodology on previous years. The details of the NIS sampling methodology are published annually by the AHRQ. Due to the de-identified nature of this data, the study was exempt from Institutional Review Board approval from the primary institution.

To assess readmissions among patients with a primary diagnosis of AF discharged between January and November 2014, we used the 2014 Nationwide Readmissions Database (NRD), developed by the AHRQ as part of the HCUP. The NRD is the largest all-payer database of hospital readmissions in the United States. In order to support readmission analyses, the NRD contains a linkage variable (NRD_visitlink) by means of which patients can be tracked across hospitalizations. The target universe for the NRD includes inpatient discharges from community hospitals that were not rehabilitation or long-term acute care facilities. The sampling frame for the NRD includes inpatient discharges from participating states, excluding rehabilitation and LTAC facilities. All discharges from the sampling frames are included. Discharge weights for the NRD were developed with the target universe as the standard. We included hospitalized patients aged ≥18 years in both the trends and readmissions analyses.

2.2 | Atrial fibrillation and diabetes ascertainment

A primary diagnosis of AF was based on the International Classification of Diseases, Ninth Revision (ICD-9) code 427.31. Diabetes was ascertained using the Clinical Classification Software (CCS) codes 49 and 50. Prior studies have shown that the use of ICD-9-CM coding has a high degree of accuracy for identifying atrial fibrillation and diabetes mellitus, with a robust sensitivity and an excellent specificity (both >90% for each condition). The complete list of codes used in the study are summarized in the Table S1.

Since the NIS and Nationwide Readmissions Database (NRD) are both administrative databases, we are able to identify a diagnosis of diabetes only by the use of ICD-9-CM diagnosis and procedure codes. There are over 50 ICD-9-CM codes for diabetes with or without complications (250.xx). The CCS coding system is developed by the AHRQ and maps similar ICD-9-CM codes to a manageable number of CCS codes (https://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccsfactsheet.jsp). We chose to use CCS codes for defining diabetes mellitus because using 2 CCS codes rather than >50 ICD-9-CM codes makes our analysis less prone to errors. The CCS coding system is designed to capture all of the disparate ICD-9 codes that are used to identify diabetes in administrative data.

2.3 | Outcomes

The study outcomes included hospitalization rate per 1000 hospitalizations related to diabetes, in-hospital outcomes (in-hospital case fatality rate, LOS, cost, utilization or rhythm control therapies), and 30-day all-cause readmission.

The rhythm control therapies included radiofrequency catheter ablation and electrical cardioversion, identified using relevant ICD-9 and CCS procedure codes (Table S1). Since codes for ablation and cardioversion are not specific to AF and could be used for other arrhythmias, we excluded records with a diagnosis of other atrial or ventricular arrhythmias as having had AF ablation or electrical cardioversion. We also excluded records with implantation of permanent pacemaker during the same hospitalization because the ablation codes
may represent a rate-controlled strategy with atrioventricular (AV) nodal ablation and pacemaker implantation.

### 2.4 Statistical analysis

We assessed the yearly prevalence of AF and estimates of the length of hospital stay and costs, and the related time trends, among patients with diabetes based on the year of admission in all patients, across four age groups, (18–45 years, 45–64 years, 65–74 years and ≥75 years) and by sex. Survey analysis techniques were used to produce national estimates as recommended by the AHRQ. Continuous variables were expressed as mean (SE) while categorical variables were expressed as percentages. Differences in continuous and categorical variables between the diabetes and no-diabetes groups were tested using linear and logistic regression models. Linear trends in continuous as well as categorical variables were examined using linear regression with year as a continuous predictor. We examined overall and subgroup specific trends in AF hospitalization rate per thousand diabetes-related hospitalizations, in-hospital case fatality rate, LOS, cost and utilization of rhythm control therapies. The costs were estimated by multiplying total charges with hospital cost-to-charge ratios supplied by the AHRQ. Costs were adjusted to 2014 US dollars using consumer price index inflation adjustment calculator from the Bureau of Labor Statistics.

The differences in in-hospital AF outcomes between the diabetes and no-diabetes groups of patients were assessed using logistic regression models. The latter included the following adjustment variables: age, sex, income quartile, Charlson comorbidity index, hypertension, chronic renal failure, congestive heart failure, obesity, peripheral vascular disease, deficiency anemia, chronic lung disease, pulmonary circulation disorders, coagulopathy, rhythm control procedure (catheter ablation and electrical cardioversion), hospital region, hospital location and teaching status.

