Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

The impact of atrial fibrillation on outcomes in patients hospitalized with COVID-19

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Studies have shown that coronavirus disease 19 (COVID-19) is an independent predictor of incident atrial fibrillation (AF) but the impact of pre-existing AF on the outcomes of patients hospitalized with COVID-19 is still unclear [1]. Some studies have reported a worse prognosis with comorbid AF in hospitalized patients with COVID-19, whereas others have reported no effect of AF on outcomes [2,3]. However, most of the published literature reporting the association between AF and COVID-19 is limited to single-center or small multi-center studies with limited sample sizes [4]. We sought to compare in-hospital outcomes in patients hospitalized with COVID-19 infection with AF vs those without AF using a national-claims-based database.

We queried the National Inpatient Sample (NIS) for the year 2020 to identify patients ≥18 years of age admitted with COVID-19 using the International Classification of Diseases, 10th revision, Clinical Modification (ICD-10 CM code- U07) [5]. We divided patients into two cohorts, based on the presence or absence of comorbid AF (ICD-10 CM code- I48.x). Baseline characteristics were compared using a Pearson χ^2 test and Fisher's exact test for categorical variables and an independent student *t*-test for continuous variables. For the assessment of the independent association of COVID-19 with in-hospital outcomes, a multivariable logistic regression model was utilized after adjusting for the variables mentioned in Table 1. The statistical analysis was performed using STATA 17.0 (StataCorp). For statistical significance, a $p<0.05$ was considered. Due to the de-identified nature of the dataset, informed consent and Institutional Review Board approval were not obtained. The NIS adheres to the 2013 Declaration of Helsinki for the conduct of human subjects research.

There was a total of 1050,045 hospitalizations for COVID-19 during the year 2020, of which 155,407 (14.8%) had comorbid AF. Baseline characteristics and crude in-hospital outcomes are reported (Table 1). Among patients hospitalized for COVID-19, those with AF were older, with a significantly lower percentage of females, and a significantly higher burden of key comorbidities like heart failure, hypertension, valvular heart disease, chronic pulmonary disease, renal failure, and peripheral vascular disorders. (Table 1)

The multivariate analysis adjusted for potential confounders showed that in patients hospitalized for COVID-19, comorbid AF was associated with significantly higher odds of in-hospital mortality (adjusted odds ratio [aOR]: 1.59; 95% confidence interval [CI]: 1.53–1.65; $p<0.01$), ischemic stroke (aOR: 1.55; 95% CI: 1.33–1.80; $p<0.01$), prolonged ventilator use >96 hrs (aOR: 1.82; 95% CI: 1.71–1.92; $p<0.01$), acute myocardial infarction (aOR: 1.19; 95% CI: 1.11–1.27; $p<0.01$), major bleeding (aOR: 1.31; 95% CI: 1.23–1.40; $p<0.01$), hemorrhagic stroke (aOR: 1.31; 95% CI: 1.04–1.64; $p = 0.02$), cardiac arrest (aOR: 1.66; 95% CI: 1.52–1.81; $p<0.01$), acute heart failure (aOR: 3.13; 95% CI: 3.02–3.23; $p<0.01$), cardiogenic shock (aOR: 2.72; 95% CI: 2.24–3.31; $p<0.01$), acute kidney injury (aOR: 1.14; 95% CI: 1.10–1.17; $p<0.01$), and requirement of dialysis (aOR: 1.29; 95% CI: 1.20–1.38; $p<0.01$). Hospitalizations for COVID-19 with AF had significantly lower odds of venous thromboembolism (aOR: 0.88; 95% CI: 0.82–0.94; $p<0.01$). Hospitalizations for COVID-19 with AF had a significantly longer length of stay (adjusted mean difference (aMD): 0.88; 95% CI: 0.76–0.99 days; $p<0.01$) and hospitalization charges (aMD: $16,584; 95% CI: $14,521-$18,647; $p<0.01$). (Table 2)

The significant findings of our analysis of a large administrative database show that in patients hospitalized with a primary diagnosis of COVID-19:

