Comparison of In-Hospital Outcomes of Patients With-Versus-Without Atrial Fibrillation and Alcohol Withdrawal Syndrome

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Alcohol withdrawal syndrome (AWS) has been associated with significant medical complications and length of stay. Cardiovascular effects from AWS include a physiologic tachycardia and hypertensive response. Although atrial fibrillation (AF) is one of the most common arrhythmias, the impact of a known history of AF on AWS is unclear. The purpose of our study is to assess the impact of history of AF on clinical outcomes, cost, and length of stay on AWS. The Nationwide Inpatient Sample was used to identify patients aged 18 years or older who underwent AWS with or without AF using the International Classification of Disease 9 Clinical Modification codes from January 2010 to December 2014. Outcomes were compared between those with or without AF using propensity score method-stratified morbidity ratio weighing- to adjust for baseline patient and hospital characteristics. A total of 280,451 patients with AWS of which 14,459 (5.2%) had history of AF. Patients with AF was older, less likely female, and more had higher burden of comorbidities. In an adjusted model, in-hospital mortality (odds ratio [OR] 1.98 95% confidence interval [CI] 1.61 to 2.45), ischemic stroke (OR 1.67 95% CI 1.42 to 1.95), acute kidney injury (OR 1.36 95% CI 1.24 to 1.49), acute kidney injury requiring dialysis (OR 1.89 95% CI 1.39 to 2.50), and cost (mean ratio 1.27 95% CI 1.21 to 1.33) were higher in the AF cohort. Length of stay was shorter in patients with AF (mean ratio 0.85 95% CI 0.81 to 0.90). In conclusion, a known history of AF increased the risk of in-hospital mortality, morbidity, and hospital expense in AWS. Published by Elsevier Inc. (Am J Cardiol 2019;124:1056−1058)

Atrial fibrillation (AF) is the most common arrhythmia worldwide with a high burden of morbidity, mortality, and increasing prevalence.[1] Excess alcohol consumption defined as greater than 3 drinks a day has been shown to increase the risk of developing AF independent of other risk factors.[2] Alcohol withdrawal syndrome (AWS) is a clinical diagnosis made with autonomic hyperactivity which may manifest as diaphoresis, tachycardia, hypertension, febrile episodes, and tremors in others.[3] If those at risk for alcohol withdrawal syndrome are not identified, most commonly with the aid of screening questionnaires such as CAGE, patients may progress to delirium tremens with mortality as high as 15%.[4,5] Despite the inherent relation between alcohol consumption and AF, to our knowledge there is limited published data available regarding the prevalence of AF in those admitted for AWS, clinical outcomes, hospital cost, and length of stay in patients with AF who undergo AWS when compared with those without AF. Therefore, we used the Nation Inpatient Sample (NIS) database to investigate the clinical impact of known AF on AWS admissions.

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Methods

Our study was conducted using the NIS database, which is part of the Healthcare Cost and Utilization Project sponsored by Agency for Healthcare Research and Quality. NIS data were queried by using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD−9−CM) codes to identify the study variables. All the patients with diagnosis of AWS (age ≥18 years) were included (ICD-9-CM code of 291.81). The presence of AF was based on ICD−9−CM code 427.31, which has been previously validated in previous studies.[6,7]

The primary outcome was the impact of AF on inpatient mortality. Secondary outcomes were the impact of AF on inpatient complications including ischemic stroke, hemorrhagic stroke, acute kidney injury with or without hemodialysis, cost, and length of stay. The ICD codes used to identify these complications are available in Supplementary Table 1. To calculate the estimated cost of hospitalization the NIS data were merged with cost−to−charge ratios available from the Healthcare Cost and Utilization Project. We estimated the cost of each inpatient stay by multiplying the total hospital charge with cost−to−charge ratios. Adjusted cost for each year was calculated in terms of the 2018 cost, after adjusting for inflation according to the latest consumer price index data. By doing this, we standardized costs over the study period.

We compared outcomes in patients with or without AF. The main end point was assessment of in-hospital mortality.

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Secondary outcomes include acute kidney injury, hemorrhagic stroke, and ischemic stroke. These complications were identified by ICD-9-CM diagnosis and procedure codes (Supplementary Table1). We identified demographic, co-morbid factors and hospital characteristics as covariates. Demographic variables were age, sex (male, female), race (White, Black, Hispanics, and other races), health insurance (Medicare, Medicaid, Private, Self-pay and others), income (stratified into 4 based on average household income of the zip-code of residence), region (Northeast, Midwest, South, and West), and hospital teaching status (rural, urban nonteaching, and teaching). We computed the modified Elixhauser co-morbidities index to summarize these co-morbid variables. Utilization of healthcare resources was performed by comparing hospital cost and length of stay among the 2 groups.