The differences in all-cause 30-day readmission among AF patients with and without diabetes were examined using a Kaplan–Meier curve and the log-rank test. A multivariable adjusted Cox proportional hazards model was also used with adjustment for age, sex, income quartile, Charlson comorbidity index, hypertension, chronic renal failure, congestive heart failure, obesity, peripheral vascular disease, deficiency anemia, chronic lung disease, pulmonary circulation disorders, coagulopathy, rhythm control procedure (catheter ablation and electrical cardioversion), hospital region, hospital location and teaching status.

A p-value of ≤0.05 was considered significant. All analyses were conducted using Stata 15.1 statistical package (Statacorp, College Station, TX).

### 3 RESULTS

#### 3.1 Trends in atrial fibrillation hospitalization in patients with diabetes mellitus

The weighted total of hospitalizations with a primary diagnosis of AF during the study period was 4,325,522, of which 1,075,770 (24.9%) had a diagnosis of diabetes. Mean age of patients with primary diagnosis of AF in the setting of diabetes was 70.4 years (SE 0.04) and 51.8% were women. There was a declining trend in the proportion of females (53%–50.5%, p-trend < .001). There was an overall increase in comorbidity burden (mean Charlson comorbidity index 2.0 [SE 0.01] to 2.5 [SE 0.01], p-trend < .001). Other trends in baseline characteristics are detailed in Table 1.

The rate of AF hospitalizations increased from 10.4 to 14.4 per thousand diabetes-related hospitalizations from 2004 to 2014 (p-trend < .001). This upward trend was evident across all age groups and sexes (Table 2). In-hospital case fatality rate improved modestly from 1.1% in 2004 to 0.9% in 2014 (p-trend = .03). In subgroup analyses, this trend was not evident in the various age groups, except for the ≥75 years age group. In subgroup analyses by sex, there was no clear downward trend in females and males (Table 2). In multivariable analyses, the improvement in case fatality rate was not fully explained by changing trends in age, sex and comorbidities (Table S2).

We observed improvements in LOS (mean of 4.0 days in 2004 to 3.7 days in 2014, p-trend < .001). This trend was significant across all but the youngest age subgroup (Table 2). Similarly, the average cost declined from $9810 in 2004 to $9125 in 2014 (p-trend < .001); and this trend was significant across all subgroups (Table 2).

The utilization of radiofrequency ablation and electrical cardioversion increased linearly in both the diabetes and no-diabetes groups of patients (p-trend < .001, Figures S1 and S2).

### 3.2 Outcomes of atrial fibrillation in patients with and without diabetes

The differences in baseline characteristics by diabetes status for patients admitted with a primary diagnosis of AF are summarized in Table S3. Patients with diabetes were older (70.4 vs. 70.2 years, p < .001), with a lower proportion of females (51.8% vs. 52.4%, p < .001), and a higher burden of comorbidities (Charlson comorbidity index 2.29 vs. 0.99, p < .001), compared to patients without diabetes.

In multivariable adjusted models (Table 3), diabetes was associated with lower in-hospital mortality (adjusted odds ratio [aOR]: 0.68; 95% CI: 0.65–0.72); lower LOS (aOR: 0.95; 95% CI: 0.94–0.96), lower rates of utilization of radiofrequency ablation (aOR: 0.96; 95% CI: 0.92–0.99) and electrical cardioversion (aOR: 0.92; 95% CI: 0.89–0.94). There was no significant difference in costs (aOR: 0.95; 95% CI: 0.94–0.96).

There were a total 359,199 index admissions for a primary diagnosis of AF in 2014 (mean age: 70.4 years [SE: 0.09], 51.8% women), among whom 28.9% had diabetes, 71.8% had a diagnosis of hypertension and 0.3% had a diagnosis of congestive heart failure. The overall rate of all-cause 30-day readmission was 15.2%. A higher proportion of patients with diabetes had at least one readmission event within 30 days (18.1% vs. 14.0%, p < .001).