1) AF has a high prevalence of 14.8%
2) Patients with comorbid AF as compared with those without AF have higher odds of in-hospital mortality, ischemic stroke, cardiac arrest, myocardial infarction, and other adverse outcomes but lower odds of venous thromboembolism
3) Patients with comorbid AF have a longer length of stay and higher cost of care

To the best of our knowledge, our study is the largest study to assess the impact of comorbid AF on in-hospital outcomes of patients hospitalized with COVID-19. While patients with AF were older and had a higher co-morbidity burden, our adjusted analysis showed AF to be independently associated with higher mortality. The likely explanation for lower venous thromboembolism in patients with comorbid AF is the significantly higher long-term use of anticoagulation compared to those without AF. However, despite higher anticoagulation use, ischemic stroke was more common and possibly due to the presence of additional risk factors such as hypertension and peripheral vascular disease. These

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Table 1
Baseline characteristics of patients hospitalized with COVID-19 based on comorbid atrial fibrillation status.

Baseline Characteristics	COVID-19 without comorbid AF (n = 894,638, 85.2%)	COVID-19 with comorbid AF (n = 155,407, 14.8%)	p-value
Female (%)	428,532 (47.9%)	66,203 (42.6%)	P<0.01
Race (%)			
Whites	483,104 (54.0%)	118,731 (76.4%)	P<0.01
Blacks	191,452 (21.4%)	20,358 (13.1%)	
Hispanics	219,186 (24.5%)	16,318 (10.5%)	
Age (mean, SE)	62.7 (0.03) yrs	75.9 (0.06) yrs	P<0.01
Comorbidities (%)			
Congestive heart failure	108,251 (12.1%)	67,913 (43.7%)	P<0.01
Valvular heart disease	22,366 (2.5%)	17,872 (11.5%)	P<0.01
Peripheral vascular disorders	31,312 (3.5%)	16,0074 (10.3%)	P<0.01
Prior Myocardial Infarction	32,207 (3.6%)	12,743 (8.2%)	P<0.01
Prior Stroke	64,414 (7.2%)	23,466 (15.1%)	P<0.01
Prior PCI	3579 (0.4%)	1399 (0.9%)	P<0.01
Prior CABG	26,839 (3.0%)	13,054 (8.4%)	P<0.01
Hypertension	579,725 (64.8%)	130,542 (84.2%)	P<0.01
COPD	197,715 (22.1%)	49,109 (31.6%)	P<0.01
Diabetes	359,644 (40.2%)	67,913 (43.7%)	P<0.01
Chronic Liver Disease	41,153 (4.6%)	6372 (4.1%)	P<0.01
Connective Tissue Disorder	27,734 (3.1%)	5439 (3.5%)	P<0.01
Coagulopathy	93,042 (10.2%)	23,933 (15.4%)	P<0.01
Iron Deficiency Anaemia	29,523 (3.3%)	6838 (4.4%)	P<0.01
Renal failure	157,456 (17.6%)	54,237 (34.9%)	P<0.01
Obesity	252,288 (28.2%)	35,123 (22.6%)	P<0.01
Weight loss	52,784 (5.9%)	14,608 (9.4%)	P<0.01
Permanent pacemaker	12,525 (1.4%)	13,831 (8.9%)	P<0.01
Implantable cardioverter defibrillator	6262 (0.7%)	5439 (3.5%)	P<0.01
Long term anticoagulation	41,153 (4.6%)	59,684 (39.3%)	P<0.01
CHA_2DS_2VASc score (%)			
≤1	263,918 (29.5%)	9014 (5.8%)	P<0.01
2	177,138 (19.8%)	13,987 (9.0%)	
3	147,615 (16.5%)	19,581 (12.6%)	
≥4	304,177 (34.0%)	112,670 (72.5%)	

Abbreviations- PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; AF: atrial fibrillation; SE: standard error; OR: odds ratio; CI: confidence interval; MD: mean difference.

Table 2
Outcomes of patients hospitalized with COVID-19 based on comorbid atrial fibrillation status.