To investigate the effect of AF on the clinical outcomes and adjusted for cofounders, stabilized inverse probability weights were used. The following data were missing; hospital region (3.91%), race (7.27%), gender (0.01), primary expected payer (0.33%), household income status (5.12%), and hospital teaching status (0.61%). Patients with missing data for any of the above variables were unable to have a propensity scores (PS) estimated and were, therefore, excluded from weighted analyses. For missing observations >6% for example, race, missing observations were replaced with the most dominant category. This method was used in previous studies.[8,9]

We estimated the controlled direct effect of AF on clinical outcomes based on variables in Supplementary Table 1. We used logistic regression calculate the PS for both the AF and the unexposed models. The denominator model for the AF probability weights (PSd) included all the variables in Supplementary Table 1; the numerator model included no explanatory variables (PSn). Inverse probability weights (IPWs) were then calculated for each patient; patients who had AF were assigned a weight of (PSn/PSd), whereas those without were weighed using (1-PSn)/(1-PSd); weights were then truncated at the first and 99th percentiles.[10]

All the data extraction and analyses were done with the Statistical Analysis System (SAS V.9.4), and p values are 2-sided with a significance threshold of <0.05. We used standardized differences (ASD) to compare the baseline characteristics. ASD (calculated as the differences in means or proportions divided by a pooled estimated of the SD) is not as sensitive to sample size compared with traditional significance testing and hence, useful in identifying clinically meaningful differences. An ASD of >0.1 is considered clinically meaningful.[11]

Stabilized IPW models were used to compare the clinical outcomes of patients with AF versus patients without. Binary outcomes were modeled with stabilized IP-weighted binomial logistic regressions. Discrete numeric variables with an overdispersed count distribution (length of stay) and continuous variables with a right skewed spread (total hospital cost) were modeled with IP-weighted generalized linear regressions, and with a negative binomial function and gamma function respectively.

Results

The study population included unweighted 14,459 patients with AF and 265,992 patients without AF who developed alcohol withdrawal syndrome from the NIS. The mean age for the those with AF was higher was 61.38 ± 11.93 years versus 48.85 ± 12.12 years for those without. AF patients were more likely to dyslipidemia, history of myocardial infarction, previous percutaneous coronary intervention and coronary artery bypass surgery procedures, chronic obstructive pulmonary disease, cerebrovascular accident, hypertension, peripheral vascular disease, hypothyroidism, diabetes mellitus, obesity, deficiency anemia, congestive heart failure, and chronic renal disease. However, they were less likely to be females and less likely to be on Medicaid insurance. All ASD >0.1. Baseline clinical characteristics between the 2 groups adequately balanced after the stabilized IPW are depicted in Supplementary Table 2 (ASD <0.1). After the IP weighing, there was a statistical difference in-hospital mortality (odds ratio [OR] 1.98 95% confidence interval [CI] 1.61 to 2.45), ischemic stroke (OR 1.67 95% CI 1.42 to 1.95), acute kidney injury (OR 1.36 95% CI 1.24 to 1.49), acute kidney injury requiring dialysis (OR 1.89 95% CI 1.39 to 2.50), and cost (mean ratio [MR] 1.27 95% CI 1.21 to 1.33) as shown in Supplementary Table 3. Conversely, in patients that survived till hospital discharge, length of stay was noted to be statistically shorter in patients with AF (MR 0.85 95% CI 0.81 to 0.90) compared with those without. A mortality subgroup analysis performed did show a higher prevalence of CHF with no difference in age or renal function shown in Supplementary Table 4.

Discussion

In the present analysis of the United States NIS database, we evaluated the potential effects of AF on in−hospital outcomes of AWS. Our study revealed 3 important findings. Firstly, the prevalence of AF in patients with AWS was 5.2% and patients were older and had more co-morbidities. Second, after adjusting for patient−level and hospital−level characteristics, there was a statistical difference regarding in-hospital mortality (OR 1.98 95% CI 1.61 to 2.45), ischemic stroke (OR 1.67 95% CI 1.42 to 1.95), acute kidney injury (OR 1.36 95% CI 1.24 to 1.49), and acute kidney injury requiring dialysis (OR 1.89 95% CI 1.39 to 2.50). Lastly, whereas length of stay in those patient's that survived the hospitalization was shorter (MR 0.85 95% CI 0.81 to 0.90), there was a statistically significant higher hospital cost (MR 1.27 95% CI 1.21 to 1.33). Of note patients in the AF group had no difference with respect to major bleeding or hemorrhagic stroke, this may be in part to the fact that these outcomes are measured in a short time frame.

Our study has several limitations that warrant recognition. Owing to the nature on the NIS database, our data is retrospective and further delineation of the type of AF is not possible (i.e., paroxysmal, persistent, or permanent). Similarly, specific parameters during the hospital course are not available including laboratory results, hemodynamic parameters/vital signs, and history of anticoagulation. Also, of note, in the NIS database because variables are identified using a coding system, the study may be subjected to coding and documentation disparities. Despite these limitations, analysis of large-scale databases including the NIS has proven to be a useful resource in identifying patient trends and aiding in clinical practice.

Important strengths of this study included the nationally representative large sample size which involves multiple centers and populations across the United States and provides the most robust evidence to date. Furthermore, we matched the study patients using propensity score to control for the discrepancies in baseline characteristics. In conclusion, this study has identified and highlighted the increased morbidity, mortality, and hospital cost associated with AF and AWS compared with those patients with AWS without AF.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.07.004.

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