In time-to-event analysis (Figure S3 and Table 3), diabetes was associated with significantly higher rates of all-cause 30-day
| Baseline characteristics | 2004–2006 (weighted n = 208 042) | 2007–2008 (weighted n = 180 042) | 2009–2010 (weighted n = 211 419) | 2011–2012 (weighted n = 239 256) | 2013–2014 (weighted n = 236 195) | Overall (weighted n = 1 075 770) | p-Trend |
|--------------------------|---------------------------------|---------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|---------|
| Age, mean (SE)           | 70.5 (0.08)                     | 70.3 (0.09)                     | 70.5 (0.10)                   | 70.5 (0.08)                   | 70.3 (0.06)                   | 70.3 (0.04)                    | .99     |
| Female (%)               | 53.0                            | 52.1                            | 51.9                          | 51.6                          | 50.5                          | 51.8                          | <.001   |
| Age group (%)            |                                 |                                 |                               |                               |                               |                               |         |
| 18–44 years              | 2.2                             | 2.4                             | 2.1                           | 2.1                           | 2.0                           | 2.1                           | .01     |
| 45–64 years              | 27.7                            | 27.9                            | 28.0                          | 27.7                          | 28.0                          | 27.9                          | .59     |
| 65–74 years              | 28.9                            | 29.3                            | 29.7                          | 30.2                          | 31.1                          | 29.9                          | <.001   |
| ≥ 75 years               | 41.3                            | 40.4                            | 40.2                          | 40.0                          | 38.9                          | 40.1                          | <.001   |
| Race (%)                 |                                 |                                 |                               |                               |                               |                               |         |
| White                    | 57.6                            | 59.8                            | 67.4                          | 72.5                          | 74.6                          | 66.8                          | <.001   |
| Black                    | 6.8                             | 7.1                             | 8.1                           | 9.2                           | 9.4                           | 8.2                           | <.001   |
| Hispanic                 | 5.4                             | 5.4                             | 6.1                           | 6.6                           | 6.9                           | 6.2                           | <.001   |
| Asian or Pacific Islander| 1.2                             | 1.5                             | 1.5                           | 1.6                           | 1.7                           | 1.5                           | .001    |
| Native American          | 0.4                             | 0.6                             | 0.6                           | 0.6                           | 0.5                           | 0.5                           | .25     |
| Others                   | 1.5                             | 1.9                             | 2.1                           | 2.1                           | 2.1                           | 2.0                           | .002    |
| SES (%)                  |                                 |                                 |                               |                               |                               |                               |         |
| Quartile 1               | 28.1                            | 28.1                            | 28.0                          | 30.1                          | 29.9                          | 28.9                          | .003    |
| Quartile 2               | 27.3                            | 28.4                            | 28.2                          | 26.3                          | 28.7                          | 27.8                          | <.001   |
| Quartile 3               | 23.8                            | 24.0                            | 24.6                          | 24.5                          | 23.3                          | 24.0                          | .63     |
| Quartile 4               | 20.8                            | 19.5                            | 19.2                          | 19.1                          | 18.1                          | 19.3                          | <.002   |
| Primary payer (%)        |                                 |                                 |                               |                               |                               |                               |         |
| Medicare                 | 70.1                            | 68.5                            | 68.5                          | 70.9                          | 70.8                          | 69.9                          | <.001   |
| Medicaid                 | 4.5                             | 4.3                             | 5.0                           | 4.8                           | 5.7                           | 4.9                           | <.001   |
| Private insurance        | 21.1                            | 22.6                            | 21.6                          | 19.5                          | 18.7                          | 20.7                          | <.001   |
| Self pay/uninsured       | 2.3                             | 2.3                             | 2.7                           | 2.6                           | 2.5                           | 2.5                           | .20     |
| AHRQ comorbidity measure|                                 |                                 |                               |                               |                               |                               |         |
| AIDS (%)                 | 0.03                            | 0.04                            | 0.04                          | 0.04                          | 0.04                          | 0.04                          | .91     |
| Alcohol abuse (%)        | 2.0                             | 2.4                             | 2.6                           | 3.1                           | 3.3                           | 2.7                           | <.001   |
| Deficiency anemias (%)   | 10.9                            | 13.7                            | 15.4                          | 17.3                          | 17.5                          | 15.1                          | <.001   |
| Rheumatoid arthritis/    | 1.9                             | 2.2                             | 2.4                           | 2.6                           | 2.9                           | 2.4                           | <.001   |
| Collagen vascular diseases (%) | 0.6                             | 0.6                             | 0.5                           | 0.6                           | 0.5                           | 0.6                           | .10     |
| Chronic blood loss anemia (%) | 0.5                             | 0.4                             | 0.4                           | 0.4                           | 0.4                           | 0.5                           | .15     |
| Congestive heart failure (%) | 0.5                             | 0.4                             | 0.6                           | 0.4                           | 0.4                           | 0.5                           | .15     |
| COPD (%)                 | 21.8                            | 22.8                            | 24.2                          | 25.8                          | 26.8                          | 24.4                          | <.001   |
| Coagulopathy (%)         | 2.2                             | 2.6                             | 3.3                           | 3.7                           | 4.0                           | 3.2                           | <.001   |
| Depression (%)           | 6.0                             | 7.5                             | 8.5                           | 9.6                           | 10.2                          | 8.5                           | <.001   |
| Diabetes, uncomplicated (%) | 87.5                            | 83.5                            | 83.1                          | 81.7                          | 80.8                          | 83.2                          | <.001   |
| Diabetes with chronic complications (%) | 10.7                            | 10.8                            | 10.6                          | 11.5                          | 12.0                          | 11.2                          | <.001   |
| Drug abuse (%)           | 0.5                             | 0.6                             | 0.7                           | 1.1                           | 1.4                           | 0.9                           | <.001   |
| Hypertension (%)         | 69.8                            | 73.4                            | 76.7                          | 79.4                          | 80.7                          | 76.3                          | <.001   |
| Hypothyroidism (%)       | 12.7                            | 14.6                            | 15.7                          | 16.9                          | 17.3                          | 15.6                          | <.001   |
| Liver disease (%)        | 1.2                             | 1.4                             | 1.8                           | 2.0                           | 2.5                           | 1.8                           | <.001   |
| Fluid and electrolyte disorders (%) | 15.7                            | 17.8                            | 20.0                          | 22.2                          | 24.7                          | 20.3                          | <.001   |