In-hospital Outcomes	COVID-19 without comorbid AF (n = 894,638, 85.2%)	COVID-19 with comorbid AF (n = 155,407, 14.8%)	p-value
In-hospital mortality	83,201 (9.3%)	34,489 (22.0%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.59 (1.53–1.65)	P<0.01
Ischemic stroke	5368 (0.6%)	2020 (1.3%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.55 (1.33–1.80)	P<0.01
Haemorrhagic stroke	2684 (0.3%)	777 (0.5%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.31 (1.04–1.64)	P = 0.02
Acute kidney injury	208,451 (23.3%)	57,500 (37.0%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.14 (1.10–1.17)	P<0.01
Major bleeding requiring blood transfusion	42,048 (4.7%)	9946 (6.4%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.31 (1.23–1.40)	P<0.01
Cardiac arrest	16,103 (1.8%)	5905 (3.8%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.66 (1.52–1.81)	P<0.01
Cardiogenic shock	2684 (0.3%)	1399 (0.9%)	P<0.01
*Adjusted OR (95% CI)	Reference	2.72 (2.24–3.31)	P<0.01
Acute heart failure	100,199 (11.2%)	64,494 (41.5%)	P<0.01
*Adjusted OR (95% CI)	Reference	3.13 (3.02–3.23)	P<0.01
Prolonged mechanical ventilator use (>96 hrs)	49,205 (5.5%)	14,608 (9.4%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.82 (1.71–1.92)	P<0.01
Requirement of dialysis	33,102 (3.7%)	10,101 (6.5%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.29 (1.20–1.38)	P<0.01
Venous thromboembolism	40,256 (4.5%)	6838 (4.4%)	P = 0.29
*Adjusted OR (95% CI)	Reference	0.88 (0.82–0.94)	P<0.01
Acute myocardial infarction	25,050 (2.8%)	10,568 (6.8%)	P<0.01
*Adjusted OR (95% CI)	Reference	1.19 (1.11–1.27)	P<0.01
Length of stay (mean, SE)	7.2 (0.02) days	8.8 (0.05) days	P<0.01
*Adjusted MD (95% CI)	Reference	0.88 (0.76–0.99) days	P<0.01
Total hospitalization charges (mean, SE)	$75,821 ($351)	$94,546 ($893)	P<0.01
*Adjusted MD (95% CI)	Reference	$16,584 ($14,521-$18,647)	P<0.01

Abbreviations- AF: atrial fibrillation; SE: standard error; OR: odds ratio; CI: confidence interval; MD: mean difference.

* Adjusted for the following variables: age, gender, hospital bed size, hospital teaching status, hypertension, diabetes mellitus, peripheral vascular disease, chronic lung disease, heart failure, chronic liver disease, prior stroke, history of percutaneous coronary intervention, history of the coronary artery bypass graft, chronic renal failure.

findings are similar to those reported in a recent meta-analysis that included approximately 15,000 patients and showed that patients admitted for COVID-19 and comorbid AF had significantly higher all-cause mortality as compared to those without AF [6]. Also, a study by Russo et al. including 467 patients hospitalized with COVID-19 demonstrated that pre-admission AF had a high prevalence and was associated with a higher risk of developing acute respiratory distress syndrome during hospitalization without any difference in the risk of death [7]. It has been suggested that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus) may directly contribute to the pathogenesis of AF through inflammation and alteration in the atrial cellular electrophysiology and through dysregulation in cellular angiotensin-converting enzyme 2 receptors [3].

The limitations of our study include the lack of patient-level data verification, coding errors related to ICD-10 codes, observational study design, lack of data on cause-specific mortality, and lack of outcome data after hospital discharge.

In conclusion, our analysis of a large national database shows that in patients admitted with COVID-19, comorbid AF has a high prevalence and is associated with higher inpatient mortality, worse in-patient outcomes, and increased resource utilization.

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Declaration of Competing Interest

None of the authors have conflicts of interest related to this manuscript.

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