(Continues)
3.3 | 30-day readmissions after an atrial fibrillation hospitalization in patients with and without diabetes

We observed significant differences in causes for readmission between those with diabetes compared to those without diabetes. Of the patients who were readmitted, a greater proportion of patients with diabetes had a primary diagnosis of congestive heart failure or sepsis compared with patients without diabetes (All \( p < .01 \)), while a lower proportion of patients with diabetes had a primary diagnosis of cardiac dysrhythmias compared with patients without diabetes (Figure S4).

4 | DISCUSSION

This study reports data on diabetes and AF comorbidities over a 10-year period in the United States, using a large nationwide sample from the NIS registry. We made several observations. A principal diagnosis of atrial fibrillation was more frequent among patients hospitalized for diabetes over time. Conversely, of all hospitalizations for a principal diagnosis of AF, nearly a quarter had coexistent diabetes. Over the 2004–2014 period, there was an increase in the frequency of AF-related hospitalizations among patients with diabetes across all age groups, but with a decrease in in-hospital fatality rate, length of hospital stay and related-costs. Among AF patients, compared to those without diabetes, patients with diabetes had a shorter hospital stay with lower costs, and a lower in-hospital mortality, but a higher 30-day readmission rate.

Despite accruing evidence on diabetes as an important precursor of AF, studies have seldom examined the trends of comorbid AF and diabetes. A prior analysis of the 2000–2010 NIS data showed that the proportion of individuals with diabetes among AF patients has been increasing over time, but this study did not focused on diabetes. We described an increasing prevalence of concomitant AF and diabetes over the 2004–2014 period. The latter trend may be related to an increase in the frequency of AF (and its detection) over time possibly due to an aging population. This could also be related to an intrinsic...
**TABLE 2** Trends in characteristics of hospitalization for atrial fibrillation among patients with diabetes mellitus

| Year         | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | Linear slope (% change/year) | p-Trend |
|--------------|------|------|------|------|------|------|------|------|------|------|------|-------------------------------|---------|
| **Hospitalization rates (per 1000)** |      |      |      |      |      |      |      |      |      |      |      |                              |         |
| Overall      | 10.4 | 10.9 | 11.6 | 12.1 | 13.1 | 13.7 | 13.6 | 14.4 | 15.0 | 14.9 | 14.4 | +4.4                           | <.001   |
| 18–44 years  | 2.1  | 2.3  | 2.5  | 2.9  | 2.9  | 2.8  | 2.8  | 3.2  | 3.1  | 2.9  | 2.9  | +3.9                           | <.001   |
| 45–64 years  | 8.0  | 8.8  | 9.5  | 9.9  | 10.3 | 10.8 | 10.5 | 11.3 | 11.6 | 11.9 | 11.4 | +4.3                           | <.001   |
| 65–74 years  | 12.8 | 13.1 | 13.7 | 15.0 | 16.2 | 16.8 | 17.3 | 17.7 | 18.5 | 18.5 | 17.6 | +4.6                           | <.001   |
| ≥75 years    | 14.2 | 14.3 | 15.2 | 15.7 | 17.2 | 18.3 | 18.2 | 19.0 | 20.0 | 19.3 | 19.5 | +4.4                           | <.001   |
| Males        | 10.4 | 11.1 | 11.7 | 12.4 | 13.3 | 13.8 | 13.4 | 13.8 | 15.2 | 15.1 | 14.6 | +4.4                           | <.001   |
| Females      | 10.4 | 10.7 | 11.4 | 11.9 | 12.9 | 13.7 | 13.4 | 13.4 | 14.3 | 14.7 | 14.2 | +4.3                           | <.001   |
| Fatality rates |     |      |      |      |      |      |      |      |      |      |      |                              |         |
| Overall      | 1.1  | 1.1  | 1.1  | 0.9  | 0.9  | 0.9  | 0.9  | 0.9  | 1.0  | 0.9  | −1.4                          | .03     |
| 18–44 years  | 0.0  | 0.0  | 0.0  | 0.5  | 0.2  | 0.5  | 0.2  | 0.2  | 0.2  | 0.2  | 0.20                          | .85     |
| 45–64 years  | 0.7  | 0.5  | 0.3  | 0.4  | 0.5  | 0.3  | 0.4  | 0.3  | 0.4  | 0.5  | 0.6                          | .94     |
| 65–74 years  | 1.0  | 0.7  | 0.7  | 0.8  | 0.7  | 0.6  | 0.6  | 0.8  | 0.8  | 0.8  | −0.3                          | .76     |
| ≥75 years    | 1.5  | 1.8  | 1.9  | 1.4  | 1.4  | 1.4  | 1.5  | 1.5  | 1.6  | 1.2  | −2.1                          | .02     |
| Males        | 1.0  | 0.9  | 0.9  | 0.8  | 0.8  | 0.7  | 0.7  | 0.9  | 0.9  | 0.8  | −1.0                          | .30     |
| Females      | 1.2  | 1.2  | 1.2  | 0.8  | 1.0  | 1.0  | 1.0  | 1.1  | 1.0  | −1.6                          | .06     |
| Length of stay |     |      |      |      |      |      |      |      |      |      |      |                              |         |
| Overall      | 4.0  | 4.0  | 4.0  | 3.9  | 3.9  | 3.9  | 3.8  | 3.7  | 3.8  | 3.7  | −0.8                          | <.001   |
| 18–44 years  | 2.9  | 3.1  | 2.8  | 3.1  | 3.1  | 2.7  | 3.0  | 2.8  | 2.9  | 2.9  | −0.3                          | .59     |
| 45–64 years  | 3.5  | 3.6  | 3.5  | 3.5  | 3.5  | 3.4  | 3.4  | 3.4  | 3.4  | 3.4  | −0.7                          | <.001   |
| 65–74 years  | 3.9  | 3.8  | 3.8  | 3.8  | 3.8  | 3.7  | 3.7  | 3.6  | 3.6  | 3.7  | −0.8                          | <.001   |
| ≥75 years    | 4.4  | 4.4  | 4.4  | 4.3  | 4.2  | 4.3  | 4.3  | 4.1  | 4.1  | 4.1  | −0.8                          | <.001   |
| Males        | 3.7  | 3.8  | 3.7  | 3.7  | 3.7  | 3.6  | 3.6  | 3.6  | 3.6  | 3.6  | −0.8                          | <.001   |
| Females      | 4.2  | 4.2  | 4.2  | 4.1  | 4.1  | 4.0  | 3.9  | 3.9  | 3.9  | 3.9  | −0.9                          | <.001   |
| Costs (USD)  |      |      |      |      |      |      |      |      |      |      |      |                              |         |
| Overall      | 9810 | 10 228 | 10 615 | 10 548 | 10 410 | 10 605 | 10 489 | 10 591 | 9 356 | 9 252 | 9 125 | −1.3                          | <.001   |
| 18–44 years  | 7990 | 8 579 | 8 823 | 10 339 | 9 638 | 8 614 | 9 420 | 8 755 | 8 347 | 8 068 | 7 976 | −1.3                          | <.001   |
| 45–64 years  | 9438 | 10 076 | 10 524 | 10 532 | 10 557 | 10 665 | 10 337 | 10 814 | 9 515 | 9 172 | 9 221 | −1.1                          | <.001   |
| 65–74 years  | 9887 | 10 210 | 10 641 | 10 757 | 10 566 | 10 783 | 10 665 | 10 914 | 9 537 | 9 549 | 9 515 | −1.0                          | <.001   |
| ≥75 years    | 10 076 | 10 426 | 10 760 | 10 420 | 10 239 | 10 535 | 10 520 | 10 293 | 9 161 | 9 130 | 8 808 | −1.7                          | <.001   |
| Males        | 9779 | 10 538 | 10 895 | 11 075 | 10 628 | 10 985 | 10 800 | 11 058 | 9 813 | 9 522 | 9 458 | −1.2                          | <.001   |
| Females      | 9838 | 9 948 | 10 367 | 10 066 | 10 211 | 10 258 | 10 199 | 10 159 | 8 922 | 8 989 | 8 797 | −1.4                          | <.001   |
Our study showed that diabetes is inversely related to in-between diabetes and clinical outcomes among individuals with AF, which may be consistent with the lower therapies (anticoagulation, rhythm and rate control medications) and thus potentially better short-term outcomes among patients with diabetes. This pattern most likely stems from the fact that diabetes is a component of the stroke risk calculators (CHADS2 and CHA2DS2-VASc). Indeed, an important fraction of patients with AF and diabetes will have a stroke risk score that makes them eligible for anticoagulation therapy.

A limited number of studies have evaluated the association between diabetes and clinical outcomes among individuals with AF. Our study showed that diabetes is inversely related to in-hospital mortality, length of hospital stay and costs among patients with AF, but is independently associated with readmissions. Prior studies have suggested that diabetes among patients with AF is associated with an increased risk of both mortality and readmission, and among those with diabetes in particular. The latter is possibly related to the fact that diabetes is a component of the stroke risk calculators (CHADS2 and CHA2DS2-VASc). Indeed, an important fraction of patients with AF and diabetes will have a stroke risk score that makes them eligible for anticoagulation therapy.

Our findings have several important implications for clinical practice, as they highlight potential gaps respect to conjoint management of diabetes and AF, which may present unique challenges, especially in the context of constantly evolving diabetes and AF therapies. While new diabetes therapies (e.g., sodium-glucose cotransporter-2 inhibitors) have been emerging and showing important cardiovascular benefits, especially in terms of heart failure outcomes. While influence of these novel therapies on atrial fibrillation remains to be fully explored, early reports have showed that investigations suggest that dapagliflozin significantly decreases the incidence of atrial fibrillation/flutter episodes among diabetes patients.

Hitherto, the association between diabetes mellitus and AF has remained under-recognized by clinicians. Our findings strengthen the potential need for active screening for diabetes among people with AF, or vice-versa; which may have a significant effect on reducing healthcare costs as suggested by our findings. Addressing diabetes in relation to AF may have a significant population-level impact, as suggested by a population-based study showing that ~5% of incident AF cases are attributable to diabetes.

The strengths of our study include a large multiethnic sample with a nationwide scope, a standardized data collection methodology, and the exploration of a variety of AF-related outcomes. However, there are limitations to our study. First, the NIS registry only captures in-hospital data, and thus may have not captured individuals in the community with both diabetes and AF. Second, we did not examine the subtypes of AF and its pharmacological therapies (anticoagulation, rhythm and rate control drugs), which may both may have a different distribution among those with diabetes and could be associated with outcomes. Third, given the reliance on clinical practice to ascertain diabetes, we may have missed the patients without a prehospitalization diagnosis of diabetes and not tested during their hospital stay, especially as up to one-fourth of all persons with diabetes in the United States are undiagnosed. The underestimation of diabetes may bias the estimate of the association of diabetes and outcomes (e.g., in-hospital mortality) towards the null. Fourth, we did not assess the type and/or severity of diabetes, as well as therapies (insulin or noninsulin-based therapies), which may influence diabetes prevalence, as well as a surge in the number of individuals diagnosed with diabetes as a result of the adoption of HbA1C as an additional diagnostic test since 2009. Our findings of decreasing trends in AF-related LOS and case-fatality in the hospital maybe related to an improvement of AF care in general, and among those with diabetes in particular. The latter is possibly related to the fact that diabetes is a component of the stroke risk calculators (CHADS2 and CHA2DS2-VASc). Indeed, an important fraction of patients with AF and diabetes will have a stroke risk score that makes them eligible for anticoagulation therapy.

### TABLE 3 Outcomes of atrial fibrillation hospitalization among patients with diabetes compared to those without diabetes

| Outcomes                               | Unadjusted OR (95% CI) | p-Value | Adjusted OR (95% CI) | p-Value |
|----------------------------------------|------------------------|---------|----------------------|---------|
| In-hospital outcomes                   |                        |         |                      |         |
| In-hospital mortality                   | 0.95 (0.90–0.99)       | .04     | 0.68 (0.65–0.72)     | <.001   |
| LOS > median                           | 1.37 (1.36–1.39)       | <.001   | 0.95 (0.94–0.96)     | <.001   |
| Cost > median                          | 1.27 (1.25–1.28)       | <.001   | 0.99 (0.98–1.00)     | .11     |
| Catheter ablation                      | 0.65 (0.62–0.68)       | <.001   | 0.96 (0.92–0.99)     | .04     |
| Direct current cardioversion           | 0.86 (0.84–0.88)       | <.001   | 0.92 (0.89–0.94)     | <.001   |
| Post-discharge outcomes                |                        |         |                      |         |
| 30-day readmission rate                | 1.33 (1.29–1.37)       | <.001   | 1.05 (1.01–1.08)     | .01     |

Abbreviations: CI, confidence interval; HR, hazard ratio; LOS, length of stay; OR, odds ratio.

*Estimates are adjusted for age, sex, and socioeconomic status, Charlson comorbidity index, comorbid conditions (congestive heart failure, chronic lung disease, hypertension, obesity, peripheral vascular disease, valvular disease, chronic kidney disease, Pulmonary circulation disorders, coagulopathy), and rhythm control procedure.
glycemic control and AF outcomes. We also lacked information on glycated hemoglobin [HbA1c] that reflects the degree of blood glucose control. Indeed, extant evidence suggests that levels of HbA1c,29 and diabetes duration are determinants of the risk of stroke and thromboembolic events among patients with AF.30,31 Fifth, given that we examined in-hospital and short-term outcomes, we may have not captured the full extent of the influence of diabetes on the outcomes of AF.

In conclusion, at least one in ten hospitalized patients with diabetes has atrial fibrillation, these proportion have been increasing with time. Approximately one quarter of AF patients have diabetes. In terms of atrial fibrillation outcomes, compared to those without diabetes, patients with diabetes tend to experience a shorter hospital stay and lower in-hospital mortality, but a higher rate of readmission.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Agency of Health Care Research and Quality. Restrictions apply to the availability of these data, which were used under license for this study. Data are available at https://www.hcup-us.ahrq.gov/nisoverview.jsp with the permission of the Agency of Health Care Research and Quality.

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REFERENCES

1. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA. 2001;285:2370-2375.
2. Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation. 2006;114:119-125.
3. Virani SS, Alonso A, Benjamin EJ, et al.; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics SubcommitteeHeart disease and stroke statistics—2020 update. Circulation. 2020;141(9):e139-e596.
4. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988-2012. JAMA. 2015;314:1021-1029.
5. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Popul Health Metr. 2010;8:29.
6. Huxley RR, Filion KB, Konety S, Alonso A. Meta-analysis of cohort and case-control studies of type 2 diabetes mellitus and risk of atrial fibrillation. Am J Cardiol. 2011;108:56-62.
7. Pitt A, McGuire DK, Giugliano RP. Atrial fibrillation, type 2 diabetes, and non-vitamin K antagonist oral anticoagulants: a review. JAMA Cardiol. 2017;2:442-448.
8. Echouffo-Tcheugui JB, Shadrer P, Thomas L, et al. Care patterns and outcomes in atrial fibrillation patients with and without diabetes: ORBIT-AF registry. J Am Coll Cardiol. 2017;70:1325-1335.
9. Zeinlik TA, Bonaca MP, Furtado R, et al. Effect of dapagliflozin on atrial fibrillation in patients with type 2 diabetes mellitus: insights from the DECLARE-TIMI 58 trial. Circulation. 2020;141:1227-1234.
10. NIS Related Report. hcup-us.ahrq.gov. http://www.hcup-us.ahrq.gov/db/nation/nis/nisrelatedreports.jsp. Accessed January 10, 2020.
11. NIS Redesign Final Report.pdf. hcup-us.ahrq.gov. http://www.hcup-us.ahrq.gov/db/nation/nis/reports/NISRedesignFinalReport040914.pdf. Accessed January 10, 2020.
12. Trend Weights for HCUP NIS Data. https://www.hcup-us.ahrq.gov/db/nation/nis/trendwghts.jsp. Accessed January 10, 2020.
13. Thigpen JL, Dillon C, Forster KB, et al. Validity of international classification of disease codes to identify ischemic stroke and intracranial hemorrhage among individuals with associated diagnosis of atrial fibrillation. Circ Cardiovasc Qual Outcomes. 2015;8:8-14.
14. Jensen PN, Johnson K, Floyd J, Heckbert SR, Carnahan R, Dublin S. A systematic review of validated methods for identifying atrial fibrillation using administrative data. Pharmacoepidemiol Drug Saf. 2012;21(suppl 1):141-147.
15. Khokhar B, Jette N, Metcalfe A, et al. Systematic review of validated case definitions for diabetes in ICD-9-coded and ICD-10-coded data in adult populations. BMJ Open. 2016;6:e009952.
16. CPI Home: U.S. Bureau of Labor Statistics. bls.gov. https://www.bls.gov/cpi/. Accessed XXX.
17. Patel NJ, Deshmukh A, Pant S, et al. Contemporary trends of hospitalization for atrial fibrillation in the United States, 2000 through 2010 implications for healthcare planning. Circulation. 2014;129:2371-2379.
18. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in obesity among adults in the United States, 2005 to 2014. JAMA. 2015;314:35-42.
19. Nathan DM, Balkau B, Bonora E, et al. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care. 2009;32:1-8.
20. Piccini JP, Xu H, Cox M, et al.; For the Get With The Guidelines-AFIB Clinical Working Group and HospitalsAdherence to guideline-directed stroke prevention therapy for atrial fibrillation is achievable. Circulation. 2019;139:1519-1526.
21. Huang B, Yang Y, Zhu J, et al. Clinical characteristics and impact of diabetes mellitus on outcomes in patients with nonvalvular atrial fibrillation. Yonsei Med J. 2015;56:62-71.
22. Klem I, Wehinger C, Schneider B, Hartl E, Finsterer J, Stößlberger C. Diabetic atrial fibrillation patients: mortality and risk for stroke or embolism during a 10-year follow-up. Diabetes Metab Res Rev. 2003;19:320-328.
23. Gómez-Outes A, Laguna-Ruiz J, Terleira-Fernández A-L, Calvo-Rojas G, Suárez-Gea ML, Vargas-Castrillón E. Causes of death in anticoagulated patients with atrial fibrillation. J Am Coll Cardiol. 2016;68:2508-2521.
24. Steinberg BA, Kim S, Fonarow GC, et al. Drivers of hospitalization for patients with atrial fibrillation: results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). Am Heart J. 2014;167:735-742.
25. Christiansen CB, Olesen JB, Gislason G, Lock-Hansen M, Torp-Pedersen C. Cardiovascular and non-cardiovascular hospital admissions associated with atrial fibrillation: a Danish nationwide, retrospective cohort study. BMJ Open. 2013;3:e001800.
26. Lee S-R, Choi E-K, Han K-D, Cha MJ, Oh S, Lip GYH. Temporal trends of antithrombotic therapy for stroke prevention in Korean patients with non-valvular atrial fibrillation in the era of non-vitamin K antagonist oral anticoagulants: a nationwide population-based study. PLoS One. 2017;12:e0189495.
27. Coyne KS, Paramore C, Grandy S, Mercader M, Reynolds M, Zimetbaum P. Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States. *Value Health*. 2006;9:348-356.

28. Wu JHY, Foote C, Blomster J, et al. Effects of sodium-glucose cotransporter-2 inhibitors on cardiovascular events, death, and major safety outcomes in adults with type 2 diabetes: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. 2016;4:411-419.

29. Saliba W, Barnett-Griness O, Elias M, Rennert G. Glycated hemoglobin and risk of first episode stroke in diabetic patients with atrial fibrillation: a cohort study. *Heart Rhythm*. 2015;12:886-892.

30. Overvad TF, Skjeth F, Lip GYH, et al. Duration of diabetes mellitus and risk of thromboembolism and bleeding in atrial fibrillation: nationwide cohort study. *Stroke*. 2015;46:2168-2174.

31. Ashburner JM, Go AS, Chang Y, et al. Effect of diabetes and glycemic control on ischemic stroke risk in AF patients. *J Am Coll Cardiol*. 2016;67:239-247.

**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of this article.